



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

26 February 2021  
EMA/CHMP/81765/2021  
Human Medicines Division

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

Final Minutes for the meeting on 07-10 December 2020

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

### Disclaimers

Some of the information contained in these 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, these 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**

The participants had no objection to hold the meeting remotely.

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 December 2020 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 07–10 December 2020.

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. 16 or more members were present remotely). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

### **1.2. Adoption of agenda**

CHMP agenda for 7-10 December 2020

The CHMP adopted the agenda.

### **1.3. Adoption of the minutes**

ORGAM minutes from meeting held on 30 November 2020.

The CHMP adopted the ORGAM minutes from the meeting held on 30 November 2020.

CHMP minutes from meeting held on 12-15 October 2020.

CHMP minutes from meeting held on 09-12 November 2020.

The CHMP adopted the October and November minutes.



## 2. Oral Explanations

### 2.1. Pre-authorisation procedure oral explanations

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

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Karyopharm Europe GmbH; treatment of patients with Relapsed Refractory Multiple Myeloma (RRMM).

Scope: Oral explanation,

Draft list of experts for the SAG Oncology meeting scheduled on 30 November 2020 adopted via written procedure on 30 November 2020,

SAG report

**Action:** Oral explanation to be held on Tuesday, 8 December 2020 at 16:00

List of Outstanding Issues adopted on 15.10.2020. 30.01.2020, 19.09.2019. List of Questions adopted on 24.04.2019.

The CHMP noted the SAG report.

An oral explanation was held on Tuesday, 8 December 2020. The presentation by the applicant focused on the clinical data in support of the application.

See 3.2

#### 2.1.2. pemigatinib - Orphan - EMEA/H/C/005266

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Incyte Biosciences Distribution B.V.; treatment of locally advanced or metastatic cholangiocarcinoma.

Scope: Oral explanation,

Draft list of experts for the SAG Oncology meeting scheduled on 3 December 2020 adopted via written procedure by 3 December 2020,

SAG report

**Action:** Oral explanation to be held on Tuesday, 8 December 2020 at 11:00

List of Outstanding Issues adopted on 17.09.2020. List of Questions adopted on 30.04.2020.

The CHMP noted the SAG report.

An oral explanation was held on Tuesday, 8 December 2020. The presentation of the applicant focused on the clinical data in support of their application.

See 3.2

#### 2.1.3. ofatumumab - EMEA/H/C/005410

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treatment of relapsing forms of multiple sclerosis.

Scope: Oral explanation

**Action:** Oral explanation to be held on Wednesday, 9 December 2020 at 11:00

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 28.05.2020.

An oral explanation was held on Wednesday, 9 December 2020. The presentation of the applicant focused on the clinical data in support of their application.

See 3.2

## 2.2. Re-examination procedure oral explanations

No items

## 2.3. Post-authorisation procedure oral explanations

### 2.3.1. WS1844 Edistride - dapagliflozin - EMEA/H/C/004161/WS1844/0039 Forxiga - dapagliflozin - EMEA/H/C/002322/WS1844/0057

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Astra Zeneca AB

Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin

Scope: "Re-categorisation of the Forxiga/Edistride PASS (D169C00011): Retrospective Cohort Study on the Risk of Diabetic Ketoacidosis (DKA) to determine the effectiveness of additional risk minimisation measures in place for DKA by assessing the impact of the risk minimisation measures on the risk of DKA in T1DM patients who are treated with dapagliflozin in Europe, from a category 1 to category 3 PASS in the RMP Version 20 and removal of the following Annex IID of the PI: Obligation to conduct the following Non-interventional PASS: In order to estimate the incidence of DKA in T1DM dapagliflozin users following implementation of RMMs in Europe, the MAH should conduct and submit the results from an observational cohort study using existing data sources in European countries where dapagliflozin will be launched for T1DM",

Oral explanation

**Action:** Oral explanation to be held on Tuesday, 8 December 2020 at 14:00

Request for Supplementary Information adopted on 15.10.2020, 23.07.2020.

An oral explanation was held on Tuesday, 8 December 2020. The presentation by the applicant focused on effectiveness data of the risk minimisation measures.

See 9.1

## 2.4. Referral procedure oral explanations

No items

## 3. Initial applications

### 3.1. Initial applications; Opinions

#### 3.1.1. Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124

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Daiichi Sankyo Europe GmbH; treatment of unresectable or metastatic HER2-positive breast cancer.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 10.11.2020. List of Questions adopted on 15.09.2020.

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

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

Furthermore, the CHMP considered that trastuzumab deruxtecan 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 medical prescription.

The summary of opinion was circulated for information.

#### 3.1.2. Heplisav B - hepatitis B surface antigen - EMEA/H/C/005063

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Dynavax GmbH; prevention of hepatitis B virus infection.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 25.07.2019.

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 CHMP noted the letter of recommendations dated 30 November 2020.

The summary of opinion was circulated for information.

### 3.1.3. Inrebic - fedratinib - Orphan - EMEA/H/C/005026

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Celgene Europe BV; treatment of primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 28.05.2020.

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 fedratinib 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 1 December 2020.

The summary of opinion was circulated for information.

### 3.1.4. Kixelle - insulin aspart - EMEA/H/C/004965

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Mylan IRE Healthcare Limited; treatment of diabetes mellitus.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 27.02.2020.

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.

The CHMP adopted the similarity assessment report.

### 3.1.5. Lenalidomide Krka d.d. Novo mesto - lenalidomide - EMEA/H/C/005348

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Krka d.d. Novo mesto; treatment of multiple myeloma.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 28.05.2020.

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

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

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

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

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

### 3.1.6. Lenalidomide Krka - lenalidomide - EMEA/H/C/005734

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KRKA, d.d., Novo mesto; treatment of multiple myeloma and follicular lymphoma.

Scope: Opinion

**Action:** For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Revlimid, Duplicate of Lenalidomide Krka d.d. Novo mesto

List of Outstanding Issues adopted on 15.10.2020.

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

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

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

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

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

### 3.1.7. Lenalidomide Krka d.d. - lenalidomide - EMEA/H/C/005729

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KRKA, d.d., Novo mesto; treatment of multiple myeloma, myelodysplastic syndromes and follicular lymphoma.

Scope: Opinion

**Action:** For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Revlimid, Duplicate of Lenalidomide Krka d.d. Novo mesto

List of Outstanding Issues adopted on 15.10.2020.

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

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

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

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

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

### 3.1.8. Lumoxiti - moxetumomab pasudotox - Orphan - EMEA/H/C/005322

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AstraZeneca AB; relapsed or refractory hairy cell leukaemia (HCL) after receiving at least two prior systemic therapies.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 30.04.2020.

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 under exceptional circumstances by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that moxetumomab pasudotox 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 medical prescription.

The CHMP noted the letter or recommendations dated 15 December 2020.

The summary of opinion was circulated for information.

### 3.1.9. Ogluo - glucagon - EMEA/H/C/005391

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Xeris Pharmaceuticals Ireland Limited; treatment of severe hypoglycaemia in adults, adolescents and children aged 2 years and over, with diabetes mellitus.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 12.11.2020, 17.09.2020. List of Questions adopted on 30.04.2020.

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.

### 3.1.10. Rukobia - fostemsavir - EMEA/H/C/005011

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ViiV Healthcare B.V.; indicated, in combination with other antiretrovirals, for the treatment of adults with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral regimen.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 28.04.2020.

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 fostemsavir 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 27 November 2020.

The summary of opinion was circulated for information

### 3.1.11. Retsevmo - selpercatinib - EMEA/H/C/005375

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Eli Lilly Nederland B.V.; indicated as monotherapy for the treatment of adults with advanced RET fusion positive non small cell lung cancer (NSCLC) who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy, advanced RET fusion positive thyroid cancer who require systemic therapy following prior treatment with sorafenib and/or lenvatinib. As monotherapy is indicated for the treatment of adults and adolescents 12 years and older with advanced RET mutant medullary thyroid cancer (MTC) who require systemic therapy following prior treatment with cabozantinib and/or vandetanib.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 28.05.2020.

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

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

Furthermore, the CHMP considered that selpercatinib 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 December 2020.

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

### 3.1.12. Sibnaya - potassium - Orphan - EMEA/H/C/005407

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Advicenne S.A.; treatment of distal renal tubular acidosis (dRTA) in patients aged 6 months and older.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 26.03.2020.

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

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



The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.  
The legal status was agreed as medicinal product subject to medical prescription.  
The summary of opinion was circulated for information.

#### 3.1.13. Sunitinib Accord - sunitinib - EMEA/H/C/005419

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Accord Healthcare S.L.U.; treatment of gastrointestinal stromal tumour (GIST) and metastatic renal cell carcinoma (MRCC) and pancreatic neuroendocrine tumours (pNET).

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 27.02.2020.

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

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

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

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

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

#### 3.1.14. Tukysa - tucatinib - EMEA/H/C/005263

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Seagen B.V.; treatment of metastatic breast cancer or brain metastases.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 28.05.2020.

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 tucatinib 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 09 December 2020.

The summary of opinion was circulated for information.

### 3.1.15. Yuflyma - adalimumab - EMEA/H/C/005188

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Celltrion Healthcare Hungary Kft.; treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, juvenile idiopathic arthritis, enthesitis-related arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa (HS), Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis, paediatric uveitis.

Scope: Opinion

**Action:** For adoption

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

List of Outstanding Issues adopted on 12.11.2020. List of Questions adopted on 23.07.2020.

