



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

27 January 2020  
EMA/CHMP/5161/2020  
Inspections, Human Medicines Pharmacovigilance and Committees Division

## Committee for medicinal products for human use (CHMP)

Final Minutes for the meeting on 11-14 November 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 ongoing 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) November 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 11-14 November 2019 (to be published post December 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 11-14 November 2019

The CHMP adopted the agenda for 11-14 November 2019.

### 1.3. Adoption of the minutes

CHMP minutes for 14 – 17 October 2019

ORGAM Minutes from 4 November 2019

The CHMP minutes for 14 – 17 October 2019 were adopted.

The Minutes of the November 2019 CHMP ORGAM meeting held on 4 November 2019, together with all decisions taken at that meeting, were adopted.

## 2. Oral Explanations

### 2.1. Pre-authorisation procedure oral explanations

#### 2.1.1. Clopidogrel/Acetylsalicylic acid Mylan - clopidogrel / acetylsalicylic acid - EMEA/H/C/004996

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Mylan S.A.S; indicated for the secondary prevention of atherothrombotic events

Scope: Possible oral explanation, opinion

**Action:** Possible oral explanation to be held on Wednesday 13 November 2019 at 11:00

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

List of Outstanding Issues adopted on 19.09.2019, 27.06.2019. List of Questions adopted on 31.01.2019.

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

See 3.1

### **2.1.2. enasidenib - Orphan - EMEA/H/C/004324**

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

Scope: Oral explanation

**Action:** Oral explanation to be held on Tuesday 12 November 2019 at 11:00

List of Outstanding Issues adopted on 19.09.2019, 26.04.2019. List of Questions adopted on 18.10.2018.

An oral explanation was held on Tuesday 12 November 2019. The presentation by the applicant focused on the clinical data supporting the sought indication and proposed post authorisation measures.

### **2.1.3. plazomicin - EMEA/H/C/004457**

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

Scope: Possible oral explanation, List of outstanding issues

**Action:** Possible oral explanation to be held on Tuesday 12 November 2019 at 09:00

List of Outstanding Issues adopted on 25.07.2019. List of Questions adopted on 28.02.2019.

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

See 3.2

## **2.2. Re-examination procedure oral explanations**

No items

## **2.3. Post-authorisation procedure oral explanations**

### **2.3.1. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0072**

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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 a new indication for Keytruda as monotherapy for the treatment of recurrent locally advanced or metastatic oesophageal cancer in adults



whose tumours express PD L1 with a CPS  $\geq$  10 and who have received prior systemic therapy; as a consequence, sections 4.1, 4.2, and 5.1 of the SmPC, and section 1 of the PL are updated accordingly. The updated RMP version 25.1 has also been submitted.”

Possible oral Explanation

**Action:** Possible oral explanation to be held on Wednesday 13 November 2019 at 09:00

Request for Supplementary Information adopted on 19.09.2019, 29.05.2019.

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

See 5.1

## 2.4. Referral procedure oral explanations

### 2.4.1. Lemtrada - Alemtuzumab - EMEA/H/A-20/1483

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Sanofi Belgium

PRAC led Referral

PRAC Rapporteur: Brigitte Keller-Stanislawski; PRAC Co-rapporteur: Ulla Wändel Liminga

CHMP Rapporteurs Lemtrada: Rapporteur: Mark Ainsworth, Co-Rapporteur: Filip Josephson

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

Oral Explanation, PRAC Recommendation, CHMP opinion

**Action:** Oral explanation to be held on Tuesday 12 November 2019 at 14:15

An oral explanation was held on Tuesday 12 November 2019. The presentation by the MAH focused on the contraindication as recommended by PRAC.

See 10.1

## 3. Initial applications

### 3.1. Initial applications; Opinions

#### 3.1.1. Clopidogrel/Acetylsalicylic acid Mylan - clopidogrel / acetylsalicylic acid - EMEA/H/C/004996

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Mylan S.A.S; indicated for the secondary prevention of atherothrombotic events

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 19.09.2019, 27.06.2019. List of Questions adopted on 31.01.2019.

See 2.1

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

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.

### 3.1.2. Deferasirox Accord - deferasirox - EMEA/H/C/005156

Accord Healthcare S.L.U.; treatment of chronic iron overload

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 19.09.2019. List of Questions adopted on 28.03.2019.

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 medical prescription.

The summary of opinion was circulated for information.

### 3.1.3. Isturisa - osilodrostat - Orphan - EMEA/H/C/004821

Novartis Europharm Limited; treatment of Cushing's syndrome

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 17.10.2019, 25.07.2019. List of Questions adopted on 28.03.2019.

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.

Furthermore, the CHMP considered that osilodrostat 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 CHMP noted the letter of recommendations dated 10 October 2019. The summary of opinion was circulated for information. The CHMP adopted the similarity assessment report.

#### 3.1.4. Mayzent - siponimod - EMEA/H/C/004712

Novartis Europharm Limited; treatment of secondary progressive multiple sclerosis (SPMS)  
Scope: Opinion, SAG Neurology report

The list of experts for the SAG Neurology meeting held on 7 November was adopted via written procedure on 6 November 2019.

**Action:** For adoption

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

List of Outstanding Issues adopted on 19.09.2019, 29.05.2019. List of Questions adopted on 31.01.2019.

The CHMP noted the report from the SAG Neurology.

The CHMP adopted a positive opinion by majority (28 positive out of 31) recommending the granting of a marketing authorisation together with the CHMP assessment report and translation timetable.

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

The Norwegian Member was in agreement with the CHMP recommendation.

The divergent position (Sinan B Sarac, Alexandre Moreau, Christian Gartner) was appended to the opinion.

The summary of opinion was circulated for information.

#### 3.1.5. Polivy - polatuzumab vedotin - Orphan - EMEA/H/C/004870

Roche Registration GmbH; treatment of mature B cell lymphomas

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 19.09.2019, 25.07.2019, 25.06.2019. List of Questions adopted on 24.04.2019.

The CHMP adopted a positive opinion by majority (24 positive out of 31) recommending the granting of a conditional marketing authorisation together with the CHMP assessment report and translation timetable.

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

The Norwegian Member was in agreement with the CHMP recommendation.

The divergent positions (Natalja Karpova, Selma Arapovic Dzakula, Concepcion Prieto Yerro, Sol Ruiz, Johann Lodewijk Hillege, Daniela Melchiorri, Kristina Dunder) were appended to the opinion.

The summary of opinion was circulated for information.

### 3.1.6. Sunosi - solriamfetol - EMEA/H/C/004893

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Jazz Pharmaceuticals Ireland Limited; indicated to improve wakefulness in patients with narcolepsy or obstructive sleep apnoea.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 25.07.2019. List of Questions adopted on 28.03.2019.

The CHMP adopted a positive opinion by majority (30 positive out of 32) recommending the granting of a marketing authorisation together with the CHMP assessment report and translation timetable.

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

The Norwegian Member was in agreement with the CHMP recommendation.

The divergent position (Johann Lodewijk Hillege, Natalja Karpova) was appended to the opinion.

The summary of opinion was circulated for information.

Post-meeting note:

The CHMP adopted the final similarity assessment report via written procedure on 21.11.2019.

### 3.1.7. Tavlesse - fostamatinib - EMEA/H/C/005012

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Rigel Pharmaceuticals B.V.; indicated for the 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 19.09.2019, 27.06.2019. 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.

Furthermore, the CHMP considered that fostamatinib 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.

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

### **3.2.1. azacitidine - EMEA/H/C/005147**

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Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML) and AML with >30% marrow blasts according to the WHO classification.

Scope: List of outstanding issues

**Action:** For adoption

List of Outstanding Issues adopted on 17.10.2019. List of Questions adopted on 29.05.2019.

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

The Committee adopted a 2<sup>nd</sup> list of outstanding issues with a specific timetable.

### **3.2.2. cefiderocol - EMEA/H/C/004829**

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Treatment of infections due to aerobic Gram-negative bacteria

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 25.06.2019.

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. insulin lispro - EMEA/H/C/005037**

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Treatment of diabetes mellitus in adults

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 25.07.2019.

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.

#### 3.2.4. bempedoic acid - EMEA/H/C/004958

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treatment of primary hypercholesterolaemia or mixed dyslipidaemia

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 27.06.2019.

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.

#### 3.2.5. bempedoic acid / ezetimibe - EMEA/H/C/004959

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treatment of primary hypercholesterolaemia or mixed dyslipidaemia

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 27.06.2019.

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.

#### 3.2.6. darolutamide - EMEA/H/C/004790

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treatment of non-metastatic castration resistant prostate cancer (nmCRPC)

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 25.07.2019.

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.

#### 3.2.7. plazomicin - EMEA/H/C/004457

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

Scope: List of outstanding issues

**Action:** For adoption

List of Outstanding Issues adopted on 25.07.2019. List of Questions adopted on 28.02.2019.

See 2.1

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

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

The Committee adopted a 2<sup>nd</sup> list of outstanding issues.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues with a specific timetable.

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

#### **3.3.1. abicipar pegol - EMEA/H/C/005103**

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treatment of neovascular (wet) age-related macular degeneration (AMD)

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. amikacin - Orphan - EMEA/H/C/005264**

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Insmed Netherlands B.V.; treatment of lung infection as part of combination antibacterial drug regimen in adults

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. avapritinib - Orphan - EMEA/H/C/005208**

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Blueprint Medicines (Netherlands) B.V.; treatment of gastrointestinal stromal tumours

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. bevacizumab - EMEA/H/C/005106**

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treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer.

First-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer.

First line treatment of patients with advanced and/or metastatic renal cell cancer.

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. [ioflupane \(<sup>123</sup>I\) - EMEA/H/C/005135](#)

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

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. [arachis hypogaea allergens - EMEA/H/C/004917](#)

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immunotherapy (OIT) for patients aged 4 to 17 years with a confirmed diagnosis of peanut allergy

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. [trastuzumab - EMEA/H/C/005066](#)

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

Scope: Letter from the applicant dated 08 October 2019 requesting an extension of clock stop to respond to the List of Questions adopted on 19.09.2019

**Action:** For adoption

List of Questions adopted on 19.09.2019.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 19.09.2019.

### 3.4.2. [selinexor - Orphan - EMEA/H/C/005127](#)

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

Scope: Letter from the applicant dated 29 October 2019 requesting an extension to the



clock stop to respond to the List of Outstanding Issues adopted on 19.09.2019

**Action:** For adoption

List of Outstanding Issues adopted on 19.09.2019. List of Questions adopted on 24.04.2019.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Outstanding Issues adopted on 19.09.2019.

#### **3.4.3. crizanlizumab - Orphan - EMEA/H/C/004874**

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Novartis Europharm Limited; Treatment of sickle cell disease

Scope: Letter from the applicant dated 04 November 2019 requesting an extension to the clock stop to respond to the List of Questions adopted on 17.10.2019

**Action:** For adoption

List of Questions adopted on 17.10.2019.

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 17.10.2019.

#### **3.4.4. idebenone - Orphan - EMEA/H/C/005123**

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Santhera Pharmaceuticals (Deutschland) GmbH; treatment of respiratory dysfunction in patients with Duchenne muscular dystrophy (DMD) not using glucocorticoids

Scope: Letter from the applicant dated 05 November 2019 requesting an extension to the clock stop to respond to the List of Questions adopted on 17.10.2019

**Action:** For adoption

List of Questions adopted on 17.10.2019.

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 17.10.2019.

#### **3.4.5. methylthioninium chloride - EMEA/H/C/002776**

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is indicated as an aid for the enhanced visualization and detection of colorectal lesions in adult patients undergoing screening / surveillance colonoscopy for colorectal cancer.

Scope: Letter from the applicant dated 06 November 2019 requesting an extension to the clock stop to respond to the List of Questions adopted on 27.06.2019.

**Action:** For adoption

List of Questions adopted on 27.06.2019.

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 27.06.2019.

#### **3.4.6. tagraxofusp - Orphan - EMEA/H/C/005031**

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

Scope: Letter from the applicant dated 30 October 2019 requesting an extension to the clock stop to respond to the List of Outstanding Issues adopted on 25.06.2019.

**Action:** For adoption

List of Outstanding Issues adopted on 25.06.2019. List of Questions adopted on 24.04.2019.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Outstanding Issues adopted on 25.06.2019.

#### 3.4.7. cholera vaccine, oral, live - EMEA/H/C/003876

indicated for active immunisation against disease caused by *Vibrio cholerae* serogroup O1 in adults and children aged 6 years and older

Scope: Letter from the applicant dated 31 October 2019 requesting an extension to the clock stop to respond to the List of Outstanding Issues adopted on 17.10.2019.

**Action:** For adoption

List of Outstanding Issues adopted on 17.10.2019. List of Questions adopted on 29.05.2019.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Outstanding Issues adopted on 17.10.2019.

#### 3.4.8. deferiprone - Orphan - EMEA/H/C/005004

Apotex B.V.; treatment of neurodegeneration with brain iron accumulation

Scope: Assessment Report on request of data exclusivity

**Action:** For adoption

List of Questions adopted on 19.09.2019.

The CHMP adopted the assessment report on request of data exclusivity.

#### 3.4.9. pexidartinib - Orphan - EMEA/H/C/004832

Daiichi Sankyo Europe GmbH; treatment of adult patients with symptomatic tenosynovial giant cell tumour (TGCT), also referred to as giant cell tumour of the tendon sheath (GCT-TS) or pigmented villonodular synovitis (PVNS)

Scope: consultation of patients

List of Questions adopted on 25.07.2019.

The CHMP noted the survey to be sent to patients. Members were asked to provide comments on the survey. Comments should be sent.

#### 3.4.10. teriparatide - EMEA/H/C/005087

treatment of osteoporosis

Scope: Letter from the applicant dated 30 October 2019 requesting an extension to the clock stop to respond to the List of Questions adopted on 19.09.2019.

**Action:** For adoption

List of Questions adopted on 19.09.2019.

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 19.09.2019.

#### 3.4.11. [teriparatide - EMEA/H/C/005388](#)

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treatment of osteoporosis

Scope: Letter from the applicant dated 30 October 2019 requesting an extension to the clock stop to respond to the List of Questions adopted on 19.09.2019.

**Action:** For adoption

List of Questions adopted on 19.09.2019.

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 19.09.2019.

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

#### 3.5.1. [Hopveus - sodium oxybate - EMEA/H/C/004962](#)

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D&A PHARMA; medium to long-term maintenance of alcohol abstinence and treatment of mild to moderate alcohol withdrawal syndrome

Scope: Appointment of re-examination Rapporteurs, draft timetable

**Action:** For adoption

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

Opinion adopted on 17.10.2019. List of Outstanding Issues adopted on 26.04.2019. List of Questions adopted on 15.11.2018.

The CHMP appointed a re-examination Rapporteur and a re-examination Co-Rapporteur.

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

#### 3.6.1. [Spravato - esketamine - EMEA/H/C/004535](#)

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Janssen-Cilag International N.V.; treatment-resistant depression

Scope: Letters from third parties

**Action:** For information

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

Opinion on 17.10.2019. List of Outstanding Issues adopted on 25.07.2019. List of Questions adopted on 28.02.2019.

The CHMP noted the third party letters. The CHMP considered that the information does not change the opinion adopted in October 2019. However revisions were made to the AR in order to provide further clarifications.

Post meeting note:

The CHMP adopted revised opinion documents via written procedure on 21 November 2019.

### **3.7. Withdrawals of initial marketing authorisation application**

#### **3.7.1. Linhaliq - ciprofloxacin - EMEA/H/C/004394**

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Aradigm Pharmaceuticals Limited; treatment of non-cystic fibrosis bronchiectasis (NCFBE) patients with chronic lung infection with *Pseudomonas aeruginosa* (*P. aeruginosa*)

Scope: Letter from the applicant dated 29 October 2019 informing about the withdrawal of marketing authorisation application

**Action:** For information

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

The CHMP noted the withdrawal of the marketing authorisation application.

#### **3.7.2. Luxceptar - viable T-cells - Orphan - ATMP - EMEA/H/C/002397**

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

Scope: Letter from the applicant dated 06 November 2019 informing about the withdrawal of marketing authorisation application

**Action:** For information

Oral explanation held on 11.10.2019. List of Outstanding Issues adopted on 21.06.2019, 14.09.2018, 25.05.2018. List of Questions adopted on 08.09.2017.

The CHMP noted the withdrawal of the marketing authorisation application.

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

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

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

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Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: Quality ". The RMP is updated (version 9.4) accordingly and in line with revision 2 of GVP module V on 'Risk management systems'."

**Action:** For adoption

List of Outstanding Issues adopted on 19.09.2019. List of Questions adopted on 26.04.2019.

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.

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

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Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: "Extension application to change process steps. The RMP is updated (version 9.4) accordingly and in line with revision 2 of GVP module V on 'Risk management systems'."

**Action:** For adoption

List of Outstanding Issues adopted on 19.09.2019. List of Questions adopted on 26.04.2019.

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.

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

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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."

**Action:** For adoption

List of Outstanding Issues adopted on 19.09.2019. 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 by consensus together with the CHMP Assessment Report and translation timetable.

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

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

### 4.2.1. Akynzeo - fosnetupitant / palonosetron - EMEA/H/C/003728/X/0018

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Helsinn Birex Pharmaceuticals Limited

Rapporteur: Peter Kiely, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Ilaria Baldelli

Scope: "Extension application to introduce the new pharmaceutical form 'powder for concentrate for solution for infusion' and a new strength for the fixed combination of fosnetupitant (pro-drug of netupitant) and palonosetron of 235 mg/0.25 mg, to be administered intravenously (new route of administration)."

**Action:** For adoption

List of Outstanding Issues adopted on 19.09.2019. List of Questions adopted on 28.03.2019.