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

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

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

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

The CHMP noted the letter of recommendation dated 07 December 2020.

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. idecabtagene vicleucel - Orphan - ATMP - EMEA/H/C/004662

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#### **Accelerated assessment**

Celgene Europe BV; treatment of multiple myeloma.

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 11.09.2020.

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

The Committee endorsed the list of outstanding issues with a specific timetable as adopted by the CAT.

### 3.2.2. bevacizumab - EMEA/H/C/005327

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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 outstanding issues

**Action:** For adoption

List of Questions adopted on 23.07.2020.

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. bevacizumab - EMEA/H/C/005286

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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 outstanding issues

**Action:** For adoption

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 28.05.2020.

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.

### 3.2.4. bevacizumab - EMEA/H/C/005611

---

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 outstanding issues

**Action:** For adoption

List of Questions adopted on 23.07.2020.

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. [remimazolam - EMEA/H/C/005246](#)

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indicated for procedural sedation.

Scope: List of outstanding issues

**Action:** For adoption

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 30.04.2020.

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.

### 3.2.6. [cenobamate - EMEA/H/C/005377](#)

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for the adjunctive treatment of focal onset seizures with or without secondary generalisation in adult patients with epilepsy who have not been adequately controlled despite a history of treatment with at least 2 anti-epileptic products.

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 23.07.2020.

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. [duvelisib - Orphan - EMEA/H/C/005381](#)

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Verastem Europe GmbH; treatment of adult patients with relapsed or refractory chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL) and relapsed or refractory follicular lymphoma (FL).

Scope: List of outstanding issues

**Action:** For adoption

List of Outstanding Issues adopted 17.09.2020. List of Questions adopted on 30.04.2020.

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.

### 3.2.8. [dostarlimab - EMEA/H/C/005204](#)

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treatment of mismatch repair deficient (dMMR)/ microsatellite instability-high (MSI-H)

endometrial cancer (EC).

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 23.06.2020.

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.

### 3.2.9. ofatumumab - EMEA/H/C/005410

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treatment of relapsing forms of multiple sclerosis.

Scope: Oral explanation, list of outstanding issues

**Action:** For adoption

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 28.05.2020.

See 2.1

An oral explanation was held on Wednesday, 9 December 2020. The presentation of the applicant focused on the clinical data in support of their application.

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

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

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Karyopharm Europe GmbH; treatment of patients with Relapsed Refractory Multiple Myeloma (RRMM).

Scope: Oral explanation, list of outstanding issues,

Draft list of experts for the SAG Oncology meeting scheduled on 30 November 2020 adopted via written procedure on 30 November 2020,

SAG report

**Action:** Oral explanation to be held on Tuesday, 8 December 2020 at 16:00

List of Outstanding Issues adopted on 15.10.2020, 30.01.2020, 19.09.2019. List of Questions adopted on 24.04.2019.

The CHMP noted the SAG report.

See 2.1

An oral explanation was held on Tuesday, 8 December 2020. The presentation by the applicant focused on the clinical data in support of the application.

The Committee adopted a 4<sup>th</sup> list of outstanding issues with a specific timetable.

### 3.2.11. berotralstat - Orphan - EMEA/H/C/005138

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BioCryst Ireland Limited; prevention of hereditary angioedema (HAE).

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 23.07.2020.

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.

### 3.2.12. bevacizumab - EMEA/H/C/005556

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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 outstanding issues

**Action:** For adoption

List of Outstanding Issues adopted on 15.10.2020. List of Questions adopted on 28.05.2020.

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.

### 3.2.13. pitolisant - EMEA/H/C/005117

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treatment of excessive day time sleepiness (EDS) in patients with obstructive sleep apnoea (OSA).

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 25.06.2020.

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.

### 3.2.14. pemigatinib - Orphan - EMEA/H/C/005266

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Incyte Biosciences Distribution B.V.; treatment of locally advanced or metastatic cholangiocarcinoma.

Scope: Oral explanation, list of outstanding issues,

Draft list of experts for the SAG Oncology meeting scheduled on 3 December 2020 adopted via written procedure by 3 December 2020,

SAG report

**Action:** Oral explanation to be held on Tuesday, 8 December 2020 at 11:00

List of Outstanding Issues adopted on 17.09.2020. List of Questions adopted on 30.04.2020.

The CHMP noted the SAG report.

See 2.1

An oral explanation was held on Tuesday, 8 December 2020. The presentation of the applicant focused on the clinical data in support of their application.

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

### 3.2.15. [sildenafil - EMEA/H/C/005439](#)

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treatment of erectile dysfunction.

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 25.06.2020.

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.

### 3.2.16. [thiotepa - EMEA/H/C/005434](#)

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conditioning treatment prior to haematopoietic progenitor cell transplantation (HPCT), treatment of solid tumours.

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 17.09.2020.

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.

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

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

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 19.09.2019.

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.

### 3.2.18. icosapent ethyl - EMEA/H/C/005398

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indicated to reduce cardiovascular risk as an adjunct to statin therapy.

Scope: List of outstanding issues

**Action:** For adoption

List of Outstanding Issues adopted on 17.09.2020. List of Questions adopted on 26.03.2020.

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.

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

### 3.3.1. bimekizumab - EMEA/H/C/005316

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treatment of plaque psoriasis.

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. evinacumab - EMEA/H/C/005449

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#### **Accelerated assessment**

treatment of homozygous familial hypercholesterolemia (HoFH).

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. icatibant - EMEA/H/C/005083

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treatment of hereditary angioedema.

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. glucarpidase - Orphan - EMEA/H/C/005467**

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Protherics Medicines Development Europe B.V.; treatment of patients at risk of methotrexate toxicity.

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. vosoritide - Orphan - EMEA/H/C/005475**

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BioMarin International Limited; indicated for the treatment of achondroplasia.

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. risperidone- EMEA/H/C/005406**

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treatment of schizophrenia.

Scope: Letter from the applicant dated 4 December 2020 requesting an extension of clock-stop to respond to the list of outstanding issues adopted in October 2020.

**Action:** For adoption

List of outstanding issues adopted on 15.10.2020. List of questions adopted on 28.05.2020.

The CHMP agreed to the request by the applicant for an extension of clock-stop to respond to the list of outstanding issues adopted in October 2020.

#### **3.4.2. sugammadex - EMEA/H/C/005403**

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treatment of neuromuscular blockade induced by rocuronium or vecuronium.

Scope: Letter from the applicant dated 3 December 2020 requesting an extension of clock-stop to respond to the list of questions adopted in September 2020.

**Action:** For adoption

List of questions adopted on 17.09.2020.

The CHMP agreed to the request by the applicant for an extension of clock-stop to respond

to the list of questions adopted in September 2020.

#### **3.4.3. COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735**

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Active immunization against COVID-19 disease.

Scope: Update on procedure

**Action:** For information

See also 15.1

The CHMP noted the update on the procedure.

#### **3.4.4. sodium thiosulfate - PUMA - EMEA/H/C/005130**

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for the prevention of ototoxicity induced by cisplatin (CIS) chemotherapy in patients 1 month to < 18 years of age with localized, non-metastatic, solid tumours.

Scope: Request by the applicant for an extension to the clock stop to respond to the list of questions adopted in June 2020.

**Action:** For adoption

List of Questions adopted on 25.06.2020.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in June 2020.

#### **3.4.5. setmelanotide - Orphan - EMEA/H/C/005089**

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TMC Pharma (EU) Limited; Treatment of obesity and the control of hunger associated with deficiencies in the leptin-melanocortin pathway

Scope: Request by the applicant for an extension to the clock stop to respond to the list of questions adopted in October 2020.

**Action:** For adoption

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

List of Questions adopted on 13.10.2020

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in October 2020.

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

No items

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

No items

### 3.7. Withdrawals of initial marketing authorisation application

#### 3.7.1. Artobend - autologous human chondrocytes *in vitro* expanded - ATMP - EMEA/H/C/004598

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Tetec Tissue Engineering Technologies AG; repair of cartilage defects of the knee joint.

Scope: Withdrawal of initial marketing authorisation application

**Action:** For information

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

The CHMP noted the withdrawal of initial 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. Xerava - eravacycline - EMEA/H/C/004237/X/0009

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Tetraphase Pharmaceuticals Ireland Limited

Rapporteur: Filip Josephson, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension application to add a new strength of 100 mg for eravacycline powder for concentrate for solution for infusion. The RMP version 3.1 is approved with this procedure. Additionally, the marketing authorisation holder took the opportunity to align the PI with the latest QRD template."

**Action:** For adoption

List of Questions adopted on 17.09.2020.

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. Sirturo - bedaquiline - Orphan - EMEA/H/C/002614/X/0036/G

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Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength (20 mg tablets) grouped with a Type II variation (C.I.6) to extend the existing Sirturo indication to include paediatric patients aged from 5 years to less than 18 years of age and weighing more than 15 kg, based on the results of the week 24 analysis of Cohort 2 (paediatric subjects aged  $\geq 5$  to  $<12$  years) of study TMC207-C211. Sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 and the product leaflet are updated to support the extended indication. The RMP (version 4.4) is updated in accordance."

**Action:** For adoption

List of Outstanding Issues adopted on 17.09.2020. List of Questions adopted on 30.04.2020.

The Committee discussed the issues identified in this application, mainly concerning the possible need for a bioequivalence study in fed state for the interchangeability of one tablet of 100 mg versus five tablets of 20 mg each. It was agreed to consult the PKWP on this question.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of outstanding issues and a specific timetable.