The Committee discussed the issues identified in this application, mainly relating to the environmental risk assessment and the wording in some SmPC sections.

The Committee adopted the CHMP recommendation and scientific discussion together with the 2<sup>nd</sup> list of outstanding issues and a specific timetable.

## 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. Halimatoz - adalimumab - EMEA/H/C/004866/X/0013

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Sandoz GmbH

Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength of 20mg (20mg/0.4ml) for Halimatoz solution for injection in pre-filled syringe.

The RMP (version 2.0) is updated in accordance. The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IB/11) and to align the PI with the latest QRD template (v.10.1)."

**Action:** For adoption

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

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

### 4.3.2. Hefiya - adalimumab - EMEA/H/C/004865/X/0013

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Sandoz GmbH

Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength of 20mg (20mg/0.4ml) for Hefiya solution for injection in pre-filled syringe.

The RMP (version 2.0) is updated in accordance. The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IB/10) and to align the PI with the latest QRD template (v.10.1).”

**Action:** For adoption

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

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

#### **4.3.3. Hyrimoz - adalimumab - EMEA/H/C/004320/X/0013**

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Sandoz GmbH

Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Extension application to add a new strength of 20mg (20mg/0.4ml) for Hyrimoz solution for injection in pre-filled syringe.

The RMP (version 2.0) is updated in accordance. The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IB/11) and to align the PI with the latest QRD template (v.10.1).”

**Action:** For adoption

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

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. Emgality - galcanezumab - EMEA/H/C/004648/X/0004**

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Eli Lilly Nederland B.V.

Rapporteur: Daniela Melchiorri (IT) (MNAT with ES for Quality), Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Kirsti Villikka

Scope: “Extension application to add a new strength of 100 mg/ml solution for injection in pre-filled syringe for Emgality, associated with a new indication (episodic cluster headache).”

List of Questions to the SAG Neurology, Request by the applicant for an extension to the clock stop to respond to the List of Outstanding Issues adopted on 17.10.2019.

**Action:** For adoption

List of Outstanding Issues adopted on 17.10.2019. List of Questions adopted on 27.06.2019.

The CHMP adopted the list of questions to the SAG Neurology. The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Outstanding Issues adopted on 17.10.2019.

#### 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. BLINCYTO - blinatumomab - Orphan - EMEA/H/C/003731/II/0030

Amgen Europe B.V.

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

Scope: "To modify the approved therapeutic indication to include the treatment of Philadelphia chromosome positive CD19 positive B-cell precursor acute lymphoblastic leukaemia (ALL) in adult and paediatric patients with relapsed or refractory ALL and adult patients in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and the PL are updated accordingly. The updated RMP version 10.0 has also been submitted."

**Action:** For adoption

The Committee discussed the issues identified in this application, concerning some uncertainties with the clinical efficacy and safety data in support of the extension of indication.

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

##### 5.1.2. Brilique - ticagrelor - EMEA/H/C/001241/II/0047/G

AstraZeneca AB

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include, in co administration with acetylsalicylic acid (ASA), the prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM) without a history of myocardial infarction who have undergone percutaneous coronary intervention (PCI) based on the final results of study D513BC00001 (THEMIS), a phase III multinational, randomised, double-blind, placebo controlled study to evaluate the effect of ticagrelor twice daily on the incidence of cardiovascular death, myocardial infarction or stroke in patients with T2DM; as



a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. Update of section 4.8 of the SmPC with new safety information on traumatic haemorrhages based on the final results from study D513BC00001 (THEMIS) and data from the ticagrelor clinical development programme and post-marketing data. The Package Leaflet is updated in accordance. The RMP version 12 has also been submitted.”

**Action:** For adoption

The Committee discussed the issues identified in this application, relating to the study conduct, the data in different subgroups as well as the indication wording.

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

### 5.1.3. [Invokana - canagliflozin - EMEA/H/C/002649/II/0046](#)

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Janssen-Cilag International NV

Rapporteur: Martina Weise, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Martin Huber

Scope: “Update of sections 4.1, 4.2, 4.8 and 5.1 of the Summary of Product Characteristics to add a new therapeutic indication for Invokana (canagliflozin) for the treatment of stage 2 or 3 chronic kidney disease and albuminuria, as an adjunct to standard of care, in adults with type 2 diabetes mellitus. The proposed new indication is based upon new clinical efficacy and safety data from the Phase 3 study: Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation Trial (CREDENCE) (DNE3001). The Package Leaflet is updated in accordance. The RMP version 8.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.”, Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

**Action:** For adoption

The Committee discussed the issues identified in this application, mainly concerning the indication wording with particular focus on the target population as well as the request for 1 year of market protection.

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

### 5.1.4. [Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0045](#)

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Roche Registration GmbH

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted

Scope: “Extension of indication to include the use of Kadcyla as a single agent for the adjuvant treatment of adult patients with HER2-positive early breast cancer who have invasive residual disease, in the breast and/or lymph nodes, after neoadjuvant taxane-based and HER2-targeted therapy; as a consequence, sections 4.1, 4.2, 4.4, 4.7, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to introduce editorial changes throughout the product information. An updated RMP version 9.2 has been agreed.

The variation leads to amendments to the Summary of Product Characteristics, Annex II and Package Leaflet and to the Risk Management Plan (RMP).”

**Action:** For adoption

Request for Supplementary Information adopted on 19.09.2019, 29.05.2019.

The Committee discussed the issues identified in this application. The members noted that the MAH withdrew the request for 1 year of market protection for a new indication.

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. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0072

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 a new indication for Keytruda as monotherapy for the treatment of recurrent locally advanced or metastatic oesophageal cancer in adults whose tumours express PD L1 with a CPS  $\geq$  10 and who have received prior systemic therapy; as a consequence, sections 4.1, 4.2, and 5.1 of the SmPC, and section 1 of the PL are updated accordingly. The updated RMP version 25.1 has also been submitted."

**Action:** For adoption

Request for Supplementary Information adopted on 19.09.2019, 29.05.2019.

See 2.3

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

The Committee discussed the issues identified in this application, mainly concerning the efficacy data in the proposed target population.

The Committee adopted a 3<sup>rd</sup> request for supplementary information with a specific timetable.

#### 5.1.6. OFEV - nintedanib - Orphan - EMEA/H/C/003821/II/0026

Boehringer Ingelheim International GmbH

Rapporteur: Peter Kiely, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include a new indication for OFEV for the treatment of Systemic Sclerosis associated Interstitial Lung Disease (SSc-ILD).

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 linguistic corrections to the Annexes for France and Sweden. The RMP version 7.0 has also

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

**Action:** For adoption

Request for Supplementary Information adopted on 27.06.2019.

The Committee discussed the issues identified in this application, mainly concerning the efficacy data in the proposed target population.

The Committee adopted a 2<sup>nd</sup> request for supplementary information with a specific timetable.

The CHMP agreed to consult an ad-hoc expert group.

#### 5.1.7. [Revlimid - lenalidomide - Orphan - EMEA/H/C/000717/II/0107](#)

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Celgene Europe BV

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

Scope: “Extension of indication to include Revlimid in combination with rituximab (anti-CD20 antibody) for the treatment of adult patients with previously treated follicular lymphoma or marginal zone lymphoma.

As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated; the PL is updated in accordance. An updated EU RMP (version 36.2) has also been submitted.”

**Action:** For adoption

Request for Supplementary Information adopted on 19.09.2019, 29.05.2019.

The Committee discussed the issues identified in this application.

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.

#### 5.1.8. [Trumenba - meningococcal group B vaccine \(recombinant, adsorbed\) - EMEA/H/C/004051/II/0013](#)

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Pfizer Europe MA EEIG

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

Scope: “Update of sections 4.2, 4.8 and 5.1 of the SmPC based on the results from the two paediatric studies B1971017 and B1971035. The Package Leaflet is updated in accordance. The RMP version 2.0 has also been submitted.”

**Action:** For adoption

Request for Supplementary Information adopted on 25.07.2019, 28.02.2019.

The Committee discussed the issues identified in this application related to clinical data in

the different paediatric age groups.

The CHMP noted that the applicant withdrew the extension of indication to convert the scope to a normal type II for inclusion of the paediatric data in the SmPC. The scope of the procedure was amended accordingly.

The Committee adopted a 3<sup>rd</sup> request for supplementary information with a specific timetable.

#### 5.1.9. [Ultomiris - ravulizumab - EMEA/H/C/004954/II/0002](#)

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Alexion Europe SAS

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of indication to include the treatment of patients with atypical hemolytic uremic syndrome (aHUS) for Ultomiris; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, Annex II.D is proposed to be updated to include the risk of thrombotic microangiopathy (TMA) with the new indication in the educational materials. The RMP version 1.6 has also been submitted."

**Action:** For adoption

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

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

#### 5.1.10. [Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0051](#)

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Janssen-Cilag International NV

Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst

Scope: "Update of sections 4.1, 4.2, 4.8 and 5.1 of the Summary of Product Characteristics to add a new therapeutic indication for Vokanamet (canagliflozin/metformin) for the treatment of stage 2 or 3 chronic kidney disease and albuminuria, as an adjunct to standard of care, in adults with type 2 diabetes mellitus. The proposed new indication is based upon new clinical efficacy and safety data from the Phase 3 study: Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation Trial (CREDENCE) (DNE3001). The Package Leaflet is updated in accordance. The RMP version 8.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

**Action:** For adoption

The Committee discussed the issues identified in this application, mainly concerning the wording of the indication in the target population, the efficacy data of the active substances in the fixed dose combination, as well as the dosing and the request for 1 year of market protection.

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

5.1.11. [WS1372](#)  
[OPDIVO - nivolumab - EMEA/H/C/003985/WS1372/0053](#)  
[Yervoy - ipilimumab - EMEA/H/C/002213/WS1372/0057](#)

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Bristol-Myers Squibb Pharma EEIG

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

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

**Action:** For adoption

Request for Supplementary Information adopted on 13.12.2018, 26.07.2018.

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

The Committee adopted a 3<sup>rd</sup> request for supplementary information with a specific timetable.

5.1.12. [WS1542](#)  
[Bretaris Genuair - acridinium - EMEA/H/C/002706/WS1542/0040](#)  
[Eklira Genuair - acridinium - EMEA/H/C/002211/WS1542/0040](#)

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AstraZeneca AB

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

Scope: "Updates of sections 4.4, 4.8 and 5.1 of the SmPC in order to add safety and efficacy information based on the ASCENT study, a phase IV double-blind, randomized, placebo-controlled, parallel-group outcome study to evaluate the effect of acridinium on cardiovascular (CV) safety and COPD exacerbations in patients with moderate to very severe COPD, and prior history of CV events or CV risk factors. 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 section 4.4, 4.6, 5.3 of the SmPC and section 2 of the PL for both Eklira Genuair and Bretaris Genuair. The worksharing procedure leads to amendments to the Summary of Product Characteristics and Package Leaflet."

**Action:** For adoption

Request for Supplementary Information adopted on 19.09.2019, 26.04.2019.

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.

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

### 5.2.1. Suliqua - insulin glargine / lixisenatide - EMEA/H/C/004243/II/0011

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sanofi-aventis groupe

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

Scope: "Extension of indication to include "treatment of adults with insufficiently controlled type 2 diabetes mellitus to improve glycaemic control as an adjunct to diet and exercise in addition to other oral medicinal products for the treatment of diabetes" 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.

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."

Request by the applicant for an extension to the clock stop to respond to the Request for Supplementary Information adopted on 17.10.2019.

**Action:** For information

Request for Supplementary Information adopted on 17.10.2019, 27.06.2019.

The CHMP agreed to the request by the applicant for an extension to the clock stop and adopted the new timetable by written procedure on 08 November 2019.

### 5.2.2. Opsumit - macitentan - Orphan - EMEA/H/C/002697/II/0029

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Janssen-Cilag International N.V.

Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication to include treatment of patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH), based on the pivotal study MERIT-1 (AC-055E201), together with 6 months of efficacy and safety data (cut-off date 17 October 2017) from its ongoing open-label extension study MERIT-2 (AC-055E202), as well as a drug-drug interaction (DDI) study (AC-055-122) of macitentan and rosuvastatine, a DDI study (AC-055-123) of macitentan and riociguat, and observational data from the OPUS Registry (OPsumit USers Registry; cut-off date of 17 April 2018).

As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 are being updated and the Package Leaflet is being updated accordingly. In addition, the MAH took the opportunity to

implement editorial changes and to align the annexes with the latest QRD template and to update the contact details of the local representatives in the Package Leaflet. An updated RMP version 9.2 was provided as part of the application.”

Letter from the MAH dated 8 November 2019 informing about the withdrawal of the extension of indication application

**Action:** For information

Request for Supplementary Information adopted on 28.03.2019, 13.12.2018.

The CHMP noted the withdrawal of the extension of indication application.

### **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. belantamab mafodotin - H0004935**

Treatment of Multiple Myeloma

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

**Action:** For adoption

The CHMP agreed to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

### 8.1.2. fostemsavir - H0005011

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indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in heavily treatment-experienced adults.

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

**Action:** For adoption

The CHMP agreed 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

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**Action:** For information

The CHMP noted the list of applications received.

### 8.2.2. Recommendation for PRIME eligibility

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**Action:** For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 8 recommendations for eligibility to PRIME: 2 were granted and 6 were 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. WS1587/G Abasaglar-EMA/H/C/002835/WS1587/0028/G Humalog-EMA/H/C/000088/WS1587/0178/G

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Eli Lilly Nederland B.V.

Lead rapporteur: Kristina Dunder

Scope: Type II variation. B.IV.z. to introduce an additional prefilled pen presentation for Abasaglar, solution for injection (EU/1/14/944/007, EU/1/14/944/008, EU/1/14/944/012, EU/1/14/944/013), Humalog, solution for injection (EU/1/96/007/002, EU/1/96/007/004, EU/1/96/007/020, EU/1/96/007/021 EU/1/96/007/023), Humalog Kwikpen solution for injection (EU/1/96/007/031, EU/1/96/007/032, EU/1/96/007/039, EU/1/96/007/040, EU/1/96/007/041, EU/1/96/007/042) and Humalog Junior Kwikpen, solution for injection (EU/1/96/007/043, EU/1/96/007/044, EU/1/96/007/045). The pack contains 5 pre-filled pens.

Type IAIN B. II.e.5.a.1 to request the 2x5 multipack.



As a consequence, the following sections of the SmPC were updated: 1, 4.2, 4.4, 6.2, 6.4, 6.5, 6.6, 8 in order to add new pre-filled pen presentation; the Package Leaflet and Labelling are updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make an editorial change (removing comma in SK address in the PL).

**Action:** For adoption

Request for Supplementary Information adopted on 19.09.2019

The Committee discussed the issues identified in this application, mainly concerning the new pen usage .

The Committee adopted a 2<sup>nd</sup> request for supplementary information with a specific timetable.

### 9.1.2. [Tyverb - lapatinib - EMEA/H/C/000795/II/0059](#)

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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

Request for Supplementary Information adopted on 26.04.2019.

The Committee discussed the issues identified in this application.

The Committee adopted a 2<sup>nd</sup> request for supplementary information with a specific timetable.

### 9.1.3. [ZOELY - Nomegestrol acetate, estradiol - EMEA/H/C/001213/II/0050](#)

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Theramex Ireland Limited

CHMP Rapporteur: Jean-Michel Race; PRAC Rapporteur: Adrien Inoubli

Scope: Update of sections 4.3 and 4.4 of the SmPC in order to add a new contraindication and a new warning regarding meningioma, upon request by PRAC following the assessment of Post-authorisation measure "LEG 014". The package leaflet is being updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in the Netherlands and Portugal in the package leaflet.

CHMP request for PRAC advice

**Action:** For adoption

Request for Supplementary Information adopted on 19.09.2019

The Committee discussed the issues identified in this application, mainly relating to previous discussions at PRAC in relation to the risk of meningioma associated with nomegestrol use.

The Committee adopted a 2<sup>nd</sup> request for supplementary information with a specific

timetable.

The CHMP adopted a request for PRAC advice.

#### 9.1.4. [Cufence - trientine dihydrochloride - EMEA/H/C/004111/II/0002/G](#)

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Univar BV

Rapporteur: Milena Stain

Scope: Quality“B.II.a.3.b.2) (type II)

B.II.b.4.b) (type IA)

B.II.b.3.a) (type IB)

B.II.a.1.a) (type IB)

B.II.d.1.a) (type IA)

B.II.f.1.d) (type IB)

C.1.4. Update of sections 4.5 and 5.2 of the SmPC in order to add information on food interaction and pk based on results from study TR-003 PK is proposed.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template.”

**Action:** For adoption

The Committee discussed the issues identified in this application, mainly relating to the wording of different sections of the SmPC.

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

#### 9.1.5. [Zydelig - idelalisib - EMEA/H/C/003843/II/0047](#)

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Gilead Sciences Ireland UC

Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber

Scope: “submission of the final clinical study report for study 101-09, A Phase 2 Study to Assess the Efficacy and Safety of Idelalisib in Subjects with Indolent BCell Non-Hodgkin Lymphomas Refractory to Rituximab and Alkylating Agents. This submission is an Annex II postauthorisation measure (ANX 002) and a category I commitment in the Zydelig Risk Management Plan (RMP). This submission also includes an update to the PI”  
Request for Supplementary Information adopted on 19.09.2019.

**Action:** For adoption

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.

#### 9.1.6. [Increlex - Mecasermin - EMEA/H/C/000704/II/0060](#)

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Ipsen Pharma

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

Scope: Update of sections 4.1, 4.2, 4.3, 4.4, 4.8 and 4.9 of the SmPC in order to update the safety information on benign or malignant neoplasia based on the EU Registry Study, the Ipsen global safety database and literature review. The Package Leaflet is updated accordingly. The MAH also submitted the updated RMP version 11.3.

In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet

**Action:** For adoption

Request for Supplementary Information adopted on 19.09.2019.

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 CHMP further discussed the potential impact of an update of the Increlex SmPC on somatropin analogues.

The CHMP agreed to consult the PRAC for advice on the SmPC discrepancies of somatropin analogues, which should be harmonised within the PSUR.

#### 9.1.7. Notice to MAHs regarding risk of nitrosamine contamination for all APIs

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**Action:** For discussion

The CHMP was informed about an update to the Q&A document. MAHs will be advised to consult the EMA/CMDh Q&A regularly and to liaise directly with the relevant authorities.

#### 9.1.8. Signal on ibuprofen/ketoprofen and serious exacerbation of infections - LOQs for the IDWP and PDCO

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The CHMP discussed the list of questions from the PRAC to the IDWP and PDCO and agreed to the consultations.

## 10. Referral procedures

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

#### 10.1.1. Lemtrada - Alemtuzumab - EMEA/H/A-20/1483

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Applicant: Sanofi Belgium

PRAC led Referral

PRAC Rapporteur: Brigitte Keller-Stanislawski; PRAC Co-rapporteur: Ulla Wändel Liminga

CHMP Rapporteurs Lemtrada: Rapporteur: Mark Ainsworth, Co-Rapporteur: Filip Josephson

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

Oral Explanation, PRAC Recommendation, CHMP opinion

**Action:** Oral explanation to be held on Tuesday 12 November 2019 at 14:15

See 2.4

An oral explanation was held on Tuesday 12 November 2019. The presentation by the MAH focused on the contraindication as recommended by PRAC.

The CHMP noted the letter from a third party.

The CHMP adopted an opinion by majority (26 out of 31 votes) based on the PRAC recommendation. The Committee recommended restriction of the use of Lemtrada due to reports of rare but serious side effects, including deaths. New measures to identify and manage the serious side effects were also recommended. The side effects include cardiovascular disorders (affecting the heart, circulation and bleeding as well as stroke) and immune-related disorders (caused by the body's defence system not working properly).

The divergent position (Dana Gabriela Marin, Alexandre Moreau, Nithyanandan Nagercoil, Concepcion Prieto Yerro, Martine Trauffler) was appended to the opinion.

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

The CHMP agreed to the DHPC and communication plan.

The public health communication was circulated for information.

#### 10.1.2. [Xeljanz - Tofacitinib - EMEA/H/A-20/1485](#)

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Applicant: Pfizer Europe MA EEIG

PRAC led Referral

PRAC Rapporteur: Liana Gross-Martirosyan; PRAC Co-rapporteur: Amelia Cupelli

CHMP Rapporteurs Xeljanz: Rapporteur: Daniela Melchiorri, Co-Rapporteur: Johann Lodewijk Hillege

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

PRAC Recommendation, CHMP opinion

**Action:** For adoption

The CHMP adopted an opinion by consensus based on the PRAC recommendation. The Committee recommended that the marketing authorisations for Xeljanz should be varied. It was recommended that Xeljanz should be used with caution in all patients at high risk of blood clots. In addition, the maintenance doses of 10 mg twice daily should not be used in patients with ulcerative colitis who are at high risk of blood clots unless there is no suitable alternative treatment. Furthermore CHMP recommended that, due to an increased risk of infections, patients older than 65 years of age should be treated with Xeljanz only when there is no alternative treatment.

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

The CHMP agreed to the DHPC and communication plan.

The public health communication was circulated for information.

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

## 11. Pharmacovigilance issue

### 11.1. Early Notification System

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

**Action:** For information

The CHMP noted the document.

## 12. Inspections

### 12.1. GMP inspections

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

### 12.2. GCP inspections

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

### 12.3. Pharmacovigilance inspections

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

### 12.4. GLP inspections

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

## 13. Innovation Task Force

### 13.1. Minutes of Innovation Task Force

**Action:** For information

### 13.2. Innovation Task Force briefing meetings

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

No items

### 14.2. Coordination with EMA Scientific Committees

#### 14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

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Summary of recommendations and advice of PRAC meeting held on 28-31 October 2019

**Action:** For information

The CHMP noted the Summary of recommendations and advice.

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

**Action:** For adoption

The CHMP adopted the EURD list.

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

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CAT draft minutes of meeting held on 06-08 November 2019

**Action:** For information

The CHMP noted the draft minutes.

#### 14.2.3. Paediatric Committee (PDCO)

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PIPs reaching D30 at November 2019 PDCO

**Action:** For information

The CHMP noted the information.

Report from the PDCO meeting held on 12-15 November 2019

**Action:** For information

The CHMP noted the report.

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

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Report from the COMP meeting held on 05-07 November 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 12-14 November 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 28-31 October 2019. Table of conclusions

**Action:** For information

The CHMP noted the report.

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

#### 14.3.2. Biologics Working Party (BWP)

---

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP November 2019 meeting to CHMP for adoption:

- 14 reports on products in scientific advice and protocol assistance
- 4 reports on products in pre-authorisation procedures
- 4 reports on products in plasma master file

**Action:** For adoption

The CHMP adopted the BWP reports.

#### 14.3.3. Antimicrobial Advice Ad Hoc Expert Group (AMEG)

---

Scope: Scientific advice on the AMEG categorisation of antimicrobials in the European Union; overview of comments

Background information: request from the EC for the update of the AMEG advice on the impact on public health and animal health of the use of antibiotics in animals ([link](#)); further extension for the deadline to submit the advice

**Action:** For discussion

The CHMP was informed that the consultation finished and the document has been updated accordingly. Final adoption of the document in December at CHMP and CVMP.



#### 14.3.4. Pharmacokinetics Working Party (PKWP)

---

Chair(s): Henrike Potthast

Election of PKWP chair

Jan Welink's second 3-year term expired in September 2019.

The CHMP elected Henrike Potthast (DE) as new chairperson.

#### 14.3.5. Oncology Working Party (ONCWP)

---

Chair(s): Sinan B. Sarac/Paolo Foggi

Pierre Demolis' participation on behalf of the Oncology Working Party in the CDDF Multi-stakeholder Workshop - The Use of Real-World Data to Optimize Oncology Drug Development and Access, 21/22 November 2019 in Amsterdam

**Action:** For adoption

The CHMP agreed for Pierre Demolis to participate at the CDDF Multi-stakeholder Workshop on behalf of the Oncology Working Party.

### 14.4. Cooperation within the EU regulatory network

No items

### 14.5. Cooperation with International Regulators

No items

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

No items

### 14.7. CHMP work plan

No items

### 14.8. Planning and reporting

No items

### 14.9. Others

No items

## 15. Any other business

### 15.1. AOB topic

#### 15.1.1. Update on EMA organisational aspects

---

**Action:** For information

The CHMP noted the update.

#### 15.1.2. Oncology Training

---

**Action:** For information

The Oncology training took place at the end of the Plenary meeting.

## 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 November 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	
Christophe Focke	Alternate	Belgium	No restrictions applicable to this meeting	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Selma Arapovic Dzakula	Alternate	Croatia	No interests declared	
Loizos Panayi	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Tomas Radimersky	Alternate	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 meetings	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meetings	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Jean-Michel Race	Alternate	France	No interests declared	
Martina Weise	Member	Germany	No restrictions applicable to this meetings	
Janet Koenig	Alternate	Germany	No interests declared	
Melinda Sobor	Member	Hungary	No restrictions applicable to this meetings	
Agnes Gyurasics	Alternate	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	Iceland	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jayne Crowe	Member	Ireland	No interests declared	
Peter Kiely	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No restrictions applicable to this meetings	
Giuseppa Pistritto	Alternate	Italy	No interests declared	
Natalja Karpova	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No interests declared	
Martine Trauffer	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
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 meetings	
Ingrid Wang	Alternate	Norway	No interests declared	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Marcin Kolakowski	Alternate	Poland	No interests declared	
Bruno Sepodes	Member (Vice-Chair)	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meetings	
Dana Gabriela Marin	Alternate	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Maria Concepcion Prieto Yerro	Member	Spain	No interests declared	
Jorge Camarero Jiménez	Alternate	Spain	No participation in final deliberations and voting on:	Polivy-EMA/H/C/004870 Kadcyla-EMA/H/C/002389/II/0045
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Nithyanandan Nagercoil	Member	United Kingdom	No restrictions applicable to this meetings	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Christian Gartner	Co-opted member	Austria	No restrictions applicable to this meetings	
Koenraad Norga	Co-opted member	Belgium	No participation in final deliberations and voting on:	H0004935
Blanka Hirschlerova	Co-opted member	Czech Republic	No interests declared	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Aaron Emmanuel Sosa Mejia	Expert in person*	Denmark	No restrictions applicable to this meetings	
Mette Toftegaard Madsen	Expert in person*	Denmark	No interests declared	
Vincent Gazin	Expert in person*	France	No interests declared	
Birgit Ahrens	Expert in person*	Germany	No interests declared	
Christoph Unkrig	Expert in person*	Germany	No interests declared	
Eva Schlosser	Expert in person*	Germany	No restrictions applicable to this meetings	
Regine Magdalene Lehnert	Expert in person*	Germany	No interests declared	
Sabine Mayrhofer	Expert in person*	Germany	No interests declared	
Kerstin Wickström	Expert in person*	Iceland	No restrictions applicable to this meetings	
Frank Holtkamp	Expert in person*	Netherlands	No interests declared	
Ron Bijleveld	Expert in person*	Netherlands	No interests declared	
Sanna Gevers	Expert in person*	Netherlands	No interests declared	
Wouter Iwema Bakker	Expert in person*	Netherlands	No interests declared	
Milena Peraita Ezcurra	Expert in person*	Spain	No interests declared	
Aleksandra Karin	Expert in person*	Sweden	No interests declared	
Maria Grünwald	Expert in person*	Sweden	No restrictions applicable to this meetings	
Matthias Loibl	Expert via telephone*	Austria	No interests declared	
Aldana Rosso	Expert via telephone*	Denmark	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Eskild Colding-Jørgensen	Expert via telephone*	Denmark	No restrictions applicable to this meetings	
Johanna Lähteenvuuo	Expert via telephone*	Finland	No interests declared	
Gérard Moulin	Expert via telephone*	France	No interests declared	
Andreas Bonertz	Expert via telephone*	Germany	No interests declared	
Jutta Dedorath	Expert via telephone*	Germany	No interests declared	
Martin Mengel	Expert via telephone*	Germany	No interests declared	
Susanna Hausmann	Expert via telephone*	Germany	No interests declared	
Susanne Kaul	Expert via telephone*	Germany	No interests declared	
Torsten Stemmler	Expert via telephone*	Germany	No restrictions applicable to this meetings	
Julia Pallos	Expert via telephone*	Hungary	No restrictions applicable to this meetings	
Agnieszka Przybyszewska	Expert via telephone*	Ireland	No interests declared	
Clare Foley	Expert via telephone*	Ireland	No interests declared	
Mair Powell	Expert via telephone*	Ireland	No interests declared	
Amelia Cupelli	Expert via telephone*	Italy	No interests declared	
Hinke Johanna van der Woude	Expert via telephone*	Netherlands	No interests declared	
Ingrid Evers van Gogh	Expert via telephone*	Netherlands	No restrictions applicable to this meetings	
Liana Gross-Martirosyan	Expert via telephone*	Netherlands	No interests declared	
Erlend Johannessen Egeland	Expert via telephone*	Norway	No interests declared	
Fabrice Eroukhmanoff	Expert via telephone*	Norway	No restrictions applicable to this meetings	
Helga Haugom	Expert via telephone*	Norway	No interests declared	
Ine Skottheim Rusten	Expert via telephone*	Norway	No interests declared	
Sigrid Klaar	Expert via telephone*	Sweden	No restrictions applicable to this meetings	
Ioanna Christodoulidou	Patient representative via telephone*	Greece	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jacobo Santamarta Barral	Patient representative via telephone*	Spain	No interests declared	
Anne Isabel Roth	Expert via Adobe*	Germany	No interests declared	
Christine Greiner	Expert via Adobe*	Germany	No interests declared	
Frauke Naumann-Winter	Expert via Adobe*	Germany	No interests declared	
Hilke Zander	Expert via Adobe*	Germany	No interests declared	
Joerg Zinserling	Expert via Adobe*	Germany	No interests declared	
Michal Zwiewka	Expert via Adobe*	Germany	No interests declared	
Susanne Mueller-Egert	Expert via Adobe*	Germany	No interests declared	
Odoardo Maria Olimpieri	Expert via Adobe*	Italy	No interests declared	
Annemarie Voute	Expert via Adobe*	Netherlands	No interests declared	
Carolien Versantvoort	Expert via Adobe*	Netherlands	No interests declared	
Elisabeth Johanne (Liesbeth) Rook	Expert via Adobe*	Netherlands	No interests declared	
Rune Kjeklen	Expert via Adobe*	Norway	No restrictions applicable to this meetings	
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** *(section 5.3)*

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 Pharmacovigilance 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/](http://www.ema.europa.eu/)



27 January 2020  
EMA/CHMP/7692/2020

## Annex to 11-14 November 2019 CHMP Minutes

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### A. PRE SUBMISSION ISSUES

#### A.1. ELIGIBILITY REQUESTS

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Report on Eligibility to Centralised Procedure for November 2019: **For adoption** Adopted

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

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Final Outcome of Rapporteurship allocation for November 2019: **For adoption** Adopted

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#### 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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<b>Brineura - cerliponase alfa - EMEA/H/C/004065/S/0018, Orphan</b> BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga Request for Supplementary Information adopted on 14.11.2019.	Request for supplementary information adopted with a specific timetable.
<b>IMVANEX - smallpox vaccine (live modified vaccinia virus Ankara) - EMEA/H/C/002596/S/0041</b> Bavarian Nordic A/S, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.  The Marketing Authorisation remains under exceptional circumstances.  The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
<b>Lojuxta - lomitapide - EMEA/H/C/002578/S/0036</b> Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 14.11.2019.	Request for supplementary information adopted with a specific timetable.
<b>Mepsevii - vestronidase alfa - EMEA/H/C/004438/S/0007, Orphan</b>	Positive Opinion adopted by consensus together with the CHMP assessment report and

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<p>Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia</p>	<p>translation timetable.</p> <p>The Marketing Authorisation remains under exceptional circumstances.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.</p>
<p><b>Naglazyme - galsulfase - EMA/H/C/000640/S/0078</b> BioMarin International Limited, Rapporteur: Fátima Ventura, PRAC Rapporteur: Ana Sofia Diniz Martins Request for Supplementary Information adopted on 14.11.2019.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>

## **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**

<p><b>Akynzeo - fosnetupitant / netupitant / palonosetron - EMA/H/C/003728/R/0024</b> Helsinn Birex Pharmaceuticals Limited, Rapporteur: Peter Kiely, Co-Rapporteur: Jean- Michel Race, PRAC Rapporteur: Ilaria Baldelli Request for Supplementary Information adopted on 17.10.2019.</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</p> <p>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.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p><b>Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMA/H/C/003852/R/0035</b> MSD Vaccins, Rapporteur: Kristina Dunder, Co- Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</p> <p>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.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p><b>IKERVIS - ciclosporin - EMA/H/C/002066/R/0017</b> Santen Oy, Rapporteur: Peter Kiely, Co- Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Jan Neuhauser Request for Supplementary Information adopted on 19.09.2019.</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</p> <p>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.</p>

	The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
<p><b>Jinarc - tolvaptan -</b>  <b>EMA/H/C/002788/R/0027</b>  Otsuka Pharmaceutical Netherlands B.V.,  Rapporteur: Daniela Melchiorri, Co-Rapporteur:  Romaldas Mačiulaitis, PRAC Rapporteur: Amelia  Cupelli  Request for Supplementary Information adopted  on 14.11.2019.</p>	Request for supplementary information adopted with a specific timetable.
<p><b>Mysimba - naltrexone hydrochloride /</b>  <b>bupropion hydrochloride -</b>  <b>EMA/H/C/003687/R/0033</b>  Orexigen Therapeutics Ireland Limited,  Rapporteur: Mark Ainsworth, Co-Rapporteur:  Andrea Laslop, PRAC Rapporteur: Martin Huber  Request for Supplementary Information adopted  on 19.09.2019.</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</p> <p>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.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p><b>Orbactiv - oritavancin -</b>  <b>EMA/H/C/003785/R/0027</b>  Menarini International Operations Luxembourg S.A., Rapporteur: Janet Koenig, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Adam Przybylkowski  Request for Supplementary Information adopted on 19.09.2019.</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</p> <p>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.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p><b>Prolia - denosumab -</b>  <b>EMA/H/C/001120/R/0082</b>  Amgen Europe B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</p> <p>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.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p><b>Sivextro - tedizolid phosphate -</b>  <b>EMA/H/C/002846/R/0031</b>  Merck Sharp &amp; Dohme B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Maria del Pilar Rayon  Request for Supplementary Information adopted on 19.09.2019.</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</p> <p>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.</p>

	The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
<p><b>Synjardy - empagliflozin / metformin - EMEA/H/C/003770/R/0044</b></p> <p>Boehringer Ingelheim International GmbH,  Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Daniela Melchiorri, PRAC  Rapporteur: Eva A. Segovia  Request for Supplementary Information adopted on 14.11.2019.</p>	Request for supplementary information adopted with a specific timetable.