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

#### 4.2.2. [Trimbow - beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004257/X/0012](#)

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Chiesi Farmaceutici S.p.A.

Rapporteur: Janet Koenig, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Jan Neuhauser

Scope: "Extension application to add a new pharmaceutical form (inhalation powder) associated with new strength (88  $\mu\text{g}$  / 5  $\mu\text{g}$  / 9  $\mu\text{g}$ ). The RMP (version 6.2) is updated in accordance."

**Action:** For adoption

List of Questions adopted on 23.07.2020.

The Committee discussed the issues identified in this application, concerning the quality part and SmPC wording.

The Committee adopted the CHMP recommendation and scientific discussion together with the 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. [Deltiba - delamanid - Orphan - EMEA/H/C/002552/X/0046/G](#)

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Otsuka Novel Products GmbH

Rapporteur: Christophe Focke, PRAC Rapporteur: Laurence de Fays

Scope: "Extension application to introduce a new pharmaceutical form (dispersible tablets)

associated with a new strength (25 mg), grouped with a Type II extension of indication variation (C.I.6.a) to include the treatment of children of at least 10 kg of body weight for the approved Delyba 50 mg film-coated tablets. As a consequence, sections 3, 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and labelling are updated accordingly. Version 3.3 of the RMP has also been submitted and Annex II is updated to remove the specific obligation related to an *in vitro* study using the HFS-TB model.”

**Action:** For adoption

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

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

#### 4.3.2. [Insulin aspart Sanofi - insulin aspart - EMEA/H/C/005033/X/0003](#)

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sanofi-aventis groupe

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Annika Folin

to introduce a new route of administration, intravenous use, for the 10 ml vial presentations only.”

**Action:** For adoption

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

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

#### 4.3.3. [Skyrizi - risankizumab - EMEA/H/C/004759/X/0012](#)

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AbbVie Deutschland GmbH & Co. KG

Rapporteur: Peter Kiely, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: “Extension application to add a new strength of 150 mg for solution for injection in a pre-filled syringe and pre-filled pen.”

**Action:** For adoption

The Committee discussed the issues identified in this application, relating to the quality and clinical part as well as 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. Diacomit - stiripentol - EMEA/H/C/000664/X/0032

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BIOCODEX

Rapporteur: Alar Irs, PRAC Rapporteur: Maia Uusküla

Scope: "Extension application to add a new strength of 100 mg capsules. The RMP (version 2.0) is updated in accordance."

Letter from the MAH dated 26 November 2020 requesting an extension of clock-stop to respond to the list of outstanding issues adopted in November 2020.

**Action:** For adoption

List of Outstanding Issues adopted on 12.11.2020. List of Questions adopted on 25.06.2020.

The CHMP agreed to the request by the MAH for an extension of clock-stop to respond to the list of outstanding issues adopted in November 2020.

### 4.4.2. Lacosamide Accord - lacosamide - EMEA/H/C/004443/X/0007

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Accord Healthcare S.L.U.

Rapporteur: John Joseph Borg, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to introduce a new pharmaceutical form (solution for infusion), a new strength (10 mg/ml) and a new route of administration (intravenous use)."

Request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted in November 2020.

**Action:** For adoption

List of Outstanding Issues adopted on 12.11.2020. List of Questions adopted on 26.03.2020.

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 in November 2020.

### 4.4.3. Pradaxa - dabigatran etexilate - EMEA/H/C/000829/X/0122/G

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Boehringer Ingelheim International GmbH

Rapporteur: Kirstine Moll Harboe, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Anette Kirstine Stark

Scope: "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 took the opportunity to update the list of local representatives in the package leaflet. The RMP 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)”

Final letter of recommendations dated 11.12.2020

**Action:** For information

Opinion adopted on 12.11.2020. List of Outstanding Issues adopted on 15.10.2020, 23.07.2020. List of Questions adopted on 27.02.2020.

The CHMP noted the final letter of recommendations.

#### **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. Bavencio - avelumab - EMEA/H/C/004338/II/0018**

Merck Europe B.V.

Rapporteur: Filip Josephson, PRAC Rapporteur: Hans Christian Siersted

Scope: “Extension of indication to include a new indication for Bavencio in the treatment as monotherapy for the first-line maintenance treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) whose disease has not progressed with first-line platinum-based induction chemotherapy. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 2.3 of the RMP has also been submitted. The marketing authorisation holder took also the occasion to include some editorial changes in the PI.”, 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 17.09.2020.

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.

#### 5.1.2. Cabometyx - cabozantinib - EMEA/H/C/004163/II/0017

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Ipsen Pharma

Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include in combination with nivolumab first line treatment of advanced renal cell carcinoma for Cabometyx. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 5.0 of the RMP has also been submitted."

**Action:** For adoption

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

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

#### 5.1.3. Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0011

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Sanofi Pasteur

Rapporteur: Christophe Focke

Scope: "To modify the approved therapeutic indication to include conditions for the eligibility to pre-vaccination serostatus screening. As a consequence, sections 4.1, 4.2 and 4.4 of the SmPC and sections 1, 2 and 3 of the package leaflet are updated accordingly."

**Action:** For adoption

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

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

#### 5.1.4. Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0012

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Sanofi Pasteur

Rapporteur: Christophe Focke

Scope: "Extension of indication to include paediatric population from 6 years of age for Dengvaxia. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC and sections 1, 2



and 4 of the package leaflet are updated. Furthermore, the marketing authorisation holder takes the opportunity to add an instruction for the installation of the needle in the SmPC and the package leaflet of the single-dose presentation.”

**Action:** For adoption

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

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

#### 5.1.5. [Doptelet - avatrombopag - EMEA/H/C/004722/II/0004/G](#)

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Swedish Orphan Biovitrum AB (publ)

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Eva A. Segovia

Scope: “Extension of indication to include the treatment of chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments. Consequently, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. Additionally, the SmPC section 5.3 is updated with data from juvenile toxicity studies. Furthermore, an additional pack size of 30 tablets has been introduced with subsequent updates of sections 6.5 and 8.0 of the SmPC. The package leaflet and labelling are updated in accordance. Version 2.1 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.1.”

**Action:** For adoption

Request for Supplementary Information adopted on 12.11.2020, 17.09.2020, 28.05.2020.

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 CHMP noted the letter of recommendations dated 08 December 2020.

The summary of opinion was circulated for information.

#### 5.1.6. [Evotaz - atazanavir / cobicistat - EMEA/H/C/003904/II/0038](#)

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Bristol-Myers Squibb Pharma EEIG

Rapporteur: Bruno Sepodes, PRAC Rapporteur: Adrien Inoubli

Scope: “Extension of indication to include the use of Evotaz in combination with other antiretroviral agents in the treatment of HIV-1 infection in adolescent patients aged  $\geq 12$  to  $< 18$  years, weighing  $\geq 35$  kg without known mutations associated with resistance to atazanavir. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 8.0 of the RMP has also been submitted. In addition, the marketing authorisation holder took the opportunity to make minor editorial corrections.”

**Action:** For adoption

The Committee discussed the issues identified in this application, relating to clinical aspects.  
The Committee adopted a request for supplementary information with a specific timetable.

#### 5.1.7. Kaftrio - ivacaftor / tezacaftor / elexacaftor - Orphan - EMEA/H/C/005269/II/0001

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Martin Huber

Scope: "Extension of indication of Kaftrio to patients with CF aged 12 years and older who have at least one F508del mutation in the CFTR gene, regardless of the second allele (F/any). Efficacy data are summarised from study 104, which was conducted in subjects heterozygous for F508del and a gating (G) or residual function (RF) mutation (F/G and F/RF genotypes). As a consequence, update of SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 are requested. Package leaflet is updated accordingly. The RMP is updated version 1.1."

**Action:** For adoption

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

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

#### 5.1.8. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0089

Vertex Pharmaceuticals (Ireland) Limited

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

Scope: "Extension of indication to extend the indication of Kalydeco (ivacaftor) tablets in combination regimen with Kaftrio (ivacaftor/tezacaftor/elexacaftor) tablets for the treatment of adults and adolescents aged 12 years and older with cystic fibrosis (CF) who have at least one F508del mutation in the CFTR gene. As a consequence, sections 4.1, 5.1, and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 9.2 of the RMP has also been submitted."

**Action:** For adoption

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

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

#### 5.1.9. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0090

Merck Sharp & Dohme B.V.

Rapporteur: Armando Genazzani, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of the currently approved therapeutic indication for the treatment of relapsed or refractory classical Hodgkin lymphoma (rrcHL) in adults to an earlier line of therapy and to include paediatric patients - as follows:

Keytruda as monotherapy is indicated for the treatment of adult and paediatric patients

aged 3 years and older with relapsed or refractory classical Hodgkin lymphoma (cHL) who have failed autologous stem cell transplant (ASCT) following at least one prior therapy when ASCT is not a treatment option.

The indication is based on the study KEYNOTE-204, a randomized, open-label, Phase 3 trial evaluating Keytruda monotherapy versus Brentuximab Vedotin (BV) for the treatment of patients with rrCHL and supportive data from updated analysis of KEYNOTE-087, which was the pivotal study supporting the initial rrCHL indication."

**Action:** For adoption

Request for Supplementary Information adopted on 17.09.2020.

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

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

#### 5.1.10. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0091

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Merck Sharp & Dohme B.V.