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

<p><b>Caprelsa - vandetanib - EMEA/H/C/002315/R/0041</b></p> <p>Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni  Request for Supplementary Information adopted on 17.10.2019.</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report.</p> <p>The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.</p> <p>The Marketing Authorisation remains conditional.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p><b>Cometriq - cabozantinib - EMEA/H/C/002640/R/0032, Orphan</b></p> <p>Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Menno van der Elst  Request for Supplementary Information adopted on 14.11.2019.</p>	Request for supplementary information adopted with a specific timetable.
<p><b>Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - EMEA/H/C/002450/R/0026, Orphan, ATMP</b></p> <p>Chiesi Farmaceutici S.p.A., Rapporteur: Egbert Flory, Co-Rapporteur: Paolo Gasparini, CHMP Coordinators: Jan Mueller-Berghaus and Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald  Request for Supplementary Information adopted on 11.10.2019.</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report.</p> <p>The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.</p> <p>The Marketing Authorisation remains conditional.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p><b>SIRTURO - bedaquiline - EMEA/H/C/002614/R/0035, Orphan</b></p> <p>Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report.</p> <p>The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.</p>



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The Marketing Authorisation remains conditional.

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

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

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

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**EMEA/H/C/PSUSA/00001751/201904**

(insulin glargine)

CAPS:

**Abasaglar** (EMEA/H/C/002835) (insulin glargine), Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder

**Lantus** (EMEA/H/C/000284) (insulin glargine), Sanofi-Aventis Deutschland GmbH, Rapporteur: Johann Lodewijk Hillege

**Semglee** (EMEA/H/C/004280) (insulin glargine), Mylan S.A.S, Rapporteur: Martina Weise

**Toujeo** (EMEA/H/C/000309) (insulin glargine), Sanofi-Aventis Deutschland GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "From: 20/04/2018 To: 20/04/2019"

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):

Update of section 4.8 of the SmPC to add cutaneous amyloidosis with frequency unknown. The Package leaflet is updated accordingly.

The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

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**EMEA/H/C/PSUSA/00002892/201903**

(tenofovir disoproxil)

CAPS:

**Tenofovir disoproxil Mylan**

(EMEA/H/C/004049) (tenofovir disoproxil), Mylan S.A.S, Rapporteur: Romaldas Mačiulaitis

**Tenofovir disoproxil Zentiva**

(EMEA/H/C/004120) (tenofovir disoproxil), Zentiva k.s., Rapporteur: John Joseph Borg

**Viread** (EMEA/H/C/000419) (tenofovir disoproxil), Gilead Sciences Ireland UC, Rapporteur: Jean-Michel Race

NAPS:

**TENOFOVIR FARMOZ** - FARMOZ - SOCIEDADE TÉCNICO MEDICINAL, S.A.

PRAC Rapporteur: Adrien Inoubli, "31/03/2018 To: 30/03/2019"

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 PSURs 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 authorisations for the medicinal products containing the above-referred active substance, concerning the following changes:

Update of section 4.4 of the SmPC to remove the description of the warnings regarding the co-administration of tenofovir disoproxil and didanosine.

Update of section 4.5 of the SmPC to replace the wording location of the interaction between tenofovir disoproxil and didanosine.

Update of section 4.6 of the SmPC to add the main safety results from the main studies with tenofovir disoproxil in the prevention of Mother-To-Child transmission of HBV infection.

Update of section 4.8 of the SmPC to add a

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paragraph describing the features of cases of lactic acidosis reported with tenofovir disoproxil and remove the warnings regarding the co-administration of tenofovir disoproxil and didanosine.

No update of package leaflet is necessary. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

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**EMA/H/C/PSUSA/00010077/201903**

(canagliflozin, canagliflozin / metformin)

CAPS:

**Invokana** (EMA/H/C/002649) (canagliflozin), Janssen-Cilag International NV, Rapporteur: Martina Weise

**Vokanamet** (EMA/H/C/002656) (canagliflozin / metformin), Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Period covered by the PSUR: 29 March 2018 to 28 March 2019"

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):

Update of section 4.8 of the SmPC to add photosensitivity as an ADR, with a frequency uncommon. The package leaflet section 4 is updated accordingly.

Update of section 4.8 of the SmPC to reclassify the urinary tract infection ADRs under the SOC: "infections and infestations"

Update of the Package Leaflet section 4 to include the signs and symptoms of serious UTI.

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**EMA/H/C/PSUSA/00010143/201903**

(dimethyl fumarate (multiple sclerosis))

CAPS:

**TECFIDERA** (EMA/H/C/002601) (dimethyl fumarate), Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "25/03/2017 To: 25/03/2019"

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):

Update of section 4.4 of the SmPC to add a warning on Fanconi syndrome. The Package leaflet is updated accordingly.

The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

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**EMA/H/C/PSUSA/00010703/201904**

(axicabtagene ciloleucel)

CAPS:

**YESCARTA** (EMA/H/C/004480) (axicabtagene ciloleucel), Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, PRAC Rapporteur: Anette

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

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Kirstine Stark, "From: 18/10/2018 To: 17/04/2019"

medicinal product(s), concerning the following change(s):  
Update of section 4.8 of the SmPC to add spinal cord oedema with a frequency uncommon, myelitis with a frequency uncommon, quadriplegia with a frequency uncommon, and dysphagia with a frequency common.  
The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

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**EMA/H/C/PSUSA/0000998/201903**

(dexmedetomidine)

CAPS:

**DEXDOR** (EMA/H/C/002268)

(dexmedetomidine), Orion Corporation,

Rapporteur: Filip Josephson, PRAC Rapporteur:

Ulla Wändel Liminga, "From: 16/03/2018 To:

15/03/2019"

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 above mentioned medicinal product(s), concerning the following change(s):  
Update of sections 4.4 and 4.8 of the SmPC in order to amend the existing warning on cardiovascular effects and to add higher degree atrioventricular block and cardiac arrest to the list of adverse drug reactions with dexmedetomidine, accordingly. The Package Leaflet is updated accordingly.  
The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

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**B.4. EPARs / WPARs**

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**BAQSIMI - glucagon - EMA/H/C/003848**

Eli Lilly Nederland B.V., treatment of severe hypoglycaemia, Known active substance (Article 8(3) of Directive No 2001/83/EC)

For information only. Comments can be sent to the PL in case necessary.

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**Ervebo - recombinant vesicular stomatitis virus - zaire ebolavirus vaccine (live) - EMA/H/C/004554**

Merck Sharp & Dohme B.V., Ebola Vaccine, New active substance (Article 8(3) of Directive No 2001/83/EC)

For information only. Comments can be sent to the PL in case necessary.

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**Evenity - romosozumab - EMA/H/C/004465**

UCB Pharma S.A., Treatment of osteoporosis, New active substance (Article 8(3) of Directive No 2001/83/EC)

For information only. Comments can be sent to the PL in case necessary.

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**Linhaliq liposomal - ciprofloxacin -**

For information only. Comments can be sent to

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<p><b>EMA/H/C/004394</b>  Aradigm Pharmaceuticals Limited, treatment of non-cystic fibrosis bronchiectasis (NCFBE) patients with chronic lung infection with Pseudomonas aeruginosa (P. aeruginosa), Known active substance (Article 8(3) of Directive No 2001/83/EC)  <b>WPAR</b></p>	the PL in case necessary.
<p><b>Luxceptar - viable T-cells - EMA/H/C/002397, Orphan, ATMP</b>  Kiadis Pharma Netherlands B.V., adjunctive treatment in haematopoietic stem cell transplantation (HSCT) for a malignant disease, New active substance (Article 8(3) of Directive No 2001/83/EC)  <b>WPAR</b></p>	For information only. Comments can be sent to the PL in case necessary.
<p><b>Pegfilgrastim Mundipharma - pegfilgrastim - EMA/H/C/005312</b>  Mundipharma Biologics S.L., treatment of neutropenia, Similar biological application (Article 10(4) of Directive No 2001/83/EC)</p>	For information only. Comments can be sent to the PL in case necessary.
<p><b>Quofenix - delafloxacin - EMA/H/C/004860</b>  A. Menarini Industrie Farmaceutiche Riunite s.r.l., treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI) in adults, New active substance (Article 8(3) of Directive No 2001/83/EC)</p>	For information only. Comments can be sent to the PL in case necessary.
<p><b>Rinvoq - upadacitinib - EMA/H/C/004760</b>  AbbVie Deutschland GmbH &amp; Co. KG, treatment of moderate to severe active rheumatoid arthritis, New active substance (Article 8(3) of Directive No 2001/83/EC)</p>	For information only. Comments can be sent to the PL in case necessary.
<p><b>Spravato - esketamine - EMA/H/C/004535</b>  Janssen-Cilag International N.V., treatment-resistant depression, Known active substance (Article 8(3) of Directive No 2001/83/EC)</p>	For information only. Comments can be sent to the PL in case necessary.
<p><b>VANFLYTA - quizartinib - EMA/H/C/004468, Orphan</b>  Daiichi Sankyo Europe GmbH, treatment of acute myeloid leukaemia, New active substance (Article 8(3) of Directive No 2001/83/EC)</p>	For information only. Comments can be sent to the PL in case necessary.
<p><b>Xyndari – glutamine - EMA/H/C/004734, Orphan</b>  Emmaus Medical Europe Ltd; treatment of sickle</p>	For information only. Comments can be sent to the PL in case necessary.

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

**WPAR**

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## **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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<b>AJOVY - fremanezumab - EMEA/H/C/004833/II/0002</b> TEVA GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 24.10.2019. Request for Supplementary Information adopted on 25.07.2019.	Positive Opinion adopted by consensus on 24.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Aripiprazole Mylan Pharma - aripiprazole - EMEA/H/C/003803/II/0012</b> Mylan S.A.S, Generic, Generic of Abilify, Rapporteur: Bjorg Bolstad Opinion adopted on 07.11.2019. Request for Supplementary Information adopted on 12.09.2019.	Positive Opinion adopted by consensus on 07.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>CellCept - mycophenolate mofetil - EMEA/H/C/000082/II/0149/G</b> Roche Registration GmbH, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 14.11.2019.	Request for supplementary information adopted with a specific timetable.
<b>Coagadex - human coagulation factor X - EMEA/H/C/003855/II/0023, Orphan</b> BPL Bioproducts Laboratory GmbH, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 24.10.2019.	Request for supplementary information adopted with a specific timetable.
<b>Eylea - aflibercept - EMEA/H/C/002392/II/0055/G</b> Bayer AG, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 07.11.2019.	Request for supplementary information adopted with a specific timetable.
<b>Eylea - aflibercept - EMEA/H/C/002392/II/0058</b> Bayer AG, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 14.11.2019.	Request for supplementary information adopted with a specific timetable.
<b>Kalydeco - ivacaftor - EMEA/H/C/002494/II/0080, Orphan</b>	Request for supplementary information adopted with a specific timetable.

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Vertex Pharmaceuticals (Ireland) Limited,  
Rapporteur: Maria Concepcion Prieto Yerro  
Request for Supplementary Information adopted  
on 24.10.2019.

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**LIBTAYO - cemiplimab -  
EMA/H/C/004844/II/0003**

Regeneron Ireland Designated Activity Company  
(DAC), Rapporteur: Sinan B. Sarac  
Request for Supplementary Information adopted  
on 24.10.2019.

Request for supplementary information adopted  
with a specific timetable.

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**Natpar - parathyroid hormone -  
EMA/H/C/003861/II/0020/G, Orphan**

Shire Pharmaceuticals Ireland Limited,  
Rapporteur: Bart Van der Schueren  
Request for Supplementary Information adopted  
on 07.11.2019.

Request for supplementary information adopted  
with a specific timetable.

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**Natpar - parathyroid hormone -  
EMA/H/C/003861/II/0021, Orphan**

Shire Pharmaceuticals Ireland Limited,  
Rapporteur: Bart Van der Schueren  
Opinion adopted on 14.11.2019.

Positive Opinion adopted by consensus on  
14.11.2019. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**NeuroBloc - botulinum toxin type B -  
EMA/H/C/000301/II/0104/G**

Sloan Pharma S.a.r.l, Rapporteur: Bruno  
Sepodes  
Request for Supplementary Information adopted  
on 31.10.2019, 26.09.2019.

Request for supplementary information adopted  
with a specific timetable.

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**Ongentys - opicapone -  
EMA/H/C/002790/II/0009**

Bial - Portela & Ca, S.A., Rapporteur:  
Nithyanandan Nagercoil  
Opinion adopted on 24.10.2019.  
Request for Supplementary Information adopted  
on 14.02.2019, 13.09.2018, 26.04.2018.

Positive Opinion adopted by consensus on  
24.10.2019. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**Palynziq - pegvaliase -  
EMA/H/C/004744/II/0002, Orphan**

BioMarin International Limited, Rapporteur:  
Johann Lodewijk Hillege  
Request for Supplementary Information adopted  
on 14.11.2019.

Request for supplementary information adopted  
with a specific timetable.

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**Pelgraz - pegfilgrastim -  
EMA/H/C/003961/II/0013/G**

Accord Healthcare S.L.U., Rapporteur: Sol Ruiz  
Request for Supplementary Information adopted  
on 31.10.2019.

Request for supplementary information adopted  
with a specific timetable.

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**Pemetrexed Hospira - pemetrexed -**

Request for supplementary information adopted

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<p><b>EMA/H/C/003970/II/0020/G</b> Pfizer Europe MA EEIG, Generic, Generic of Alimta, Rapporteur: Alar Irs Request for Supplementary Information adopted on 24.10.2019, 12.09.2019.</p>	with a specific timetable.
<p><b>Praluent - alirocumab - EMA/H/C/003882/II/0049/G</b> sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 14.11.2019.</p>	Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<p><b>Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMA/H/C/001104/II/0180/G</b> Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 07.11.2019, 12.09.2019.</p>	Request for supplementary information adopted with a specific timetable.
<p><b>RotaTeq - rotavirus vaccine (live, oral) - EMA/H/C/000669/II/0079/G</b> MSD Vaccins, Rapporteur: Kristina Dunder Opinion adopted on 14.11.2019. Request for Supplementary Information adopted on 12.09.2019.</p>	Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<p><b>Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMA/H/C/000973/II/0141</b> GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder Opinion adopted on 07.11.2019.</p>	Positive Opinion adopted by consensus on 07.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<p><b>Tepadina - thiotepa - EMA/H/C/001046/II/0034, Orphan</b> ADIENNE S.r.l., Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 14.11.2019, 19.09.2019.</p>	Request for supplementary information adopted with a specific timetable.
<p><b>Tepadina - thiotepa - EMA/H/C/001046/II/0035/G, Orphan</b> ADIENNE S.r.l., Rapporteur: Alexandre Moreau Opinion adopted on 14.11.2019. Request for Supplementary Information adopted on 19.09.2019.</p>	Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<p><b>Xofigo - radium-223 - EMA/H/C/002653/II/0037</b> Bayer AG, Rapporteur: Janet Koenig Opinion adopted on 31.10.2019.</p>	Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<p><b>Zessly - infliximab -</b></p>	Positive Opinion adopted by consensus on

<p><b>EMA/H/C/004647/II/0009/G</b> Sandoz GmbH, Rapporteur: Bjorg Bolstad Opinion adopted on 24.10.2019.</p>	<p>24.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p><b>WS1587/G</b> <b>Abasaglar-EMA/H/C/002835/WS1587/0028/G</b> <b>Humalog-EMA/H/C/000088/WS1587/0178/G</b> Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder“Type II variation. B.IV.z. to introduce an additional prefilled pen presentation for Abasaglar, solution for injection (EU/1/14/944/007, EU/1/14/944/008, EU/1/14/944/012, EU/1/14/944/013), Humalog, solution for injection (EU/1/96/007/002, EU/1/96/007/004, EU/1/96/007/020, EU/1/96/007/021 EU/1/96/007/023), Humalog Kwikpen solution for injection (EU/1/96/007/031, EU/1/96/007/032, EU/1/96/007/039, EU/1/96/007/040, EU/1/96/007/041, EU/1/96/007/042) and Humalog Junior Kwikpen, solution for injection (EU/1/96/007/043, EU/1/96/007/044, EU/1/96/007/045). The pack contains 5 pre-filled pens. Type IAIN B. II.e.5.a.1 to request the 2x5 multipack. As a consequence, the following sections were updated 1, 4.2, 4.4, 6.2, 6.4, 6.5, 6.6, 8 of the SmPC in order to add new pre-filled pen presentation; the Package Leaflet and Labelling are updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make an editorial change (removing comma in SK address in the PL)” Request for Supplementary Information adopted on 14.11.2019, 19.09.2019.</p>	<p>See 9.1 Request for supplementary information adopted with a specific timetable.</p>
<p><b>WS1612/G</b> <b>Herceptin-EMA/H/C/000278/WS1612/0155/G</b> <b>Kadcyla-EMA/H/C/002389/WS1612/0047/G</b> Roche Registration GmbH, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 07.11.2019. Request for Supplementary Information adopted on 12.09.2019.</p>	<p>Positive Opinion adopted by consensus on 07.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p><b>WS1678</b> <b>Rixathon-EMA/H/C/003903/WS1678/</b></p>	<p>Positive Opinion adopted by consensus on 07.11.2019. The Icelandic and Norwegian CHMP</p>



<p><b>0027</b>  <b>Riximyo-EMA/H/C/004729/WS1678/0028</b>  Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus  Opinion adopted on 07.11.2019.  Request for Supplementary Information adopted on 19.09.2019.</p>	<p>Members were in agreement with the CHMP recommendation.</p>
<p><b>WS1700/G</b>  <b>Humalog-EMA/H/C/000088/WS1700/0180/G</b>  <b>Liprolog-EMA/H/C/000393/WS1700/0141/G</b>  Eli Lilly Nederland B.V., Informed Consent of Humalog, Lead Rapporteur: Kristina Dunder  Request for Supplementary Information adopted on 24.10.2019.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p><b>B.5.2. CHMP assessed procedures scope: Non-Clinical and Clinical aspects</b></p>	
<p><b>Abraxane - paclitaxel - EMA/H/C/000778/II/0097</b>  Celgene Europe BV, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC based on the results of study ABI-007-PST-001. This was a phase 1/2, multicenter, open-label, dose-finding study to assess the safety, tolerability and efficacy of weekly abraxane in paediatric patients with recurrent or refractory solid tumours, listed in the PIP, submitted in order to fulfil Article 46."  Request for Supplementary Information adopted on 14.11.2019.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p><b>Advagraf - tacrolimus - EMA/H/C/000712/II/0054</b>  Astellas Pharma Europe B.V., Rapporteur: Jayne Crowe, "Update of section 4.2 of the SmPC, to reinforce the existing wording regarding the switching between different oral formulations of tacrolimus with different release characteristics."  Opinion adopted on 24.10.2019.  Request for Supplementary Information adopted on 12.09.2019, 14.06.2019.</p>	<p>Positive Opinion adopted by consensus on 24.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p><b>Afstyla - lonoctocog alfa - EMA/H/C/004075/II/0024</b>  CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.4 and 4.8 of</p>	<p>Negative Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP</p>

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the SmPC with safety information regarding the development of factor VIII inhibitors in patients treated with Afstyla based on clinical trial and post-marketing data reviewed recently with data lock point 03 January 2019. The PL is updated accordingly. Additionally, local representatives' details for Bulgaria and Croatia have been updated.”  
Opinion adopted on 14.11.2019.  
Request for Supplementary Information adopted on 10.10.2019.

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**Aptivus - tipranavir -  
EMA/H/C/000631/II/0083/G**  
Boehringer Ingelheim International GmbH,  
Rapporteur: Jean-Michel Race, “C.I.4 (type II) -  
Update section 5.3 of the SmPC of the oral  
formulation in order to update the preclinical  
safety information based on the outcome of ICH  
M7 assessment which identified 5-trifluoro-2-  
methylpyridinol (5-TFMP), a class 2 mutagen.  
B.I.b.1.h (type IB)  
B.II.b.2.a (type IA)  
B.II.d.1.g (type IB)  
B.II.f.1.a.1 (type IB)  
B.II.f.1.d (type IB)  
B.II.f.1.e (type IB)  
The Package Leaflet and Labelling are updated  
accordingly.”  
Opinion adopted on 14.11.2019.

Positive Opinion adopted by consensus on  
14.11.2019. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**Brintellix - vortioxetine -  
EMA/H/C/002717/II/0022/G**  
H. Lundbeck A/S, Rapporteur: Bart Van der  
Schueren, “Update of sections 4.8 and 5.1 of  
the SmPC in order to describe effects of  
vortioxetine on treatment-emergent sexual  
dysfunction based on the outcome of 2  
prospective clinical studies (Studies 318 and  
4001).  
Update of sections 4.4 and 5.2 of the SmPC in  
order to reflect the outcome of study 401 in  
subjects with severe hepatic impairment.”  
Request for Supplementary Information adopted  
on 14.11.2019, 27.06.2019.

Request for supplementary information adopted  
with a specific timetable.

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**Cufence - trientine dihydrochloride -  
EMA/H/C/004111/II/0002/G**  
Univar BV, Rapporteur: Milena  
Stain“B.II.a.3.b.2) (type II)  
B.II.b.4.b) (type IA)  
B.II.b.3.a) (type IB)

See 9.1

Request for supplementary information adopted  
with a specific timetable.

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B.II.a.1.a) (type IB)

B.II.d.1.a) (type IA)

B.II.f.1.d) (type IB)

C.1.4. Update of sections 4.5 and 5.2 of the SmPC in order to add information on food interaction and pk based on results from study TR-003 PK are proposed.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template.”

Request for Supplementary Information adopted on 14.11.2019.

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**Deltyba - delamanid -  
EMA/H/C/002552/II/0037, Orphan**

Otsuka Novel Products GmbH, Rapporteur: Koenraad Norga, “C.I.13 MIC report as amendment to CSR 242-09-213.”

Opinion adopted on 24.10.2019.

Request for Supplementary Information adopted on 11.07.2019.

Positive Opinion adopted by consensus on 24.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Dovato - dolutegravir / lamivudine -  
EMA/H/C/004909/II/0001**

ViiV Healthcare B.V., Rapporteur: Filip Josephson, “Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegravir. The SmPC is updated accordingly. The RMP is not submitted.”

Request for Supplementary Information adopted on 14.11.2019.

Request for supplementary information adopted with a specific timetable.

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**Eurartesim - piperazine tetraphosphate /  
artenimol - EMA/H/C/001199/II/0036**

Alfasigma S.p.A., Rapporteur: Janet Koenig, “Changes to sections 4.2, 4.4 and 4.6 of the SmPC with reference to the posology and the recommendation during pregnancy; sections 2 and 3 of the leaflet (PL) are amended accordingly and reference to the pregnancy register deleted from Annex II.”

Request for supplementary information adopted with a specific timetable.

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Request for Supplementary Information adopted on 07.11.2019, 19.09.2019.

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**Faslodex - fulvestrant -  
EMA/H/C/000540/II/0067**

AstraZeneca AB, Rapporteur: Filip Josephson, "To update a warning in section 4.6 of the SmPC following an overview of non-clinical data, clinical pharmacology simulation/modelling data, supporting documentation and safety data. The Package Leaflet is updated accordingly. In addition, the applicant has taken the opportunity to correct a minor mistake in the address of one of the manufacturers responsible for batch release in Annex II and PL."

Opinion adopted on 07.11.2019.

Positive Opinion adopted by consensus on 07.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Feraccru - ferric maltol -  
EMA/H/C/002733/II/0022**

Norgine B.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of sections 4.2, 4.4 and 5.1 of the SmPC to include information on patients with chronic kidney disease, following the submission of the final study report of study ST10-01-303."

Opinion adopted on 14.11.2019.

Request for Supplementary Information adopted on 12.09.2019.

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Herceptin - trastuzumab -  
EMA/H/C/000278/II/0157**

Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, "To submit the results from biopharmaceutic studies and clinical pharmacology studies on the improved sensitivity of the assay developed and validated to assess rHuPH20, included as a recommendation."

Opinion adopted on 31.10.2019.

Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**IBRANCE - palbociclib -  
EMA/H/C/003853/II/0016**

Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC based on the final results from the pivotal Study A5481023 (A double blind, Phase 3 trial of fulvestrant with or without palbociclib in pre- and postmenopausal women with hormone receptor positive, HER2-negative metastatic breast cancer that progressed on prior endocrine therapy) listed as a recommendation at the time of initial MA. The

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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package leaflet is updated accordingly. The MAH also took the opportunity to update the list of local representatives in the PL.”

Opinion adopted on 14.11.2019.

Request for Supplementary Information adopted on 26.09.2019, 25.07.2019, 02.05.2019, 31.01.2019.

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**IBRANCE - palbociclib -  
EMA/H/C/003853/II/0024**

Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, “Update of section 5.1 of the SmPC based on the final report from a non-clinical study (PD-0332991) evaluating the correlation of palbociclib response to RB1 status.”

Opinion adopted on 31.10.2019.

Request for Supplementary Information adopted on 12.09.2019.

Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**IDELVION - albutrepenonacog alfa -  
EMA/H/C/003955/II/0034, Orphan**

CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, “Submission of a variation to update the dosing regimen as follows:

-21-day prophylaxis regimen with rIX-FP at a dose of 100 IU/kg body weight for patients ≥ 12 years who are well controlled on a 14-day prophylaxis regimen.

-10- or 14-day prophylaxis regimen with rIX-FP at a dose of 75 IU/kg body weight for patients < 12 years who are well controlled on a 7-day prophylaxis regimen.

This submission also updates the existing population PK model with additional intravenous and subcutaneous (SC) data from the PTPs in the PTP arm of study CSL654\_3003 and re-evaluates the covariates that are possible determinants of PK variability.”

Request for Supplementary Information adopted on 14.11.2019.

Request for supplementary information adopted with a specific timetable.

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**Juluca - dolutegravir / rilpivirine -  
EMA/H/C/004427/II/0016**

ViiV Healthcare B.V., Rapporteur: Filip Josephson, “Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status

Request for supplementary information adopted with a specific timetable.

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and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted.”

Request for Supplementary Information adopted on 14.11.2019.

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**Kisqali - ribociclib -  
EMA/H/C/004213/II/0018**

Novartis Europharm Limited, Rapporteur: Filip Josephson, “Update of section 5.2 of the SmPC to include updated information about the use of Kisqali in patients with mild or moderate renal impairment based on the results of Study CLEE011A2116 Part II and additional data from breast cancer patients with mild or moderate renal impairment.”

Request for Supplementary Information adopted on 14.11.2019.

Request for supplementary information adopted with a specific timetable.

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

Retrophin Europe Ltd, Rapporteur: Konstantinos Markopoulos, “Update of section 5.1. of the SmPC based on the submission of the final report from study CAC-002-01, listed as a category 3 study in the RMP. This is a Phase 3, open-label, single arm, non-randomized study investigating cholic acid in the treatment of subjects with inborn errors of bile acid metabolism.

The study was a continuation study that included eligible subjects who had previously received cholic acid in studies CAC-91-10-10 or CAC-001-01 as well as newly diagnosed subjects.

In addition, the MAH also took the opportunity to make editorial changes and to correct typographical mistakes throughout the product information.”

Opinion adopted on 14.11.2019.

Request for Supplementary Information adopted on 19.09.2019, 29.05.2019, 28.02.2019.

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Maviret - glecaprevir / pibrentasvir -  
EMA/H/C/004430/II/0027**

AbbVie Deutschland GmbH & Co. KG,  
Rapporteur: Jean-Michel Race, “Submission of the final clinical study report from study M16-

Request for supplementary information adopted with a specific timetable.

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133, this is a phase 3b, single Arm, open label, multicenter study aimed to evaluate the efficacy and safety of glecaprevir (GLE)/pibrentasvir (PIB) in treatment of naïve adults with chronic Hepatitis C Virus (HCV) Genotypes 1 – 6 infection and aspartate aminotransferase to platelet ratio index (APRI)  $\leq 1$ .”  
Request for Supplementary Information adopted on 24.10.2019.

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**Mimpara - cinacalcet -  
EMA/H/C/000570/II/0065**

Amgen Europe B.V., Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC in order to the new ADR ‘chondrocalcinosis pyrophosphate’ with a frequency of unknown. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to implement a minor correction to the List of Excipients in section 6.1 of the SmPC.”  
Request for Supplementary Information adopted on 14.11.2019.

Request for supplementary information adopted with a specific timetable.

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**Ongentys - opicapone -  
EMA/H/C/002790/II/0020**

Bial - Portela & C<sup>a</sup>, S.A., Rapporteur: Martina Weise, “Update of sections 4.5 and 5.2 of the SmPC to add information on drug interaction and pharmacokinetic properties of opicapone based on final results from drug interaction studies NBI-OPC-1708 and NBI-OPC-1707. Study NBI-OPC-1708 is a phase 1, open-label, one-sequence crossover, drug-interaction study to evaluate and compare the pharmacokinetics of repaglinide when administered alone and concomitantly with opicapone. Study NBI-OPC-1707 is a Phase 1, randomized, open-label, 2-period crossover drug interaction study of the effect of administration of single dose of quinidine on the pharmacokinetics of opicapone. In addition, the marketing authorisation holder took the opportunity to delete the local representative for UK from the PL, according to the guidance provided on UK's withdrawal from the EU regarding medicinal products for human and veterinary use within the framework of the Centralised Procedure”  
Request for Supplementary Information adopted on 24.10.2019.

Request for supplementary information adopted with a specific timetable.

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**OPDIVO - nivolumab -**

Positive Opinion adopted by consensus on

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**EMA/H/C/003985/II/0073**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, "To update sections 4.8 and 5.1 of the SmPC based on the final results from two studies: CA209017 (Open-label Randomized Phase III Trial comparing Nivolumab Versus Docetaxel in Previously Treated Advanced or Metastatic Squamous Cell Non-small Cell Lung Cancer) and CA209057 (Open-label Randomized Phase III Trial comparing Nivolumab Versus Docetaxel in Previously Treated Metastatic Non-Squamous Non-small Cell Lung Cancer)."  
Opinion adopted on 24.10.2019.

24.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Pradaxa - dabigatran etexilate -  
EMA/H/C/000829/II/0118/G**

Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth, "Update of sections 4.3 and 4.5 of the SmPC in order to add a contraindication and a warning regarding the interaction between Pradaxa and the fixed-dose combination of the P-gp inhibitors glecaprevir and pibrentasvir based on the results of the phase I drug-drug interaction study. The Package Leaflet was updated accordingly.  
Update of section 4.8 of the SmPC with new safety information regarding adverse reaction alopecia following the confirmation of signal "alopecia associated with dabigatran" and the cumulative review of cases of alopecia and related terms that was provided in PSUR submitted by 27 May 2019. In addition, small editorial corrections under "Adverse reaction" Table 2 were made to highlight that information on some side effects was obtained from post-marketing data. The Package Leaflet was updated accordingly."  
Opinion adopted on 14.11.2019.  
Request for Supplementary Information adopted on 12.09.2019.

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) -  
EMA/H/C/001104/II/0181**

Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to update efficacy information based on results from a public health analysis and publication of data from the CAPITA

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.



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(Community-Acquired Pneumonia Immunization Trial in Adults), a double-blind, randomized, placebo-controlled efficacy trial of 13-valent pneumococcal conjugate vaccine (PCV13)."

Opinion adopted on 14.11.2019.

Request for Supplementary Information adopted on 19.09.2019.

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**Qtern - saxagliptin / dapagliflozin -  
EMA/H/C/004057/II/0024**

AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.2, 4.4 and 5.1 of the SmPC with information on the glycaemic efficacy and renal safety of dapagliflozin in patients with Type 2 Diabetes Mellitus and moderate renal impairment (CKD 3A) based on final results from study D1690C00024 (DERIVE) (dapagliflozin), and to reflect a change in renal cut-off value for saxagliptin. The package leaflet is updated accordingly.

The RMP version 4.1 has also been submitted.

In addition, the MAH took the opportunity to update SmPC sections 2, 4.8, 5.2 and Annex II to include the required excipient information in relation to sodium levels and lactose following the update to the Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use", as well as to bring the PI in line with EMA guidance ("Compilation of QRD decisions on stylistic matters in product information", EMA/25090/2002 Rev.18, published 08 December 2017)."

Request for Supplementary Information adopted on 14.11.2019, 27.06.2019.

Request for supplementary information adopted with a specific timetable.

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**Repatha - evolocumab -  
EMA/H/C/003766/II/0038**

Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update the safety information based on final results from study 20140213. This is a phase 1 open-label interventional study to evaluate the safety, pharmacokinetics, and pharmacodynamics of evolocumab after a single 140 mg subcutaneous dose in subjects with normal renal function or severe renal insufficiency or end stage renal disease receiving haemodialysis. The Package Leaflet is updated accordingly."

Request for Supplementary Information adopted

Request for supplementary information adopted with a specific timetable.

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on 14.11.2019.

**Resolor - prucalopride -  
EMA/H/C/001012/II/0049/G**

Shire Pharmaceuticals Ireland Limited,  
Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to update the safety information following the final results from study SHP555-802 (a cohort Study of the Relative Incidence of Major Cardiovascular Events) and based on an analysis of all potential major adverse cardiovascular events (MACE) from completed Phase 2/4 clinical studies in adult subjects. In addition, the Marketing authorisation holder (MAH) took the opportunity to update typographical errors in sections 4.4 and 5.1"  
Request for Supplementary Information adopted on 31.10.2019.

Request for supplementary information adopted with a specific timetable.

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**Rezolsta - darunavir / cobicistat -  
EMA/H/C/002819/II/0035**

Janssen-Cilag International NV, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 of the SmPC to reflect the safety and efficacy information of Rezolsta based on the 48-week results from study TMC114FD2HTX3001 (AMBER), an ongoing Phase 3, randomized, active-controlled, double-blind study to evaluate efficacy and safety of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) once daily fixed dose combination (FDC) regimen versus a regimen consisting of darunavir/cobicistat (DRV/COBI) FDC co-administered with emtricitabine/tenofovir disoproxil fumarate FDC in antiretroviral treatment-naïve human immunodeficiency virus type 1 infected subjects.  
The MAH took the opportunity to update section 4.5 of the SmPC to remove the interaction with simeprevir, following the withdrawal of Olysio Marketing Authorization. In addition, the MAH has implemented some minor administrative updates throughout the Product Information. The Package Leaflet is updated accordingly."  
Opinion adopted on 14.11.2019.

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Rizmoic - naldemedine -  
EMA/H/C/004256/II/0004**

Shionogi B.V., Rapporteur: Mark Ainsworth, "Submission of the final report from non-clinical

Request for supplementary information adopted with a specific timetable.

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study S-297995-PF-360-N as agreed in letter of recommendation to CHMP: In-vitro data determining whether naldemedine inhibits in a time dependent manner the OATP1B1, OATP1B3, OAT1 and OAT3 transporters.” Request for Supplementary Information adopted on 14.11.2019.

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**RoActemra - tocilizumab -  
EMA/H/C/000955/II/0089**

Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, “Submission of the final report from study WA28119. This is a Phase III, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of tocilizumab in subjects with giant cell arteritis.” Opinion adopted on 14.11.2019.