Rapporteur: Armando Genazzani, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: "C.I.6 -Extension of indication to include first-line treatment of metastatic microsatellite instability-high (MSI H) or mismatch repair deficient (dMMR) colorectal cancer in adults for Keytruda based on the results from KEYNOTE-177 (an international, randomised, open-label Phase 3 trial of pembrolizumab versus chemotherapy in MSI-H or dMMR Stage IV Colorectal Carcinoma). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, a minor correction has been made in section 4.4, "Immune related endocrinopathies" subsection. Version 29.0 of the RMP has also been submitted."

**Action:** For adoption

Request for Supplementary Information adopted on 15.10.2020.

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.

#### 5.1.11. Libtayo - cemiplimab - EMEA/H/C/004844/II/0011

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Regeneron Ireland Designated Activity Company (DAC)

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Johanna Lähteenvuo, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication for Libtayo as monotherapy indicated for the first-line treatment of adult patients with non-small cell lung cancer (NSCLC) expressing PD-L1 (in ≥

50% tumor cells), with no EGFR, ALK or ROS1 aberrations, who have:

- locally advanced NSCLC and who are not candidates for surgical resection or definitive chemoradiation, or have progressed after treatment with definitive chemoradiation, or
- metastatic NSCLC.

The package leaflet is revised accordingly. A revised RMP is submitted.”, 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, relating to clinical aspects and the request for 1 year of market protection.

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

#### 5.1.12. Libtayo - cemiplimab - EMEA/H/C/004844/II/0012

Regeneron Ireland Designated Activity Company (DAC)

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Johanna Lähteenvuo, PRAC Rapporteur: Menno van der Elst

Scope: “Extension of indication to include: Libtayo as monotherapy is indicated for the treatment of adult patients with locally advanced basal cell carcinoma (BCC) previously treated with a hedgehog pathway inhibitor. SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 have been revised. The package leaflet has been updated accordingly. A revised RMP has been submitted.”, 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 relating to clinical aspects and the request for 1 year of market protection.

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

#### 5.1.13. Nordimet - methotrexate - EMEA/H/C/003983/II/0016

Nordic Group B.V.

Rapporteur: Bruno Sepodes, PRAC Rapporteur: Martin Huber

Scope: “Extension of indication to include the new indication “Induction of remission in moderate steroid-dependent Crohn's disease in adult patients, in combination with corticosteroids and for maintenance of remission, as monotherapy, in patients who have responded to methotrexate” for Nordimet; 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 5.3 has been adopted. The MAH took the opportunity to update the RMP with changes related to GVP V version 2 template and the outcome of MTX referral.”

**Action:** For adoption

Request for Supplementary Information adopted on 17.09.2020, 30.04.2020.

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.

#### 5.1.14. Nplate - romiplostim - EMEA/H/C/000942/II/0077

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Amgen Europe B.V.

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

Scope: "Extension of indication to add the use of romiplostim in adult patients who have had ITP for  $\leq 12$  months and who have had an insufficient response to corticosteroids or immunoglobulins. Sections 4.1, 4.4., 4.8, 5.1 and 5.2 of the SmPC have been updated. In addition, the marketing authorisation holder has taken the opportunity to implement minor editorial changes in sections 4.2, 4.4, 4.8 and 5.1 of the SmPC. Furthermore, the PI is being brought in line with the latest QRD template (version 10.1). The package leaflet has been updated accordingly. The updated RMP version 20.0 has also been submitted."

**Action:** For adoption

Request for Supplementary Information adopted on 17.09.2020.

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.

#### 5.1.15. Opdivo - nivolumab - EMEA/H/C/003985/II/0092

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Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of indication to include in combination with cabozantinib for the first-line treatment of advanced renal cell carcinoma for Opdivo. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 19.0 of the RMP has also been submitted."

**Action:** For adoption

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

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

#### 5.1.16. Rinvoq - upadacitinib - EMEA/H/C/004760/II/0004

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AbbVie Deutschland GmbH & Co. KG

Rapporteur: Kristina Dunder, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include the treatment of active psoriatic arthritis in adult patients for Rinvoq; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Minor updates were made to the Annex II. Version 2.3 of the RMP has been adopted."

**Action:** For adoption

Request for Supplementary Information adopted on 17.09.2020.

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.

#### 5.1.17. Rinvoq - upadacitinib - EMEA/H/C/004760/II/0005

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AbbVie Deutschland GmbH & Co. KG

Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include the treatment of active ankylosing spondylitis in adult patients for Rinvoq; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Minor editorial changes to the SmPC and Annex II are also agreed. Version 3.3 of the RMP has been adopted."

**Action:** For adoption

Request for Supplementary Information adopted on 17.09.2020.

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.

#### 5.1.18. Sarclisa - isatuximab - Orphan - EMEA/H/C/004977/II/0003

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sanofi-aventis groupe

Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Eva A. Segovia

Scope: "An extension of indication for Sarclisa to add combination with carfilzomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy. As a consequence, the sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 have been updated. The package leaflet is updated accordingly. The marketing authorisation holder took the opportunity to introduce minor changes in the SmPC sections 4.9, 6.3 and 6.6 and update the details of local representatives. Revised RMP version 1 has been submitted."

**Action:** For adoption

The Committee discussed the issues identified in this application, concerning clinical aspects and the RMP.

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

#### 5.1.19. Spravato - esketamine - EMEA/H/C/004535/II/0001/G

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Janssen-Cilag International N.V.

Rapporteur: Martina Weise, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kirsti Villikka

Scope: "C.I.6(a): Extension of indication to include a new indication for Spravato for the rapid reduction of depressive symptoms in adult patients with a moderate to severe depressive episode of MDD who have current suicidal ideation with intent.

As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 the SmPC are updated. The RMP version 2.1 has also been submitted.

B.II.e.5.a.2: addition of a new pack size corresponding to 4 weeks of treatment in the new indication. The package leaflet and labelling are updated in accordance. In addition, the marketing authorisation holder took the opportunity to clarify the wording in Annex II.D."

**Action:** For adoption

Request for Supplementary Information adopted on 15.10.2020, 30.04.2020.

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.

#### 5.1.20. Tagrisso - osimertinib - EMEA/H/C/004124/II/0039/G

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AstraZeneca AB

Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication of Tagrisso to include the adjuvant treatment after complete tumour resection in EGFR mutant non-small cell lung cancer (NSCLC) patients, based on the results from the pivotal Phase 3 randomised, placebo-controlled study ADAURA

(D5164C00001). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.3 of the SmPC are updated. The package leaflet is updated accordingly. Version 14.1 of the RMP has also been submitted.”

**Action:** For adoption

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

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

#### 5.1.21. [Tecentriq - atezolizumab - EMEA/H/C/004143/II/0042](#)

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Roche Registration GmbH

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

Scope: “Extension of indication to include, in combination with platinum-based chemotherapy, first-line treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) for Tecentriq. As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. Version 14.0 of the RMP has also been submitted.”

**Action:** For adoption

Request for Supplementary Information adopted on 25.06.2020.

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

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

#### 5.1.22. [WS1769](#) [Iscover - clopidogrel - EMEA/H/C/000175/WS1769/0140](#) [Plavix - clopidogrel - EMEA/H/C/000174/WS1769/0138](#)

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sanofi-aventis groupe

Lead Rapporteur: Bruno Sepodes, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: “Extension of indication in combination with aspirin to include adult patients with moderate to high risk Transient Ischemic Attack (TIA) (ABCD2 score  $\geq 4$ ) or minor Ischemic Stroke (IS) (NIHSS  $\leq 3$ ) within 24 hours of either the TIA or IS event for Iscover and Plavix. The new indication is based on the results of two double-blind, randomised, placebo-controlled phase III trials (studies POINT & CHANCE); as a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated, the PL is updated accordingly. Version 2.3 of the RMP has also been submitted.”

**Action:** For adoption

Request for Supplementary Information adopted on 17.09.2020, 30.04.2020.

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.

5.1.23. [WS1881](#)  
[Opdivo - nivolumab - EMEA/H/C/003985/WS1881/0091](#)  
[Yervoy - ipilimumab - EMEA/H/C/002213/WS1881/0085](#)

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Bristol-Myers Squibb Pharma EEIG

Lead Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include first-line treatment of adult patients with unresectable malignant pleural mesothelioma (MPM) for Opdivo in combination with Yervoy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 20.0 for Opdivo and version 30.0 for Yervoy of the RMP has also been submitted."

**Action:** For adoption

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

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

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

5.2.1. [Xtandi - enzalutamide - EMEA/H/C/002639/II/0047/G](#)

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Astellas Pharma Europe B.V.

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

Scope: "C.1.6: Extension of indication to include the treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) for Xtandi in combination with androgen deprivation therapy; As a consequence, sections 4.1, 4.7, 4.8, 5.1, 5.3 and 6.6 of the SmPC are updated. Furthermore the MAH took the opportunity to make corrections to section 4.7. The Package Leaflet is updated in accordance. The RMP version 13.0 has also been submitted.

C.1.4: Update of section 5.1 of the SmPC based the 5-year Overall Survival (OS) results obtained from the PREVAIL study (MDV310003), a phase 3 study of enzalutamide in chemotherapy naïve patients with metastatic prostate cancer that progressed on ADT."

Request by the applicant for an extension to the clock stop to respond to the Request for Supplementary Information adopted on 28.05.2020.

**Action:** For adoption

Request for Supplementary Information adopted on 28.05.2020, 17.10.2019.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the Request for Supplementary Information adopted on 28.05.2020.

### **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. amivantamab - H0005454**

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indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal-growth factor receptor (EGFR) exon 20 insertion mutations, after failure of platinum-based chemotherapy.