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**RXULTI - brexpiprazole -  
EMA/H/C/003841/II/0003**

Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Daniela Melchiorri, “Based on the Company Core Data Sheet of brexpiprazole, update of section 4.4 of the SmPC to add information regarding Impulse-control disorders and section 4.8 to add the adverse reactions ‘Gambling disorder’, ‘Impulsive behaviour’, ‘Binge eating’, ‘Compulsive shopping’ and ‘Compulsive sexual behaviour’ with a frequency ‘unknown’. The Package Leaflet (PL) is updated accordingly. In addition, the MAH took the opportunity to clarify the wording regarding the posology in ‘Patients taking strong CYP3A4 inducers’ in SmPC section 4.2 as requested by EMA, and to perform additional editorials and minor changes throughout the Product Information.” Opinion adopted on 14.11.2019. Request for Supplementary Information adopted on 12.09.2019.

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Shingrix - herpes zoster vaccine  
(recombinant, adjuvanted) -  
EMA/H/C/004336/II/0016**

GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, “Update of section 4.5 of the SmPC in order to reflect information related to coadministration based on the final results from studies ZOSTER-035 and ZOSTER-042; these are immunogenicity and safety studies in which Shingrix was co-administered

Positive Opinion adopted by consensus on 24.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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either with Merck's 23-valent pneumococcal polysaccharide vaccine (Pneumovax 23; ZOSTER-035) or with GSK's reduced-antigen-content diphtheria and tetanus toxoids and acellular pertussis (dTpa) vaccine (Boostrix; ZOSTER-042); the Package Leaflet is updated accordingly."

Opinion adopted on 24.10.2019.

Request for Supplementary Information adopted on 19.09.2019, 25.07.2019.

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**SIMBRINZA - brinzolamide / brimonidine - EMEA/H/C/003698/II/0018/G**

Novartis Europharm Limited, Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 5.1 of the SmPC in order to update the safety information with adjunctive use of BID Simbrinza with a PGA therapy based on final results from study CQVJ499A2401; this is a phase 4, multicenter, randomized, double-masked, parallel-group study.

Update of section 5.1 of the SmPC in order to update the safety information with adjunctive use of BID Simbrinza with a PGA/beta-blocker combination therapy based on final results from study CQVJ499A2402; this is a phase 4, multicenter, randomized, double-masked, parallel-group study."

Opinion adopted on 07.11.2019.

Request for Supplementary Information adopted on 12.09.2019.

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Positive Opinion adopted by consensus on 07.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0032**

Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes, "To update the Marketing Authorization for Sivextro with the final report from Phase 3 study for the treatment of Hospital-Acquired Bacterial Pneumonia and Ventilator-Associated Bacterial Pneumonia (HABP/VABP) MK-1986-002; protocol TR701-132."

Opinion adopted on 31.10.2019.

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Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Tivicay - dolutegravir - EMEA/H/C/002753/II/0052**

ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a

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Request for supplementary information adopted with a specific timetable.

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birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted.”

Request for Supplementary Information adopted on 14.11.2019.

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**Translarna - ataluren -  
EMA/H/C/002720/II/0053/G, Orphan**

PTC Therapeutics International Limited,  
Rapporteur: Johann Lodewijk Hillege, “C.I.4: Update of section 5.3 of the SmPC in order to update the safety information based on final results Charles River 9001126 Three-month juvenile toxicology and toxicokinetic study planned in neonatal dogs listed as category 3 study in the RMP (MEA-005).

C.I.13 Submission of the final report from study WIL-523008 listed as category 3 study in the RMP (MEA/003). This is a Seven-day tolerability and pharmacokinetic study in neonatal dogs.

C.I.13 Submission of the final report from study WIL-523009 listed as category 3 study in the RMP (MEA/004). This is a One-month juvenile dose range-finding toxicology and toxicokinetic study planned in neonatal dogs age correlating with dosing in newborn paediatric patients to 2 years of age.

C.I.13 Submission of the final report from study (Charles River 5700755 listed as category 3 study in the RMP (MEA/0024). This is a 28-day investigational toxicology and toxicokinetic study of ataluren in juvenile beagle dogs with an 8-week recovery period – Category 3.”

Opinion adopted on 24.10.2019.

Request for Supplementary Information adopted on 18.07.2019.

Positive Opinion adopted by consensus on 24.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Triumeq - dolutegravir / abacavir /  
lamivudine - EMA/H/C/002754/II/0069**

ViiV Healthcare B.V., Rapporteur: Filip Josephson, “Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a

Request for supplementary information adopted with a specific timetable.

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birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted.”

Request for Supplementary Information adopted on 14.11.2019.

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**Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0161**

Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, “Submission of the final clinical study report for the non-interventional study GS-US-276-0103, ‘A Prospective, Observational Study of Individuals Who Seroconvert While Taking Truvada for Pre-Exposure Prophylaxis (PrEP)’, listed as a Category 3 study in the Truvada RMP.”

Opinion adopted on 14.11.2019.

Request for Supplementary Information adopted on 12.09.2019.

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Tyverb - lapatinib - EMEA/H/C/000795/II/0059**

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

Request for Supplementary Information adopted on 14.11.2019, 26.04.2019.

See 9.1

Request for supplementary information adopted with a specific timetable.

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**Verzenio - abemaciclib - EMEA/H/C/004302/II/0006**

Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, “Update of section 4.8 of the SmPC in order to add interstitial lung disease (ILD)-like events (including pneumonitis) as a new adverse drug reaction. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.”

Request for Supplementary Information adopted

Request for supplementary information adopted with a specific timetable.

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on 14.11.2019, 19.09.2019.

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**XALKORI - crizotinib -  
EMA/H/C/002489/II/0064**

Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the SmPC in order to reflect updated efficacy data from Study A8081001 in patients with ROS1-positive NSCLC. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1."

Opinion adopted on 31.10.2019.

Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Xermelo - telotristat ethyl -  
EMA/H/C/003937/II/0014, Orphan**

Ipsen Pharma, Rapporteur: Martina Weise, "To update sections 4.2 and 5.2 of the SmPC following final results from study LX1606-111; this is a Phase 1, open-label, parallel-group study to evaluate the single-dose pharmacokinetics of Telotristat Ethyl in Male and Female Subjects with Severe Hepatic Impairment and Matched Subjects with Normal Function; the Package Leaflet is updated accordingly."

Request for Supplementary Information adopted on 14.11.2019, 19.09.2019, 11.07.2019.

Request for supplementary information adopted with a specific timetable.

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**Zoely - norgestrel acetate / estradiol -  
EMA/H/C/001213/II/0050**

Theramex Ireland Limited, Rapporteur: Jean-Michel Race, "Update of sections 4.3 and 4.4 of the SmPC in order to add a new contraindication and a new warning regarding meningioma, upon request by PRAC following the assessment of Post-authorisation measure "LEG 014". The Package Leaflet is being updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in the Netherlands and Portugal in the Package Leaflet."

Request for Supplementary Information adopted on 14.11.2019, 19.09.2019.

Request for supplementary information adopted with a specific timetable.

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PRAC Led

**WS1601**

**Glyxambi-EMA/H/C/003833/WS1601/  
0022**

**Jentaducto-EMA/H/C/002279/WS1601/  
0051**

**Trajenta-EMA/H/C/002110/WS1601/  
0038**

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Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.1 of the Trajenta SmPC, update of sections 4.2, 4.4 and 5.1 of the Jentaducto SmPC and section 5.1 of the Glyxambi SmPC, based on the final results from study 1218.74 (CAROLINA study) listed as a category 3 study in the RMP of Jentaducto and Trajenta, in order to fulfil Trajenta MEA 008.1 and Jentaducto MEA 001.1; this is a phase III randomized, parallel group, double blind study to evaluate Cardiovascular safety of linagliptin versus glimepiride in patients with type 2 diabetes mellitus at high cardiovascular risk. The Package Leaflet for Trajenta is updated accordingly. The RMP version 13.0 for Jentaducto and Trajenta and version 5.0 for Glyxambi have also been submitted. In addition, the Worksharing applicant (WSA) took the opportunity to make corrections throughout the product information for Glyxambi and Jentaducto and to make corrections to the Bulgarian, French, Swedish translations for Glyxambi."

Opinion adopted on 31.10.2019.  
Request for Supplementary Information adopted on 11.07.2019.

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**WS1605**  
**Lyrica-EMA/H/C/000546/WS1605/0097**  
**Pregabalin Pfizer-EMA/H/C/003880/**  
**WS1605/0027**

Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, "Addition of a warning in section 4.4. regarding an increased risk for opioid related death in patients who took concomitant opioids. A statement on the observation of a trend for a greater risk at higher doses was also included. Section 4.5 has been updated to reflect the findings of the case-control study regarding concomitant use of pregabalin and opioids."

Opinion adopted on 14.11.2019.  
Request for Supplementary Information adopted on 12.09.2019, 23.05.2019.

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**WS1701**  
**Epclusa-EMA/H/C/004210/WS1701/**  
**0040**  
**Vosevi-EMA/H/C/004350/WS1701/0032**

Request for supplementary information adopted with a specific timetable.



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Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add new safety information on rash and angioedema following a cumulative review of hypersensitivity with Eplusa and Vosevi, prompted by routine pharmacovigilance and signal detection activities. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes throughout the Product Information."

Request for Supplementary Information adopted on 14.11.2019.

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**WS1705**

**Aluvia-EMA/H/W/000764/WS1705/0111**  
**Kaletra-EMA/H/C/000368/WS1705/0180**

AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Jean-Michel Race, "Change of section 4.8 of the SmPC to update the safety information following a cumulative safety review of the incidence rate of Stevens-Johnson syndrome, erythema multiforme and jaundice during clinical trials. This variation closes LEG 110. The Package Leaflet is updated accordingly."

Opinion adopted on 31.10.2019.

Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

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**Aranesp - darbepoetin alfa -**  
**EMA/H/C/000332/II/0150**

Amgen Europe B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of the SmPC sections 4.4, 4.8, 5.1 based on the study data from Study 20070782 - a phase 3, randomized, double-blind, placebo-controlled, noninferiority study in subjects with chemotherapy-induced anemia receiving multi-cycle chemotherapy for the treatment of advanced stage non-small-cell lung cancer (NSCLC); study of epoetin alfa in metastatic breast cancer (EPO-ANE-3010) and the Company Core Data Sheet.

In addition, the section 4.6 has been revised based on the recommendation from last Periodic Safety Update Report Number 33 dated 15 January 2018. Furthermore, the MAH took the opportunity to introduce minor editorial changes, update the information on local representatives and align the PI with the

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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requirements of the QRD template 10.0. The PL is updated accordingly. The revised RMP version 9.3 has been also submitted.”

Opinion adopted on 14.11.2019.

Request for Supplementary Information adopted on 25.07.2019, 28.03.2019.

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**Avastin - bevacizumab -  
EMA/H/C/000582/II/0110**

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, “Submission of the final report from study NEJ026 listed as an obligation in the Annex II of the Product Information. This is an open-label, randomized, Phase III study conducted in Japan to compare erlotinib + bevacizumab combination therapy versus erlotinib monotherapy as first-line therapies for patients with NSCLC with EGFR gene mutations (exon 19 deletion or exon 21 L858R substitution).

The RMP version 30.0 has also been submitted. In addition, the Package leaflet is updated to reflect information on sodium content in compliance with the revised Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use".”

Request for Supplementary Information adopted on 31.10.2019, 05.09.2019.

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Request for supplementary information adopted with a specific timetable.

**Brinavess - vernakalant -  
EMA/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

Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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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 as 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)."

Opinion adopted on 31.10.2019.

Request for Supplementary Information adopted on 05.09.2019, 14.06.2019.

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**Increlex - mecasecamin -**

**EMA/H/C/000704/II/0060**

Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.1, 4.2, 4.3, 4.4, 4.8 and 4.9 of the SmPC in order to update the safety information on benign or malignant neoplasia based on the EU Registry Study, the Ipsen global safety database and literature review. The Package Leaflet is updated accordingly. The MAH also submitted the updated RMP version 11.3.

In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet"

Opinion adopted on 14.11.2019.

Request for Supplementary Information adopted on 19.09.2019.

See 9.1

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Mircera - methoxy polyethylene glycol-epoetin beta - EMA/H/C/000739/II/0068**

Roche Registration GmbH, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "Update of sections 4.4 and 4.8 of the SmPC to include information on the availability of anti-erythropoietin antibody (AEAB) testing and to amend the frequency of adverse drug reactions, respectively, based on the final report of study BH21260, listed as a category 3 study in the RMP (MEA008.5); this is a randomized, controlled, open-label,

Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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multicenter, parallel- group study to assess all-cause mortality and cardiovascular morbidity in patients with chronic kidney disease on dialysis and those not on renal replacement therapy under treatment with Mircera or reference ESAs. In addition, reference to the educational materials related to AEAB testing is removed from the Annex II. The RMP (version 12.3) is updated accordingly and transitioned to the new EU RMP template in line with the revised Good Pharmacovigilance Practice (GVP) Module V (Revision 2) guideline.”

Opinion adopted on 31.10.2019.

Request for Supplementary Information adopted on 14.06.2019, 17.01.2019, 04.10.2018.

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**NovoEight - turoctocog alfa -  
EMA/H/C/002719/II/0030/G**

Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC based on results of the Guardian 4 (NN7008-3809) Clinical Trial in Previously Untreated Patients (PUPs) and the Guardian 9 (NN7008-4239) PK Clinical Trial. The MAH has also updated the SmPC to align with the 'EMA Core SmPC for human plasma derived and recombinant coagulation factor VIII products, revision 3' and Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. Further, some administrative updates have also been applied.”

Opinion adopted on 31.10.2019.

Request for Supplementary Information adopted on 05.09.2019.

Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Odomzo - sonidegib -  
EMA/H/C/002839/II/0024**

Sun Pharmaceutical Industries Europe B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Željana Margan Koletić, “To submit the final report of study CLDE225X2116, listed as a category 3 study in the RMP. This is an interventional Phase Ib/II, open-label, multi-center, dose-finding study to assess the safety and efficacy of the oral combination of LDE225 and INC424 (Ruxolitinib) in subjects with myelofibrosis. The RMP version 7.1 has also been submitted.”

Request for Supplementary Information adopted

Request for supplementary information adopted with a specific timetable.

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on 31.10.2019.

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**Orkambi - lumacaftor / ivacaftor -  
EMA/H/C/003954/II/0049**

Vertex Pharmaceuticals (Ireland) Limited,  
Rapporteur: Daniela Melchiorri, PRAC  
Rapporteur: Rhea Fitzgerald, "Updated of  
section 4.8 of the SmPC with the safety data  
from the Phase 3, open-label, rollover study for  
Studies 109 and 011 Part B (Study 011B)  
designed to evaluate the long-term safety and  
tolerability of Orkambi treatment for 96 weeks  
in patients with cystic fibrosis, 6 years of age  
and older, homozygous for F508del."  
Request for Supplementary Information adopted  
on 31.10.2019, 05.09.2019.

Request for supplementary information adopted  
with a specific timetable.

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**Raxone - idebenone -  
EMA/H/C/003834/II/0018, Orphan**

Santhera Pharmaceuticals (Deutschland) GmbH,  
Rapporteur: John Joseph Borg, PRAC  
Rapporteur: Amelia Cupelli, "Submission of the  
final report from study SNT-EAP-001 listed as a  
Specific Obligation (SOB11, former SOB4) in the  
Annex II of the Product Information. This is a  
follow-up study of patients in the Expanded  
Access Program (SNT-EPA-001) for Raxone in  
the treatment of patients with Leber's  
Hereditary Optic Neuropathy (LHON). The goal  
is to collect further long-term real-world efficacy  
and safety data. Annex II is modified  
accordingly. An updated RMP version 1.10  
submitted accordingly."  
Opinion adopted on 14.11.2019.

Positive Opinion adopted by consensus on  
14.11.2019. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**TECFIDERA - dimethyl fumarate -  
EMA/H/C/002601/II/0058**

Biogen Netherlands B.V., Rapporteur: Martina  
Weise, PRAC Rapporteur: Martin Huber,  
"Submission of CSR of study 109MS310, an  
open-label study to assess the effects of  
Tecfidera on lymphocyte subsets in subjects  
with relapsing remitting multiple sclerosis, listed  
as category 3 study in the RMP.  
The RMP (version 10.1) has been updated as a  
consequence of the completion of this study.  
The revised RMP also includes updates to reflect  
safety information available through to the data  
lock point of 24 January 2019 and to align with  
the EU RMP Module V (revision 2.01)."  
Request for Supplementary Information adopted  
on 31.10.2019, 11.07.2019.

Request for supplementary information adopted  
with a specific timetable.

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**TECFIDERA - dimethyl fumarate -  
EMA/H/C/002601/II/0062**

Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 and 4.8 of the SmPC to add a warning on the newly identified risk of herpes zoster and to add the adverse reaction herpes zoster with a frequency not known. The update is based on cumulative review data submitted in PSUSA/00010143/201903. The Package Leaflet is updated accordingly."

Opinion adopted on 14.11.2019.

Request for Supplementary Information adopted on 19.09.2019.

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**UDENYCA - pegfilgrastim -  
EMA/H/C/004413/II/0003**

ERA Consulting GmbH, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, "To update section 4.6 of the SmPC to remove reference to the pregnancy and lactation registry listed as a category 3 study in the RMP. The Package Leaflet is updated accordingly. The updated RMP version 1.5 has also been submitted."

Opinion adopted on 31.10.2019.

Request for Supplementary Information adopted on 05.09.2019.

Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**VeraSeal - human fibrinogen / human thrombin - EMA/H/C/004446/II/0006/G**

Instituto Grifols, S.A., Rapporteur: Andrea Laslop, PRAC Rapporteur: Amelia Cupelli "B.IV.1.a.3 – Type II - To add a new CE marked applicator tip as a replacement for the current application cannula which allows the application of the product both by dripping and spraying without gas assistance. The safety concern of air or gas embolism that is currently included in the Risk Management Plan (RMP) is no longer applicable, consequently the RMP has been updated accordingly (version 4.0) and is provided in Module 1.8.2. RMP version 4.0 has been restructured in order to adapt to the new format of GVP Module V.

B.II.e.6.a – Type 1B

B.II.e.6.a – Type 1B

B.II.b.3.a – Type 1A

B.II.b.3.a – Type 1A

Opinion adopted on 14.11.2019.

Request for Supplementary Information adopted

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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on 17.10.2019.

**Zelboraf - vemurafenib -  
EMA/H/C/002409/II/0054**

Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Update of sections 4.4 and 4.5 of the SmPC in order to add information and a precaution regarding concomitant strong CYP3A4 inhibitors based on final results from study GO29475 (MEA-011), a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PL in line with the excipients guideline (EMA/CHMP/302620/2017) by adding information about the product's sodium content."

Opinion adopted on 31.10.2019.

Request for Supplementary Information adopted on 05.09.2019.

Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Zydelig - idelalisib -**

**EMA/H/C/003843/II/0047**

Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber, "Update of sections 4.8 and 5.1 of the SmPC based on final results from study 101-09 (A Phase 2 Study to Assess the Efficacy and Safety of Idelalisib in Subjects with Indolent B Cell Non-Hodgkin Lymphomas Refractory to Rituximab and Alkylating Agents); the relevant obligation is removed from the Annex II and the RMP version 5.0 is agreed. Finally, section 4.1 of the SmPC and the Package Leaflet are updated to remove references to combination with ofatumumab further to the withdrawal of the marketing authorisation of Arzerra and the SmPC and Package Leaflet are also updated to remove references to additional monitoring."

Opinion adopted on 14.11.2019.

Request for Supplementary Information adopted on 19.09.2019.

See 9.1

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**WS1690**

**Clopidogrel Zentiva-EMA/H/C/000975/  
WS1690/0066**

**DuoPlavin-EMA/H/C/001143/WS1690/  
0053**

**Iscover-EMA/H/C/000175/WS1690/  
0136**

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Plavix-EMA/H/C/000174/WS1690/0133**

sanofi-aventis groupe, Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "To modify the Product Information (PI) in section 4.5

"Interaction with other medicinal products and other forms of interaction" of the SmPC and the corresponding section of the PL to add the signal of interaction of clopidogrel with boosted antiviral HIV therapy leading to insufficient inhibition of platelet aggregation in line with EPITT 19325. The MAH has made minor adjustments to the wording."

Opinion adopted on 14.11.2019.

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**B.5.4. PRAC assessed procedures**

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PRAC Led

**Adempas - riociguat -****EMA/H/C/002737/II/0030, Orphan**

Bayer AG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Tuomo Lapveteläinen, "Submission of the final report from risk management plan (RMP) category 3 study 16657, EXPERT (EXPosurE Registry Riociguat in patients with pulmonary hypertension) to collect information about the long term use of Adempas in real clinical practice. The RMP version 7.1 has also been submitted."

Request for Supplementary Information adopted on 31.10.2019.

Clockstop extension Adopted.

Letter from the applicant dated 11.11.2019 requesting a clock stop extension.

Request for supplementary information adopted with a specific timetable.

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PRAC Led

**AUBAGIO - teriflunomide -****EMA/H/C/002514/II/0025**

sanofi-aventis groupe, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the patients and HCPs final survey reports to assess the effectiveness of the education materials; the survey reports are part of the additional pharmacovigilance activities in the RMP (category 3 studies). Within this submission the MAH is proposing a revised patient card with the following revisions: the patient card was restructured (general guidance, possible side

Request for supplementary information adopted with a specific timetable.

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effects, pregnancy), details related to the Accelerated Elimination Procedure were deleted and symptoms related to liver and infections are described.”

Request for Supplementary Information adopted on 31.10.2019, 05.09.2019.

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PRAC Led

**Colobreathe - colistimethate sodium -  
EMA/H/C/001225/II/0044/G**

Teva B.V., Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski, PRAC-CHMP liaison: Ewa Balkowiec Iskra, “Submission of the final Post-authorisation safety study report for CLB-MD-05: An observational safety study of Colobreathe (colistimethate sodium dry powder for inhalation) compared with other inhaled anti-pseudomonal antibiotics in cystic fibrosis patients using cystic fibrosis registries. The MAH is also providing an updated RMP, reflecting results from CLB-MD-05 but also the results from CLB-MD-08 that had been provided previously.”

Request for Supplementary Information adopted on 31.10.2019.

Request for supplementary information adopted with a specific timetable.

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PRAC Led

**Cubicin - daptomycin -  
EMA/H/C/000637/II/0074**

Merck Sharp & Dohme B.V., PRAC Rapporteur: Pernille Harg, PRAC-CHMP liaison: Bjorg Bolstad, “Submission of an updated RMP version 11.1 in order to delete all risks and additional risk minimisation measures in line with GVP module V revision 2. Annex II of the Product Information is updated accordingly. In addition, the MAH took the opportunity to align the Product Information with the QRD template version 10.1 and update the list of local representatives.”

Request for Supplementary Information adopted on 31.10.2019.

Request for supplementary information adopted with a specific timetable.

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PRAC Led

**Flixabi - infliximab -  
EMA/H/C/004020/II/0039**

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

Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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registries (CEDUR, CREDIT, and DREAM)”  
Opinion adopted on 31.10.2019.  
Request for Supplementary Information adopted  
on 11.07.2019, 11.04.2019.

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PRAC Led

**Invokana - canagliflozin -  
EMA/H/C/002649/II/0045/G**

Janssen-Cilag International NV, Rapporteur:  
Martina Weise, PRAC Rapporteur: Martin Huber,  
PRAC-CHMP liaison: Martina Weise, “Submission  
of the final report from 3 non-interventional  
studies (listed as category 3 studies in the  
RMP):

- Study RRA-21410, an Epidemiology Study to  
characterize the risk of LLA in subjects in the  
overall T2DM population and in a subpopulation  
with established CVD.
- NAP4001, a Meta-Analysis from CANVAS,  
CANVAS-R and CREDENCE Studies to  
characterize the risk of LLA in subjects at high  
risk for CV events and/or progression of kidney  
disease.
- Meta-Analysis from CANVAS, CANVAS-R and  
CREDENCE to evaluate the incidence of bladder  
cancer in the canagliflozin group compared to  
the placebo group.”

Opinion adopted on 31.10.2019.

Positive Opinion adopted by consensus on  
31.10.2019. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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PRAC Led

**Praluent - alirocumab -  
EMA/H/C/003882/II/0050/G**

sanofi-aventis groupe, Rapporteur: Johann  
Lodewijk Hillege, PRAC Rapporteur: Brigitte  
Keller-Stanislawski, PRAC-CHMP liaison: Jan  
Mueller-Berghaus, “Submission of an updated  
RMP version 5.0 in order to amend the list of  
safety concerns (removing ‘cataract (in the  
context of very low LDL-C)’ as important  
potential risk; ‘long-term use (>5years)’ and  
‘clinical impact of very low LDL-C for extended  
period of time’ as missing information; and  
consequentially to remove the following  
additional Pharmacovigilance activities (category  
3 studies in the RMP) from the RMP: study  
R727-CL-1609 (MEA 016), study OBS14697  
(MEA 019) and study ALIROC07997 (MEA 017)  
based on a review of data since the MA was  
granted including the 1st interim report for  
study OBS14697, a drug utilisation study (DUS)  
of alirocumab in Europe to assess the  
effectiveness of the dosing recommendation to

Request for supplementary information adopted  
with a specific timetable.

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avoid very low LDL-C levels, in order to fulfil MEA 019.4.”  
Request for Supplementary Information adopted on 31.10.2019.

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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 CC-5013-PASS-001 final study report dated 2 Nov 2018; this is a non-interventional post-authorisation safety study (PASS) to further characterise the safety profile of lenalidomide plus dexamethasone in the treatment of relapsed and/or refractory (R/R) MM in a real-world setting.”  
Opinion adopted on 31.10.2019.  
Request for Supplementary Information adopted on 14.06.2019.

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Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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PRAC Led  
**Selincro - nalmefene - EMEA/H/C/002583/II/0025**  
H. Lundbeck A/S, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, “submission for the Final Study Reports for the PASS 15649A: Use of Nalmefene (Selincro) in European databases: Cohort design using longitudinal electronic medical records or claims databases and PASS 14910A a non-interventional multicountry prospective cohort study to investigate the pattern of use of Selincro and frequency of selected adverse reactions in routine clinical practice. The RMP version 8.0 has been updated accordingly.”  
Request for Supplementary Information adopted on 31.10.2019, 05.09.2019.

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Request for supplementary information adopted with a specific timetable.

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PRAC Led  
**SIMBRINZA - brinzolamide / brimonidine - EMEA/H/C/003698/II/0019**  
Novartis Europharm Limited, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, “Submission of an updated RMP version 3.0 in order to remove metabolic acidosis/renal impairment as an important potential risk from the list of safety concerns and in addition update the Risk management plan to comply

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Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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with the new GVP module V rev 2 RMP template.”  
Opinion adopted on 31.10.2019.  
Request for Supplementary Information adopted on 05.09.2019.

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PRAC Led  
**Slentyto - melatonin -  
EMA/H/C/004425/II/0010**  
RAD Neurim Pharmaceuticals EEC SARL,  
Rapporteur: Kristina Dunder, PRAC Rapporteur:  
Ana Sofia Diniz Martins, PRAC-CHMP liaison:  
Bruno Sepodes, “Submission of the Annual  
report #3 of the French RTU with data collected  
from 01 October 2015 to 01 October 2018.  
Update of the RMP to version 1.5 to reflect the  
interim RTU result and commit to submit final  
results when available.”  
Opinion adopted on 31.10.2019.  
Request for Supplementary Information adopted  
on 05.09.2019.

Positive Opinion adopted by consensus on  
31.10.2019. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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PRAC Led  
**VELCADE - bortezomib -  
EMA/H/C/000539/II/0093**  
Janssen-Cilag International NV, Rapporteur:  
Daniela Melchiorri, PRAC Rapporteur: Amelia  
Cupelli, PRAC-CHMP liaison: Daniela Melchiorri,  
“Submission of an updated RMP version 30.1 in  
order to revise the list of safety concerns. This  
revision has been triggered by the PRAC  
recommendation received in outcome of the EU-  
PSUR covering the period from 26 April 2017 to  
25 April 2018. As a consequence, the Annex II  
of the PI has been updated to reflect the  
removal of the additional risk minimisation  
activities. In addition, the applicant took the  
opportunity to update the list of local  
representatives in the PL. Furthermore, the PI is  
being brought in line with the latest QRD  
template (version 10.1).”  
Request for Supplementary Information adopted  
on 31.10.2019.

Request for supplementary information adopted  
with a specific timetable.

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PRAC Led  
**Vokanamet - canagliflozin / metformin -  
EMA/H/C/002656/II/0050/G**  
Janssen-Cilag International NV, Rapporteur:  
Martina Weise, PRAC Rapporteur: Menno van  
der Elst, PRAC-CHMP liaison: Johann Lodewijk  
Hillege, “Submission of the final report from 3  
non-interventional studies (listed as category 3

Positive Opinion adopted by consensus on  
31.10.2019. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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studies in the RMP):

- Study RRA-21410, an Epidemiology Study to characterize the risk of LLA in subjects in the overall T2DM population and in a subpopulation with established CVD.

- NAP4001, a Meta-Analysis from CANVAS, CANVAS-R and CREDENCE Studies to characterize the risk of LLA in subjects at high risk for CV events and/or progression of kidney disease .

- Meta-Analysis from CANVAS, CANVAS-R and CREDENCE to evaluate the incidence of bladder cancer in the canagliflozin group compared to the placebo group.”

Opinion adopted on 31.10.2019.

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PRAC Led

**WS1654**

**Enbrel-EMEA/H/C/000262/WS1654/0228**  
**LIFMIOR-EMEA/H/C/004167/WS1654/0022**

Pfizer Europe MA EEIG, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, “C.I.13: Submission of the final report from study (B1801311 - BADBIR) listed as a category 3 study in the RMP. This is a prospective cohort study that compared patients treated with biologic interventions (etanercept, adalimumab, and ustekinumab) and patients with similar disease characteristics but exposed only to conventional non-biologic systemic therapies.”

Opinion adopted on 31.10.2019.

Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

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**Alofisel - darvadstrocel -**  
**EMEA/H/C/004258/II/0009, Orphan,**  
**ATMP**

Takeda Pharma A/S, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder  
Request for Supplementary Information adopted on 08.11.2019.

Request for supplementary information adopted with a specific timetable.

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**Kymriah - tisagenlecleucel -**  
**EMEA/H/C/004090/II/0014, Orphan,**  
**ATMP**

Novartis Europharm Limited, Rapporteur: Rune Kjekken, CHMP Coordinator: Ingrid Wang

Request for supplementary information adopted with a specific timetable.

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Request for Supplementary Information adopted on 08.11.2019.

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**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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**WS1656/G**  
**Copalia-EMEA/H/C/000774/WS1656/0108/G**  
**Copalia HCT-EMEA/H/C/001159/WS1656/0079/G**  
**Dafiro-EMEA/H/C/000776/WS1656/0111/G**  
**Dafiro HCT-EMEA/H/C/001160/WS1656/0081/G**  
**Exforge HCT-EMEA/H/C/001068/WS1656/0078/G**

Positive Opinion adopted by consensus on 31.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Novartis Europharm Limited, Lead Rapporteur:  
Mark Ainsworth  
Opinion adopted on 31.10.2019.  
Request for Supplementary Information adopted on 19.09.2019.

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**WS1661/G**  
**Entresto-EMEA/H/C/004062/WS1661/0026/G**  
**Neparvis-EMEA/H/C/004343/WS1661/0025/G**

Positive Opinion adopted by consensus on 24.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Novartis Europharm Limited, Lead Rapporteur:  
Johann Lodewijk Hillege  
Opinion adopted on 24.10.2019.

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**WS1669**  
**Ryzodeg-EMEA/H/C/002499/WS1669/0035**  
**Tresiba-EMEA/H/C/002498/WS1669/0042**  
**Xultophy-EMEA/H/C/002647/WS1669/0032**

Positive Opinion adopted by consensus on 07.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder  
Opinion adopted on 07.11.2019.  
Request for Supplementary Information adopted on 12.09.2019.

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**WS1673**  
**Infanrix hexa-EMEA/H/C/000296/WS1673/0263**

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

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Opinion adopted on 14.11.2019.

**WS1685**

**Juluca-EMA/H/C/004427/WS1685/0017**  
**Tivicay-EMA/H/C/002753/WS1685/0053**  
**Triumeq-EMA/H/C/002754/WS1685/0072**

ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson

Opinion adopted on 14.11.2019.

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**WS1692/G**

**Edistride-EMA/H/C/004161/WS1692/0033/G**  
**Forxiga-EMA/H/C/002322/WS1692/0052/G**

AstraZeneca AB, Lead Rapporteur: Kristina Dunder

Opinion adopted on 14.11.2019.

Positive Opinion adopted by consensus on 14.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**WS1706**

**Enurev Breezhaler-EMA/H/C/002691/WS1706/0030**  
**Seebri Breezhaler-EMA/H/C/002430/WS1706/0030**  
**Tovanor Breezhaler-EMA/H/C/002690/WS1706/0034**

Novartis Europharm Limited, Duplicate, Duplicate of Seebri Breezhaler, Lead Rapporteur: Mark Ainsworth, "To introduce a modification of the Instructions for Use (IFU) for the Breezhaler devices affecting the labelling (SmPC and PL) through simplification of its content and layout - condensing textual instructions, optimizing illustrations, and clustering of content to aid comprehension of the procedure of use.

In addition both the packaging and IFU in the SmPC and PL have included device-specific information in precise locations in order to meet the MDR requirements. This is because the device does not have its own packaging or leaflet."

Request for Supplementary Information adopted on 07.11.2019.

Request for supplementary information adopted with a specific timetable.

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**WS1707**

**Ultibro Breezhaler-EMA/H/C/002679/WS1707/0031**  
**Ulunar Breezhaler-EMA/H/C/003875/WS1707/0032**  
**Xoterna Breezhaler-EMA/H/C/003755/WS1707/0035**

Negative Opinion adopted by consensus on 07.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, "To add onto the packaging and IFU in the SmPC and PL device-specific information in precise locations in order to meet the MDR requirements. This is because the device does not have its own packaging or leaflet."

Opinion adopted on 07.11.2019.

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**WS1708**

**Hirobriz Breezhaler-EMEA/H/C/001211/WS1708/0055**

**Onbrez Breezhaler-EMEA/H/C/001114/WS1708/0053**

**Oslif Breezhaler-EMEA/H/C/001210/WS1708/0053**

Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, "To introduce a modification of the Instructions for Use (IFU) for the Breezhaler devices affecting the labelling (SmPC and PL) through simplification of its content and layout - condensing textual instructions, optimizing illustrations, and clustering of content to aid comprehension of the procedure of use.

In addition both the packaging and IFU in the SmPC and PL have included device-specific information in precise locations in order to meet the MDR requirements. This is because the device does not have its own packaging or leaflet.

Finally, as notified to the Agency, the MAH took this opportunity to remove unnecessary details from the quality module 3.2.P.7 currently registered for Onbrez/ Hirobriz/ Oslif Breezhaler."

Request for Supplementary Information adopted on 07.11.2019.

Request for supplementary information adopted with a specific timetable.