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

**Action:** For adoption

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

## 8.2. Priority Medicines (PRIME)

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

### 8.2.1. List of applications received

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**Action:** For information

The CHMP noted the information.

### 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 3 recommendations for eligibility to PRIME: 1 was accepted and 2 were denied.

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

## 9. Post-authorisation issues

### 9.1. Post-authorisation issues

#### 9.1.1. Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0013

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Sanofi Pasteur

Rapporteur: Christophe Focke

Scope: "To update sections 4.2, 4.8 and 5.1 of the SmPC in order to introduce a new posology regimen from 3 doses to 2 doses for individuals from 9 years of age based on interim results from study CYD65 listed as a category 3 study in the RMP. This is a Phase II, observer-blind, placebo-controlled trial in order to assess immunogenicity and safety of tetravalent dengue vaccine given in 1-, 2-, or 3-dose schedules followed by a single booster; section 3 of the package leaflet is updated accordingly."

**Action:** For adoption

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

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

#### 9.1.2. Halimatoz - adalimumab - EMEA/H/C/04866

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Sandoz GmbH

Rapporteur: Milena Stain, Co-Rapporteur: Peter Kiely

Scope: Withdrawal of marketing authorisation

**Action:** For information

The CHMP noted the withdrawal of marketing authorisation.

9.1.3. [Hexaxim - diphtheria, tetanus, pertussis \(acellular, component\), hepatitis b \(rdna\), poliomyelitis \(inactivated\) and haemophilus influenzae type b conjugate vaccine \(adsorbed\) - EMEA/H/W/002495](#)

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Sanofi Pasteur

Rapporteur: Jan Mueller-Berghaus

Scope: Stop of the maintenance of the scientific opinion under Article 58 of Hexaxim, suspension for injection

**Action:** For information

The CHMP noted the stop of the maintenance of the scientific opinion under Article 58 of Hexaxim, suspension for injection.

9.1.4. [Prepandrix - split influenza virus inactivated - EMEA/H/C/0822](#)

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GlaxoSmithkline Biologicals SA

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Jan Mueller-Berghaus

Scope: Withdrawal of marketing authorisation

**Action:** For information

The CHMP noted the withdrawal of marketing authorisation.

9.1.5. [Remsima - infliximab - EMEA/H/C/002576/II/0095](#)

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Celltrion Healthcare Hungary Kft.

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Addition of a new posology for the rheumatoid arthritis indication that does not include IV induction doses."

**Action:** For adoption

The Committee discussed the issues identified in this application, concerning clinical aspects.

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

9.1.6. [Truberzi - eluxadoline - EMEA/H/C/4098](#)

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Allergan Pharmaceuticals International Limited

Rapporteur: Martina Weise, Co-Rapporteur: Johann Lodewijk Hillege

Scope: Withdrawal of marketing authorisation

**Action:** For information

The CHMP noted the withdrawal of marketing authorisation.

#### 9.1.7. [Veklury - remdesivir - EMEA/H/C/005622/II/0012](#)

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Gilead Sciences Ireland UC

Rapporteur: Janet Koenig, Co-Rapporteur: Filip Josephson

Scope: "Submission of the final D28 mortality data by ordinal scale categories of study COUS-540-5776 (NIAID-ACTT1), listed as a specific obligation in the Annex II of the product information, in order to confirm the efficacy and safety of remdesivir in patients on invasive mechanical ventilation and extracorporeal membrane oxygenation (IMV/ECMO). In addition, the marketing authorisation holder discuss the potential imbalance in the use of corticosteroids and effect modification in study CO-US-540-5776. As a consequence, Annex II is updated accordingly."

**Action:** For adoption

Request for supplementary information adopted on 12.11.2020.

The CHMP adopted a positive opinion by consensus recommending a change to the terms of the marketing authorisation for the medicinal product Veklury.

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

The summary of opinion was circulated for information.

#### 9.1.8. [WS1844](#) [Edistride - dapagliflozin - EMEA/H/C/004161/WS1844/0039](#) [Forxiga - dapagliflozin - EMEA/H/C/002322/WS1844/0057](#)

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Astra Zeneca AB

Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin

Scope: "Re-categorisation of the Forxiga/Edistride PASS (D169C00011): Retrospective Cohort Study on the Risk of Diabetic Ketoacidosis (DKA) to determine the effectiveness of additional risk minimisation measures in place for DKA by assessing the impact of the risk minimisation measures on the risk of DKA in T1DM patients who are treated with dapagliflozin in Europe, from a category 1 to category 3 PASS in the RMP Version 20 and removal of the following Annex IID of the PI: Obligation to conduct the following Non-interventional PASS: In order to estimate the incidence of DKA in T1DM dapagliflozin users following implementation of RMMs in Europe, the MAH should conduct and submit the results from an observational cohort study using existing data sources in European countries where dapagliflozin will be launched for T1DM",

Oral explanation

**Action:** For adoption

Request for Supplementary Information adopted on 15.10.2020, 23.07.2020.

See 2.3

An oral explanation was held on Tuesday, 8 December 2020. The presentation by the applicant focused on effectiveness data of the risk minimisation measures.

The CHMP further discussed the presented data.

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

#### 9.1.9. [Xeljanz - tofacitinib - EMEA/H/C/004214/II/0027](#)

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Pfizer Europe MA EEIG

Rapporteur: Armando Genazzani, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Update of sections 4.1, 4.2, 4.4 , 4.8, 5.1 and 5.2 of Xeljanz 11 mg prolonged-release tablets SmPC in order to include the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior disease modifying antirheumatic drug therapy. As an alternative to the immediate release film-coated tablets section 4.2 of Xeljanz film-coated tablets is also updated to include switching with the prolonged-release tablet in the treatment of PsA. The package leaflet is updated accordingly. The RMP version 13.1 has also been submitted."

**Action:** For adoption

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

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

## 10. Referral procedures

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

No items

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

#### 10.2.1. [Presence of nitrosamine impurities in human medicinal products containing chemically synthesised active pharmaceutical ingredients EMEA/H/A-5\(3\)/1490](#)

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MAHs: various

Referral Rapporteur: Martina Weise, Referral Co-Rapporteur: Kristina Dunder

Scope: Letter from third parties

**Action:** For adoption

The CHMP noted the letter from third parties and adopted the response.

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

No items

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

No items

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

#### **10.5.1. Varilrix - EMEA/H/A-30/1499**

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MAH: GlaxoSmithKline Biologicals

Referral Rapporteur: Jan Mueller-Berghaus, Referral Co-Rapporteur: Sol Ruiz

Scope: List of Outstanding Issues

**Action:** For adoption

Harmonisation exercise for Varilrix and associated names. Product information harmonisation was triggered by the MAH.

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

CHMP list of outstanding issues: 10.12.2020

Submission of responses: 22.01.2021

Re-start of the procedure: 28.01.2021

Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 12.02.2021

Comments: 17.02.2021

Updated Rapporteur / co-rapporteur joint assessment report circulated to CHMP: 19.02.2021

CHMP list of outstanding issues/CHMP opinion: February 2021 CHMP

### **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**

December 2020 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

**Action:** For information

# **12. Inspections**

## **12.1. GMP inspections**

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

## **12.2. GCP inspections**

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

## **12.3. Pharmacovigilance inspections**

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



#### **12.4. GLP inspections**

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

### **13. Innovation Task Force**

#### **13.1. Minutes of Innovation Task Force**

No items

#### **13.2. Innovation Task Force briefing meetings**

No items

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

No items

#### **13.4. Nanomedicines activities**

No items

### **14. Organisational, regulatory and methodological matters**

#### **14.1. Mandate and organisation of the CHMP**

No items

#### **14.2. Coordination with EMA Scientific Committees**

##### **14.2.1. Paediatric Committee (PDCO)**

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PIPs reaching D30 at December 2020 PDCO

**Action:** For information

The CHMP noted the information.

Report from the PDCO meeting held on 8-11 December 2020

**Action:** For information

The CHMP noted the information.

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

---

Summary of recommendations and advice of PRAC meeting held on 23-26 November 2020

**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 December 2020

**Action:** For adoption

The CHMP adopted the EURD list.

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

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

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Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP December 2020 meeting to CHMP for adoption:

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

**Action:** For adoption

The CHMP adopted the BWP reports.

#### 14.3.2. Infectious disease working party (IDWP)

---

Product information update across all medicinal products with indication in human immunodeficiency virus (HIV) – proposal

**Action:** For discussion

The CHMP noted the update.

It was noted that mandatory information introduced in 4.4 and 4.6 is related to the risk associated to the product itself. Therefore, information related to the transmission of the infection itself is not mandatory.

The CHMP agreed to the proposal. The outcome will be presented at the next ORGAM.

#### 14.3.3. Safety Working Party (SWP)

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Chair(s): Jan Willem Van der Laan/Susanne Brendler-Schwaab

Updated list of questions from CMDh to SWP on the issue related to the MeNP limit in

rifampicin

**Action:** For information

The CHMP noted to the updated list of questions from CMDh to SWP.

#### 14.3.4. Name Review Group (NRG)

---

Adoption of November 2020 NRG ad-hoc ToD and overview of accepted names to date

Action: For adoption

The CHMP adopted the NRG report.

Name request for a thalidomide-containing product initially submitted as an invented name

**Action:** For information

The CHMP noted the information.

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

---

Chair: Anja Schiel

Report from the SAWP meeting held on 23-26 November 2020. 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.

### 14.4. Cooperation within the EU regulatory network

#### 14.4.1. Nitrosamines Multidisciplinary Expert Group (NMEG) on metformin

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List of participants for the Nitrosamines Multidisciplinary Expert Group on metformin scheduled on 01 December 2020 adopted via written procedure on 27 November 2020

**Action:** For information

The CHMP noted the list of participants.

### 14.5. Cooperation with International Regulators

#### 14.5.1. OPEN project – International collaboration in time of COVID-19

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**Action:** For information

The CHMP noted the update and welcomed a close collaboration with International

Agencies.

#### **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**

##### **14.8.1. Update of the Business Pipeline report for the human scientific committees**

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Q4/2020 initial marketing authorisation application submissions with eligibility request to central procedure

**Action:** For information

The CHMP noted the information.

#### **14.9. Others**

No items

### **15. Any other business**

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#### **15.1. AOB topic**

##### **15.1.1. New Executive Director at the EMA**

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Introduction of the new EMA Executive Director - Emer Cooke

The CHMP welcomed Emer Cooke as new EMA Executive Director.

##### **15.1.2. Update on COVID-19**

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**Action:** For information

The CHMP noted the update.

##### **15.1.3. COVID-19 vaccine (Ad26.COV2-S (recombinant)) - H0005737**

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active immunisation for prevention of coronavirus disease-2019 (COVID-19) caused by SARS-CoV-2 in adults >18 years old.

Scope: Rolling review timetable adopted via written procedure on 30 November 2020

**Action:** For information

The CHMP noted the rolling review timetable which was adopted via written procedure.

#### **15.1.4. COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735**

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active immunisation against COVID-19 disease.

Scope: Conditional marketing authorisation application timetable adopted at the ORGAM meeting on 30 November 2020

**Action:** For information

The CHMP noted the conditional marketing authorisation application timetable which was adopted at ORGAM.

See also 3.4

#### **15.1.5. COVID-19 mRNA Vaccine (nucleoside-modified) - EMEA/H/C/005791**

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indicated for active immunisation against coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus in adults aged 18 years and older.

Scope: Conditional marketing authorisation application timetable adopted at the ORGAM meeting on 30 November 2020

**Action:** For information

The CHMP noted the conditional marketing authorisation application timetable which was adopted at ORGAM.

## 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 07-10 December 2020 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	
Christophe Focke	Member	Belgium	No restrictions applicable to this meeting	
Karin Janssen van Doorn	Alternate	Belgium	No interests declared	
Ilko Getov	Member	Bulgaria	No interests declared	
Margareta Bego	Member	Croatia	No interests declared	
Emilia Mavrokordatou	Alternate	Cyprus	No participation in final deliberations and voting on	COVID-19 vaccines
Ondřej Slanař	Member	Czech Republic	No restrictions applicable to this meeting	
Tomas Radimersky	Alternate	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Kirstine Moll Harboe	Alternate	Denmark	No interests declared	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Edward Laane	Alternate	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Johanna Lähteenvuio	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 meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Janet Koenig	Alternate	Germany	No interests declared	
Konstantinos Markopoulos	Member	Greece	No interests declared	
Eleftheria Nikolaidi	Alternate	Greece	No interests declared	
Agnes Gyurasics	Alternate	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	Iceland	No interests declared	
Hrefna Gudmundsdottir	Alternate	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	
Peter Kiely	Alternate	Ireland	No interests declared	
Armando Genazzani	Member	Italy	No interests declared	
Elita Poplavska	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No participation in final deliberations and voting on	COVID-19 vaccines
Martine Trauffler	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 meeting	
Ingrid Wang	Alternate	Norway	No interests declared	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Bruno Sepodes	Member (Vice-Chair)	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No participation in final deliberations and voting on	COVID-19 vaccines
Simona Badoi	Member	Romania	No interests declared	
Dana Gabriela Marin	Alternate	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Dorota Distlerova	Alternate	Slovakia	No restrictions applicable to this meeting	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Maria Concepcion Prieto Yerro	Member	Spain	No interests declared	
Blanca Garcia-Ochoa	Alternate	Spain	No interests declared	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Christian Gartner	Co-opted member	Austria	No restrictions applicable to this meeting	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Blanka Hirschlerova	Co-opted member	Czech Republic	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Doris Hovgaard	Expert - via telephone*	Denmark	No interests declared	
Helga Haugom Olsen	Expert - via telephone*	Norway	No interests declared	
Rune Kjeklen	Expert - via telephone*	Norway	No restrictions applicable to this meeting	
Janusz Szyndler	Expert - via telephone*	Poland	No interests declared	
Piotr Maciejak	Expert - via telephone*	Poland	No interests declared	
Mario Miguel Coelho da Silva Rosa	Expert - via telephone*	Portugal	No interests declared	
Diederica Claeys	Expert - via Adobe*	Belgium	No interests declared	
Edwige Haelterman	Expert - via Adobe*	Belgium	No interests declared	
Flora Musuamba	Expert - via Adobe*	Belgium	No interests declared	
Joelle Warlin	Expert - via Adobe*	Belgium	No interests declared	
Stefan Bonne	Expert - via Adobe*	Belgium	No interests declared	
Violette Dirix	Expert - via Adobe*	Belgium	No interests declared	
Filip Kukulski	Expert - via Adobe*	Health Canada	No interests declared	
Aaron Sosa	Expert - via Adobe*	Denmark	No restrictions applicable to this meeting	
Anne-Marie Dalseg	Expert - via Adobe*	Denmark	No interests declared	



Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ebru Karakoc Madsen	Expert - via Adobe*	Denmark	No restrictions applicable to this meeting	
Mette Linnert Jensen	Expert - via Adobe*	Denmark	No interests declared	
Ole Weis Bjerrum	Expert - via Adobe*	Denmark	No restrictions applicable to this meeting	
Antero Kallio	Expert - via Adobe*	Finland	No restrictions applicable to this meeting	
Elina Asikanius	Expert - via Adobe*	Finland	No restrictions applicable to this meeting	
Juha Vakkilainen	Expert - via Adobe*	Finland	No interests declared	
Karin Punnonen	Expert - via Adobe*	Finland	No interests declared	
Karri Penttila	Expert - via Adobe*	Finland	No interests declared	
Clemens Mittmann	Expert - via Adobe*	Germany	No interests declared	
Georgios Aislaitner	Expert - via Adobe*	Germany	No interests declared	
Martina Schuessler-Lenz	Expert - via Adobe*	Germany	No interests declared	
Miriam Fuerst-Wilmes	Expert - via Adobe*	Germany	No interests declared	
Regine Lehnert	Expert - via Adobe*	Germany	No interests declared	
Stephanie Buchholz	Expert - via Adobe*	Germany	No interests declared	
Susanne Brendler-Schwaab	Expert - via Adobe*	Germany	No interests declared	
Cristina Migali	Expert - via Adobe*	Italy	No interests declared	
OdoardoMaria Olimpieri	Expert - via Adobe*	Italy	No interests declared	
Kristine Supe	Expert - via Adobe*	Latvia	No interests declared	
Liga Kunrade	Expert - via Adobe*	Latvia	No interests declared	
Edward Bojtor	Expert - via Adobe*	Netherlands	No restrictions applicable to this meeting	
Esther Brandon	Expert - via Adobe*	Netherlands	No interests declared	
Illiana Meurs	Expert - via Adobe*	Netherlands	No interests declared	
Ingrid Evers van Gogh	Expert - via Adobe*	Netherlands	No restrictions applicable to this meeting	
Loes den Otter	Expert - via Adobe*	Netherlands	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Martijn van Gils	Expert - via Adobe*	Netherlands	No interests declared	
Miki Hew	Expert - via Adobe*	Netherlands	No interests declared	
Monique van Raamsdonk	Expert - via Adobe*	Netherlands	No interests declared	
Anja Schiel	Expert - via Adobe*	Norway	No interests declared	
Greger Abrahamsen	Expert - via Adobe*	Norway	No interests declared	
Mats Okvist	Expert - via Adobe*	Norway	No interests declared	
Nina Pettersen Hessvik	Expert - via Adobe*	Norway	No interests declared	
Meeting run with the help of EMA staff				

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

## 17. Explanatory notes

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

### Oral explanations (section 2)

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

### Initial applications (section 3)

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

### **Re-examination procedures** *(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 lists 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/)



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

26 February 2021  
EMA/CHMP/82797/2021

## Annex to 07-10 December 2020 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 December 2020: <b>For adoption</b>	Adopted.
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#### **A.2. Appointment of Rapporteur / Co-Rapporteur Full Applications**

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Final Outcome of Rapporteurship allocation for December 2020: <b>For adoption</b>	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 -</b> <b>EMA/H/C/004065/S/0028, Orphan</b> BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga Request for Supplementary Information adopted on 12.11.2020.	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>Increlex - mecasermin -</b> <b>EMA/H/C/000704/S/0064</b> Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka Request for Supplementary Information adopted on 10.12.2020.	Request for supplementary information adopted with a specific timetable.
<b>Lojuxta - lomitapide -</b> <b>EMA/H/C/002578/S/0043</b> Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst	Request for supplementary information adopted with a specific timetable.

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Request for Supplementary Information adopted on 10.12.2020.

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**Mepsevii - vestronidase alfa -**  
**EMA/H/C/004438/S/0017, Orphan**  
Ultragenyx Germany GmbH, Rapporteur:  
Johann Lodewijk Hillege, PRAC Rapporteur: Eva  
A. Segovia  
Request for Supplementary Information adopted  
on 12.11.2020.

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.