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

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**Vepacel - prepandemic influenza vaccine H5N1 (whole virion, vero cell derived, inactivated) - EMEA/H/C/002089/II/0021**

Ology Bioservices Ireland Limited, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of an updated RMP version 2.0 to update the summary of safety concerns in line with updated Summary of Product Characteristics (SmPC) of Prepandemic and Pandemic influenza vaccine H5N1 (whole virion, Vero cell derived,

The MAH withdrew the procedure on 06.11.2019.



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inactivated) suspension for injection and current scientific knowledge. The RMP has been submitted in accordance with the new format of Good Pharmacovigilance Practices (GVP) module V (Rev 2)."

Withdrawal request submitted on 06.11.2019.

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

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##### **Jakavi - ruxolitinib -**

##### **EMA/H/C/002464/II/0044**

Novartis Europharm Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Annika Folin, "Update of the SmPC sections 5.1 and 4.8 with the efficacy and safety information to reflect the 5-year follow-up data from the B2301 Week 256 final clinical study report (CSR). The final analyses presented in the CSR are submitted to fulfil the Post-Authorisation Measure, therefore the Annex II.D of the Product Information is updated accordingly. The changes have been reflected in the RMP version 11 submitted with the procedure II/43."

Request for Supplementary Information adopted on 03.10.2019.

Clockstop extension request **For adoption.**

Request by the applicant for an extension of the clock stop.

The CHMP agreed to the request by the applicant for an extension to the clock stop with a specific timetable.

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PRAC Led

##### **Jakavi - ruxolitinib -**

##### **EMA/H/C/002464/II/0043**

Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Filip Josephson, "Submission of the final report from a safety study (INC424AIC01T) of ruxolitinib in myelofibrosis (MF) listed as a category 3 study in the RMP. This is a non-interventional, observational post-authorisation safety study (PASS) intended to provide real-world safety data on patients with MF who were exposed and non-exposed to ruxolitinib and thereby provide insights into disease management and the safety profile of ruxolitinib.

The RMP version 11 has also been submitted. The updated RMP v11 reflects the completion of additional pharmacovigilance studies including the above-mentioned PASS (INC424AIC01T, Category 3) as well as the RESPONSE study (INC424B2301, Category 1). This RMP is

Request by the applicant for an extension of the clock stop

The CHMP agreed to the request by the applicant for an extension to the clock stop with a specific timetable.

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incorporated in this variation and will be cross-referred in the variation forthcoming submission for the RESPONSE study within a month of this submission.”

Request for Supplementary Information adopted on 03.10.2019.

Clockstop extension request **For adoption.**

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

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

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#### **acalabrutinib - EMEA/H/C/005299, Orphan**

AstraZeneca AB, Treatment of adult patients with chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL)

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#### **bulevirtide - EMEA/H/C/004854, Orphan      Accelerated review**

MYR GmbH, indicated for the treatment of chronic hepatitis delta virus (HDV) infection in adult patients with compensated liver disease.

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#### **ellexacaftor / tezacaftor / ivacaftor - EMEA/H/C/005269, Orphan      Accelerated review**

Vertex Pharmaceuticals (Ireland) Limited, treatment of cystic fibrosis

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#### **insulin aspart - EMEA/H/C/004965**

treatment of diabetes mellitus

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#### **Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/005084, Article 28**

immunization against Neisseria meningitidis serogroups A, C, W-135 and Y

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#### **caffeine citrate - EMEA/H/C/005435**

treatment of primary apnoea

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#### **salmeterol xinafoate / fluticasone propionate - EMEA/H/C/004881**

for treatment of asthma

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#### **sunitinib - EMEA/H/C/005419**

treatment of gastrointestinal stromal tumour (GIST) and metastatic renal cell carcinoma (MRCC) and pancreatic neuroendocrine tumours (pNET)

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#### **influenza quadrivalent vaccine (rDNA) - EMEA/H/C/005159**

prevention of influenza disease

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

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**Epclusa - sofosbuvir / velpatasvir -  
EMA/H/C/004210/X/0043/G**

Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "Extension application to introduce a new strength (200/50 mg film-coated tablets).

The new formulation is indicated for the treatment of chronic hepatitis C (CHC) in patients aged 6 years and older.

The extension application is grouped with a type II variation (C.I.6.a) to include paediatric use in patients aged 6 to < 18 years who weigh greater than or equal to 35 kg to the existing presentation (400/100 mg film-coated tablets). Sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and the Package Leaflet are updated to support the extended indication.

The RMP (version 5.1) is updated in accordance."

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**Pemetrexed Hospira - pemetrexed -  
EMA/H/C/003970/X/0021**

Pfizer Europe MA EEIG, Generic, Generic of Alimta, Rapporteur: Alar Irs, "Extension application to introduce a new pharmaceutical form with its associated strength (25 mg/ml concentrate for solution for infusion)."

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**Pradaxa - dabigatran etexilate -  
EMA/H/C/000829/X/0122/G**

Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Anette Kirstine Stark, "Extension application to add two new pharmaceutical forms for PRADAXA (coated granules (20 mg, 30 mg, 40 mg, 50 mg, 110 mg, 150 mg) and powder and solvent for oral solution (6.25 mg/ml)), grouped with:  
-A type II variation (C.I.6.a) - Extension of indication to include new indication for Pradaxa 75 mg, 110 mg, 150 mg capsules based on the paediatric trials 1160.106 and 1160.108.

As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet and Labelling are 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

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version 37.0 has also been submitted.

- Type IB (B.I.b.1.c)
  - Type IA (B.I.b.1.b)
  - Type IB (B.I.b.1.d)
  - Type IA (B.I.b.2.a)
  - Type IA (B.I.b.1.d)
  - Type IA (B.I.d.1.a.1)
  - Type IA (B.II.d.1.a)
  - Type IB (B.II.d.1.d)
  - Type IA (B.II.d.2.a)
  - Type IA (B.II.c.1.c)
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### **B.6.3. Restart of procedure - responses received to Day 120 List of Questions timetables: for information**

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#### **givosiran - EMEA/H/C/004775, Orphan**

Alnylam Netherlands B.V., Treatment of acute hepatic porphyria (AHP) in adults and adolescents aged 12 years and older.  
List of Questions adopted on 15.10.2019.

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

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#### **Increlex - mecasermin - EMEA/H/C/000704/S/0061**

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

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#### **Myalepta - metreleptin - EMEA/H/C/004218/S/0009, Orphan**

Aegerion Pharmaceuticals B.V., Rapporteur:  
Bart Van der Schueren, PRAC Rapporteur: Adam  
Przybylkowski

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#### **Raxone - idebenone - EMEA/H/C/003834/S/0019, Orphan**

Santhera Pharmaceuticals (Deutschland) GmbH,  
Rapporteur: John Joseph Borg, PRAC  
Rapporteur: Amelia Cupelli

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

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#### **Aripiprazole Zentiva - aripiprazole - EMEA/H/C/003899/R/0012**

Zentiva, k.s., Generic, Generic of Abilify,  
Rapporteur: John Joseph Borg, PRAC  
Rapporteur: Ana Sofia Diniz Martins

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#### **Bortezomib Accord - bortezomib -**

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**EMA/H/C/003984/R/0022**

Accord Healthcare S.L.U., Generic, Generic of  
VELCADE, Rapporteur: Milena Stain, PRAC  
Rapporteur: Amelia Cupelli

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**Daxas - roflumilast -****EMA/H/C/001179/R/0039**

AstraZeneca AB, Rapporteur: Maria Concepcion  
Prieto Yerro, Co-Rapporteur: Jayne Crowe,  
PRAC Rapporteur: Maria del Pilar Rayon

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**Ivabradine Anpharm - ivabradine -****EMA/H/C/004187/R/0014**

ANPHARM Przedsiębiorstwo Farmaceutyczne  
S.A., Rapporteur: Johann Lodewijk Hillege, Co-  
Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur:  
Menno van der Elst

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**Odomzo - sonidegib -****EMA/H/C/002839/R/0028**

Sun Pharmaceutical Industries Europe B.V.,  
Rapporteur: Paula Boudewina van Hennik, Co-  
Rapporteur: Daniela Melchiorri, PRAC  
Rapporteur: Željana Margan Koletić

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**Pregabalin Sandoz - pregabalin -****EMA/H/C/004010/R/0012**

Sandoz GmbH, Generic, Generic of Lyrica,  
Rapporteur: Tomas Radimersky, PRAC  
Rapporteur: Liana Gross-Martirosyan

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**Pregabalin Sandoz GmbH - pregabalin -****EMA/H/C/004070/R/0013**

Sandoz GmbH, Generic, Duplicate, Generic of  
Lyrica, Duplicate of Pregabalin Sandoz,  
Rapporteur: Tomas Radimersky, PRAC  
Rapporteur: Liana Gross-Martirosyan

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**Pregabalin Zentiva - pregabalin -****EMA/H/C/003900/R/0021**

Zentiva k.s., Generic, Generic of Lyrica,  
Rapporteur: Alar Irs, PRAC Rapporteur: Liana  
Gross-Martirosyan

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**Repatha - evolocumab -****EMA/H/C/003766/R/0040**

Amgen Europe B.V., Rapporteur: Johann  
Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC  
Rapporteur: Kimmo Jaakkola

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**Strensiq - asfotase alfa -****EMA/H/C/003794/R/0044, Orphan**

Alexion Europe SAS, Rapporteur: Daniela  
Melchiorri, Co-Rapporteur: Jayne Crowe, PRAC

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### **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**

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#### **CRYSVITA - burosumab -**

##### **EMA/H/C/004275/II/0010/G, Orphan**

Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of indication to include treatment of adults with X-linked hypophosphataemia (XLH), and modification of the currently approved indication in children and adolescents, by removing the qualification 'with growing skeletons', in order to include treatment in all children with radiographic evidence of bone disease.

The application provides new week-48 data from Study UX023-CL304; a randomized, double-blind, placebo-controlled, phase 3 study with open-label extension to assess the efficacy and safety of KRN23 in adults with XLH.

As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated and the Package Leaflet is updated in accordance.

Furthermore, the PI is brought in line with the latest QRD template version 10.1.

The updated RMP version 2.0 has also been submitted."

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#### **INTELENCE - etravirine -**

##### **EMA/H/C/000900/II/0058**

Janssen-Cilag International NV, Rapporteur: Jean-Michel Race, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Adrien Inoubli, "To extend the approved therapeutic indication of Intelence in order to include patient population from 2 to 6 years of age based on the 48 week study results from study TMC125-C234/P1090 (A Phase I/II, Open-label Trial to Evaluate the Safety, Tolerability, Pharmacokinetics and Antiviral Activity of Etravirine (ETR) in Antiretroviral (ARV) Treatment-experienced HIV-1 Infected Infants and Children, Aged ≥2 Months to <6 Years). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and sections 1, 2 and 3 of the PL are updated accordingly. The updated RMP version 13.1 has

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also been submitted.

The RMP (version 13.1) of the product has been updated to remove the completed additional pharmacovigilance activities (TMC125-C234/P1090 (Week 48) and TMC125-EPPICC) from the pharmacovigilance plan of the RMP). The RMP has also been updated to meet the requirements and updated definitions in the European Medicines Agency (EMA) Guideline on good pharmacovigilance practices (GVP) Module V Revision 2 (EMA/838713/2011; Rev 2) and Guidance on the format of the RMP in the European Union (EMA/164014/2018 Rev 2.0.1) including proposed removal of safety concerns. The MAH took the opportunity to include some typographic changes in Annex II C and D.”

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**Kalydeco - ivacaftor -**

**EMA/H/C/002494/II/0082, Orphan**

Vertex Pharmaceuticals (Ireland) Limited,  
Rapporteur: Maria Concepcion Prieto Yerro,  
PRAC Rapporteur: Maria del Pilar Rayon,  
“Extension of indication to include new population for Kalydeco 150 mg tablets to extend the use to patients with cystic fibrosis (CF) aged 6 years and older and weighing 25 kg or more who have an R117H mutation in the CFTR gene and for Kalydeco granules 75 mg and 50 mg, to add patients with CF aged 12 months and older and weighing 7 kg to less than 25 kg who have an R117H mutation in the CFTR gene. This is based on a clinical trial and literature data, and post-marketing experience with Kalydeco. As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 8.5 has also been submitted.”

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**Kineret - anakinra -**

**EMA/H/C/000363/II/0070**

Swedish Orphan Biovitrum AB (publ),  
Rapporteur: Mark Ainsworth, Co-Rapporteur:  
Fátima Ventura, PRAC Rapporteur: Hans  
Christian Siersted, “Extension of indication to include the treatment of Familial Mediterranean Fever (FMF) for Kineret, to be given in combination with colchicine, if appropriate; as a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 5.0 has also been submitted.”

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**Ruconest - conestat alfa -  
EMA/H/C/001223/II/0053/G**

Pharming Group N.V., Rapporteur: Andrea Laslop, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Jan Neuhauser, "Update of indication to include children in the treatment of acute angioedema attacks with hereditary angioedema

(HAE) due to C1 esterase inhibitor deficiency. This is based from Study C1 1209 in children. In addition final efficacy and safety data from the OLE phases of Studies C1 1304 and 1205 and the completed Study C1 1310 are submitted together with final study results of Studies C1 1207 and 3201, concerning prophylactic treatment of HAE patients. Consequently the product information has been updated.

Furthermore, the company is requesting an extension for the completion of registry Study C1 1412. The current RMP (V 18.0) states that completion of the final study report for Study C1 1412 is anticipated 31 March 2020.

Although patient enrolment has increased, the study will not be completed on time. The MAH would therefore like to request an extension of the study completion date to submit the final report date for Study C1 1412 of 30 June 2022. In addition the RMP has also been aligned to RMP template version 2.0.1. The product information has also been updated to align with the most recent QRD template, version 10.1."

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**Taltz - ixekizumab -  
EMA/H/C/003943/II/0031**

Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of indication to include the treatment of moderate to severe plaque psoriasis in children from the age of 6 years and adolescents who are candidates for systemic therapy for Taltz; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated with new safety and efficacy 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 RMP version 7.1 has also been submitted."



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**Tremfya - guselkumab -  
EMA/H/C/004271/II/0017**

Janssen-Cilag International N.V., Rapporteur:  
Melinda Sobor, Co-Rapporteur: Peter Kiely,  
PRAC Rapporteur: Brigitte Keller-Stanislawski,  
"Addition of a new indication for the treatment  
of active psoriatic arthritis in adult patients who  
have had an inadequate response or who have  
been intolerant to a prior disease-modifying  
antirheumatic drug (DMARD) therapy.  
Consequently sections 4.1, 4.2, 4.5, 4.8, 5.1  
and 5.2 of the SmPC are updated. The Package  
leaflet is updated accordingly.  
Additionally minor QRD changes are introduced  
in annex II."

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**WS1695  
Braftovi-EMA/H/C/004580/WS1695/  
0008  
Mektovi-EMA/H/C/004579/WS1695/  
0007**

Pierre Fabre Medicament, Lead Rapporteur:  
Janet Koenig, "Extension of indication to include  
encorafenib in combination with binimetinib and  
cetuximab, for the treatment of adult patients  
with metastatic colorectal cancer (CRC) with a  
BRAF V600E mutation, who have received prior  
systemic therapy, as a consequence, sections  
4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3 of the  
SmPC are updated. The Package Leaflet is  
updated in accordance. The RMP version 1.1 has  
also been submitted. Furthermore, the PI is  
brought in line with the latest QRD template  
version 10.1."  
Request for 1 year of market protection for a  
new indication (Article 14(11) of Regulation  
(EC) 726/2004)

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

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**Ruconest - conestat alfa -  
EMA/H/C/001223/II/0052**  
Pharming Group N.V, Rapporteur: Andrea Laslop

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

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

**B.6.11. PRAC assessed procedures**

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

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

**B.6.14. PRAC assessed ATMP procedures**

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

**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**

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

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

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

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

**G. ANNEX G**

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

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

**G.2. 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 11-14 November 2019 CHMP plenary:**

<i>Neurology</i>	
1. Treatment of Amyotrophic Lateral Sclerosis	The CHMP denied eligibility to PRIME and adopted the critical summary report.
2. (SME) Treatment of children with Rett Syndrome	The CHMP denied eligibility to PRIME and adopted the critical summary report.
3. (SME) Treatment of early Alzheimer's Disease	The CHMP denied eligibility to PRIME and adopted the critical summary report.
<i>Endocrinology-Gynaecology-Fertility-Metabolism</i>	
4. (SME) Treatment of Postbariatric Hypoglycemia	The CHMP denied eligibility to PRIME and adopted the critical summary report.
5. (SME) Treatment of inherited disorders of oxidative phosphorylation	The CHMP denied eligibility to PRIME and adopted the critical summary report.
<i>Oncology</i>	
6. <b>Autologous CD4+ and CD8+ T-cell populations transduced with a genetically-engineered replication-incompetent, self-inactivating lentiviral vector to express a BCMA-specific CAR (JCAR125);</b> ATMP; Treatment of relapsed / refractory multiple myeloma	The CHMP granted eligibility to PRIME <i>in the treatment of relapsed / refractory multiple myeloma whose prior therapies included autologous stem cell transplant if they were eligible, a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody</i> and adopted the critical summary report.
<i>Haematology - Hemostaseology</i>	
7. <b>Danicopan;</b> (SME); Treatment of paroxysmal nocturnal hemoglobinuria	The CHMP granted eligibility to PRIME <i>in the treatment of PNH patients who are not adequately responding to a C5 inhibitor</i> and adopted the critical summary report.
<i>Infectious diseases</i>	
8. (SME) Treatment of chronic Hepatitis D Virus Infection	The CHMP denied eligibility to PRIME and adopted the critical summary report.

**G.3.2. List of procedures starting in November 2019 for December 2019 CHMP adoption of outcomes**

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