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**Strensiq - asfotase alfa -**  
**EMA/H/C/003794/S/0048, Orphan**  
Alexion Europe SAS, Rapporteur: Armando  
Genazzani, PRAC Rapporteur: Rhea Fitzgerald

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.

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## **B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES**

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

**Neparvis - sacubitril / valsartan -**  
**EMA/H/C/004343/R/0032**  
Novartis Europharm Limited, Rapporteur:  
Johann Lodewijk Hillege, Co-Rapporteur:  
Kristina Dunder, PRAC Rapporteur: Anette  
Kirstine Stark

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

Based on the review of the available information, the CHMP was of the opinion that an additional five-year renewal was required.

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

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

**Alprolix - eftrenonacog alfa -**  
**EMA/H/C/004142/R/0032, Orphan**  
Swedish Orphan Biovitrum AB (publ),  
Rapporteur: Andrea Laslop, Co-Rapporteur:  
Maria Concepcion Prieto Yerro, PRAC Rapporteur:  
Brigitte Keller-Stanislawski  
Request for Supplementary Information adopted  
on 15.10.2020.

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

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.

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

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**Coagadex - human coagulation factor X -**  
**EMA/H/C/003855/R/0031, Orphan**  
BPL Bioproducts Laboratory GmbH, Rapporteur:

The CHMP agreed to the request by the applicant for an extension of the clock stop to respond to the RSI adopted on 15.10.2020.

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Andrea Laslop, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, Request for Supplementary Information adopted on 15.10.2020.

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**EndolucinBeta - lutetium (<sup>177</sup>Lu) chloride - EMEA/H/C/003999/R/0019**

ITM Medical Isotopes GmbH, Rapporteur: Peter Kiely, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Rugile Pilviniene

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

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.

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

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**Flixabi - infliximab - EMEA/H/C/004020/R/0064**

Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Ulla Wändel Liminga Request for Supplementary Information adopted on 12.11.2020.

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

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.

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

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**GalaFold - migalastat - EMEA/H/C/004059/R/0027, Orphan**

Amicus Therapeutics Europe Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Ulla Wändel Liminga Request for Supplementary Information adopted on 12.11.2020.

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

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.

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

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**IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/R/0047, Orphan**

CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 12.11.2020.

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

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.

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

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**Ongentys - opicapone - EMEA/H/C/002790/R/0031**

Bial - Portela & C<sup>a</sup>, S.A., Rapporteur: Martina Weise, Co-Rapporteur: Kirstine Moll Harboe,

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

PRAC Rapporteur: Maria del Pilar Rayon	<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>Palonosetron Accord - palonosetron - EMEA/H/C/004129/R/0009</b></p> <p>Accord Healthcare S.L.U., Generic, Generic of Aloxi, Rapporteur: Alar Irs, PRAC Rapporteur: Rhea Fitzgerald</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>Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - EMEA/H/C/003854/R/0029, Orphan, ATMP</b></p> <p>Orchard Therapeutics (Netherlands) BV, Rapporteur: Sol Ruiz, Co-Rapporteur: Egbert Flory, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 04.12.2020.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p><b>Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/R/0024</b></p> <p>Pfizer Ireland Pharmaceuticals, Rapporteur: Bjorg Bolstad, Co-Rapporteur: Simona Stankeviciute, PRAC Rapporteur: Rugile Pilvinienė</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>

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

<p><b>Bosulif - bosutinib - EMEA/H/C/002373/R/0045</b></p> <p>Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Martin Huber</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</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</p>
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	conditional.  The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
<b>Cometriq - cabozantinib -</b> <b>EMA/H/C/002640/R/0042, Orphan</b> Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Menno van der Elst	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.  The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.  The Marketing Authorisation remains conditional.  The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
<b>Deltyba - delamanid -</b> <b>EMA/H/C/002552/R/0047, Orphan</b> Otsuka Novel Products GmbH, Rapporteur: Christophe Focke, PRAC Rapporteur: Laurence de Fays Request for Supplementary Information adopted on 10.12.2020.	Request for supplementary information adopted with a specific timetable.
<b>Natpar - parathyroid hormone -</b> <b>EMA/H/C/003861/R/0027, Orphan</b> Shire Pharmaceuticals Ireland Limited, Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Rhea Fitzgerald Request for Supplementary Information adopted on 10.12.2020.	Request for supplementary information adopted with a specific timetable.
<b>Ondexxya - andexanet alfa -</b> <b>EMA/H/C/004108/R/0015</b> Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.  The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.  The Marketing Authorisation remains conditional.  The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
<b>WAYLIVRA - volanesorsen -</b> <b>EMA/H/C/004538/R/0009, Orphan</b> Akcea Therapeutics Ireland Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Martin Huber	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.  The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.

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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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#### SIGNAL DETECTION

PRAC recommendations on signals adopted at the PRAC meeting held on 23-26 November 2020:

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**Signal of anaphylactic reaction**

Adopted.

Xeloda, Capecitabine Accord, Capecitabine Medac, Capecitabine Teva, Ecansya - capecitabine, Rapporteur: various, Co-Rapporteur: various  
Scope: PRAC recommendation on a variation  
**Action:** For adoption

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**Signal of vasculitis**

Adopted.

Keytruda - pembrolizumab, Rapporteur: Armando Genazzani, Co-Rapporteur: Jan Mueller-Berghaus  
Scope: PRAC recommendation on a variation  
**Action:** For adoption

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#### PSUR PROCEDURES

PRAC recommendation for variation of the terms of the MA at the PRAC meeting held on 23-26 November 2020:

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**EMA/H/C/PSUSA/00000424/202004**

(bortezomib)

CAPS:

**Bortezomib Accord** (EMA/H/C/003984)

(bortezomib), Accord Healthcare S.L.U., Rapporteur: Milena Stain

**Bortezomib Fresenius Kabi**

(EMA/H/C/005074) (bortezomib), Fresenius Kabi Deutschland GmbH, Rapporteur: Kolbeinn Gudmundsson

**Bortezomib Hospira** (EMA/H/C/004207)

(bortezomib), Pfizer Europe MA EEIG, Rapporteur: Milena Stain

**Bortezomib SUN** (EMA/H/C/004076)

(bortezomib), Sun Pharmaceutical Industries Europe B.V., Rapporteur: Margareta Bego

**VELCADE** (EMA/H/C/000539) (bortezomib), Janssen-Cilag International NV, Rapporteur:

The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following change(s):

Update of section 4.8 of the SmPC to add 'Guillain-Barré syndrome' and 'Demyelinating polyneuropathy', with a frequency 'rare'. The Package Leaflet is updated accordingly for Guillain-Barré syndrome. No amendment to the Package Leaflet is considered necessary for reflecting the ADR of 'Demyelinating polyneuropathy' since it is considered sufficiently

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<p>Armando Genazzani NAPS: <b>NAPs</b> - EUR PRAC Rapporteur: Amelia Cupelli, "26/04/2019 To: 25/04/2020"</p>	<p>covered by the existing overarching sentence: Sensitivity, numbness, tingling or burning sensation of the skin, or pain in the hands or feet, due to nerve damage, which accounts for all forms of neuropathies. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>
<p><b>EMA/H/C/PSUSA/00002772/202003</b> (somatropin) CAPS: <b>NutropinAq</b> (EMA/H/C/000315) (somatropin), Ipsen Pharma, Rapporteur: Kirstine Moll Harboe <b>Omnitrope</b> (EMA/H/C/000607) (somatropin), Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege NAPS: <b>NAP</b> - EU PRAC Rapporteur: Anette Kirstine Stark, "Period covered by the PSUR: 31/03/2017 To: 31/03/2020"</p>	<p>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 pancreatitis. Update of section 4.8 of the SmPC to add the adverse reaction "gynecomastia" with a frequency uncommon. The Package Leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>
<p><b>EMA/H/C/PSUSA/00010044/202004</b> (meningococcal group A, C, W135, Y conjugate vaccines (conjugated to tetanus toxoid carrier protein)) CAPS: <b>Nimenrix</b> (EMA/H/C/002226) (meningococcal group A, C, W135 and Y conjugate vaccine), Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: David Olsen, "20/04/2019 To: 19/04/2020"</p>	<p>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 lymphadenopathy as a new ADR with a frequency of 'unknown'. The Package Leaflet has been updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>
<p><b>EMA/H/C/PSUSA/00010550/202005</b> (mycophenolate mofetil, mycophenolic acid) CAPS: <b>CellCept</b> (EMA/H/C/000082) (mycophenolate mofetil), Roche Registration GmbH, Rapporteur: Kirstine Moll Harboe <b>Myclausen</b> (EMA/H/C/001218) (mycophenolate mofetil), Passauer Pharma GmbH, Rapporteur: Andrea Laslop <b>Mycophenolate mofetil Teva</b></p>	<p>The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substances, concerning the following change:</p>

<p>(EMA/H/C/000882) (mycophenolate mofetil), Teva B.V., Rapporteur: Ondřej Slanař</p> <p><b>Myfenax</b> (EMA/H/C/000884) (mycophenolate mofetil), Teva B.V., Rapporteur: Ondřej Slanař</p> <p>NAPS:</p> <p><b>NAPs</b> - EU</p> <p>PRAC Rapporteur: Hans Christian Siersted, "03/05/2019 To: 02/05/2020"</p>	<p>Update of section 4.8 of the SmPC to add the adverse reaction de novo purine synthesis inhibitors-associated acute inflammatory syndrome with a frequency uncommon.</p> <p>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>
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#### B.4. EPARs / WPARs

<p><b>Artobend (WD) - autologous human chondrocytes in vitro expanded - EMA/H/C/004598, ATMP</b></p> <p>Tetec Tissue Engineering Technologies AG, repair of cartilage defects of the knee joint, New active substance (Article 8(3) of Directive No 2001/83/EC)</p> <p><b>WPAR</b></p>	<p>For information only. Comments can be sent to the PL in case necessary.</p>
<p><b>Gamifant - emapalumab - EMA/H/C/004386, Orphan</b></p> <p>Swedish Orphan Biovitrum AB (publ), treatment of paediatric patients with primary haemophagocytic lymphohistiocytosis (HLH)., New active substance (Article 8(3) of Directive No 2001/83/EC)</p>	<p>For information only. Comments can be sent to the PL in case necessary.</p>
<p><b>Onbevzi - bevacizumab - EMA/H/C/005640</b></p> <p>Samsung Bioepis NL B.V., treatment of carcinoma of the colon or rectum, breast cancer, non-small cell lung cancer, renal cell cancer, epithelial ovarian, fallopian tube or primary peritoneal cancer, and carcinoma of the cervix, Similar biological application (Article 10(4) of Directive No 2001/83/EC)</p>	<p>For information only. Comments can be sent to the PL in case necessary.</p>
<p><b>Phesgo - pertuzumab / trastuzumab - EMA/H/C/005386</b></p> <p>Roche Registration GmbH, treatment of early breast cancer, metastatic breast cancer, Fixed combination application (Article 10b of Directive No 2001/83/EC)</p>	<p>For information only. Comments can be sent to the PL in case necessary.</p>
<p><b>Roclanda - latanoprost / netarsudil - EMA/H/C/005107</b></p> <p>Aerie Pharmaceuticals Ireland Limited, reduction of elevated intraocular pressure, Fixed combination application (Article 10b of Directive No 2001/83/EC)</p>	<p>For information only. Comments can be sent to the PL in case necessary.</p>
<p><b>Tibsovo (WD) - ivosidenib -</b></p>	<p>For information only. Comments can be sent to</p>

<b>EMEA/H/C/005056, Orphan</b> FGK Representative Service, treatment of adult patients (≥ 18 years old) with relapsed or refractory Acute Myeloid Leukaemia (AML) with an Isocitrate Dehydrogenase-1 (IDH1) R132 mutation, New active substance (Article 8(3) of Directive No 2001/83/EC) <b>WPAR</b>	the PL in case necessary.
<b>Xofluza - baloxavir marboxil - EMEA/H/C/004974</b> Roche Registration GmbH, Treatment of influenza in patients aged 12 and above, including patients at high risk of developing influenza-related complications and for post-exposure prophylaxis of influenza in individuals aged 12, 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.

## 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

<b>ADYNOVI - ruriotocog alfa pegol - EMEA/H/C/004195/II/0013</b> Baxalta Innovations GmbH, Rapporteur: Andrea Laslop Opinion adopted on 26.11.2020. Request for Supplementary Information adopted on 23.07.2020.	Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>AMGEVITA - adalimumab - EMEA/H/C/004212/II/0023</b> Amgen Europe B.V., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 19.11.2020.	Request for supplementary information adopted with a specific timetable.
<b>Beovu - brolucizumab - EMEA/H/C/004913/II/0005/G</b> Novartis Europharm Limited, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 10.12.2020.	Request for supplementary information adopted with a specific timetable.
<b>Beromun - tasonermin - EMEA/H/C/000206/II/0050</b> Belpharma s.a., Rapporteur: Sinan B. Sarac Opinion adopted on 10.12.2020.	Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.



<b>Beromun - tasonermin -</b> <b>EMA/H/C/000206/II/0051</b> Belpharma s.a., Rapporteur: Sinan B. Sarac Opinion adopted on 10.12.2020.	Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Cerezyme - imiglucerase -</b> <b>EMA/H/C/000157/II/0118</b> Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 19.11.2020.	Positive Opinion adopted by consensus on 19.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Cinquaero - reslizumab -</b> <b>EMA/H/C/003912/II/0037/G</b> Teva B.V., Rapporteur: Johann Lodewijk Hillege Opinion adopted on 19.11.2020.	Positive Opinion adopted by consensus on 19.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Cinryze - c1 esterase inhibitor (human) -</b> <b>EMA/H/C/001207/II/0082/G</b> Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 10.12.2020.	Request for supplementary information adopted with a specific timetable.
<b>Daptomycin Hospira - daptomycin -</b> <b>EMA/H/C/004310/II/0014/G</b> Pfizer Europe MA EEIG, Generic, Generic of Cubicin, Rapporteur: Kolbeinn Gudmundsson Opinion adopted on 10.12.2020. Request for Supplementary Information adopted on 17.09.2020.	Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Efavirenz/Emtricitabine/Tenofovir disoproxil Zentiva - efavirenz / emtricitabine / tenofovir disoproxil -</b> <b>EMA/H/C/004250/II/0019</b> Zentiva k.s., Generic, Generic of Atripla, Rapporteur: Tomas Radimersky Opinion adopted on 03.12.2020. Request for Supplementary Information adopted on 03.09.2020.	Positive Opinion adopted by consensus on 03.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Emtricitabine/Tenofovir disoproxil Zentiva - emtricitabine / tenofovir disoproxil -</b> <b>EMA/H/C/004137/II/0015</b> Zentiva k.s., Generic, Generic of Truvada, Rapporteur: Alar Irs Opinion adopted on 03.12.2020. Request for Supplementary Information adopted on 03.09.2020, 28.05.2020.	Positive Opinion adopted by consensus on 03.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Eylea - aflibercept -</b> <b>EMA/H/C/002392/II/0062/G</b> Bayer AG, Rapporteur: Alexandre Moreau Opinion adopted on 10.12.2020.	Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Request for Supplementary Information adopted on 10.09.2020.	recommendation.
<b>Herzuma - trastuzumab -</b> <b>EMA/H/C/002575/II/0032/G</b> Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 10.12.2020. Request for Supplementary Information adopted on 01.10.2020.	Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Hulio - adalimumab -</b> <b>EMA/H/C/004429/II/0021</b> Mylan S.A.S, Rapporteur: Christophe Focke Opinion adopted on 10.12.2020.	Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>IDELVION - albutrepenonacog alfa -</b> <b>EMA/H/C/003955/II/0041/G, Orphan</b> CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 10.12.2020. Request for Supplementary Information adopted on 15.10.2020, 16.07.2020.	Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>IMVANEX - smallpox vaccine (live modified vaccinia virus Ankara) -</b> <b>EMA/H/C/002596/II/0050</b> Bavarian Nordic A/S, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 19.11.2020. Request for Supplementary Information adopted on 03.09.2020.	Positive Opinion adopted by consensus on 19.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>IMVANEX - smallpox vaccine (live modified vaccinia virus Ankara) -</b> <b>EMA/H/C/002596/II/0055</b> Bavarian Nordic A/S, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 26.11.2020. Request for Supplementary Information adopted on 08.10.2020.	Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Invokana - canagliflozin -</b> <b>EMA/H/C/002649/II/0052/G</b> Janssen-Cilag International NV, Rapporteur: Martina Weise Opinion adopted on 10.12.2020. Request for Supplementary Information adopted on 17.09.2020.	Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Kentera - oxybutynin -</b> <b>EMA/H/C/000532/II/0059</b> Teva B.V., Rapporteur: Karin Janssen van Doorn Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 26.11.2020.	
<b>Kyprolis - carfilzomib -</b> <b>EMA/H/C/003790/II/0050/G, Orphan</b> Amgen Europe B.V., Rapporteur: Blanca Garcia-Ochoa Request for Supplementary Information adopted on 03.12.2020.	Request for supplementary information adopted with a specific timetable.
<b>Lonquex - lipegfilgrastim -</b> <b>EMA/H/C/002556/II/0060</b> Teva B.V., Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 10.12.2020.	Request for supplementary information adopted with a specific timetable.
<b>Lyumjev - insulin lispro -</b> <b>EMA/H/C/005037/II/0006/G</b> Eli Lilly Nederland B.V., Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 26.11.2020.	Request for supplementary information adopted with a specific timetable.
<b>M-M-RVAXPRO - measles, mumps and rubella vaccine (live) -</b> <b>EMA/H/C/000604/II/0103</b> MSD Vaccins, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 10.12.2020.	Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Mysimba - naltrexone hydrochloride / bupropion hydrochloride -</b> <b>EMA/H/C/003687/II/0042</b> Orexigen Therapeutics Ireland Limited, Rapporteur: Kirstine Moll Harboe Request for Supplementary Information adopted on 03.12.2020, 23.07.2020.	Request for supplementary information adopted with a specific timetable.
<b>Nulojix - belatacept -</b> <b>EMA/H/C/002098/II/0071</b> Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson Request for Supplementary Information adopted on 10.12.2020, 15.10.2020.	Request for supplementary information adopted with a specific timetable.
<b>Nulojix - belatacept -</b> <b>EMA/H/C/002098/II/0072/G</b> Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson Opinion adopted on 10.12.2020. Request for Supplementary Information adopted on 22.10.2020.	Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Palynziq - pegvaliase -</b> <b>EMA/H/C/004744/II/0014, Orphan</b> BioMarin International Limited, Rapporteur:	Request for supplementary information adopted with a specific timetable.

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Johann Lodewijk Hillege  
Request for Supplementary Information adopted  
on 03.12.2020.

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**Pemetrexed Sandoz - pemetrexed -  
EMA/H/C/004011/II/0009**

Sandoz GmbH, Generic, Generic of Alimta,  
Rapporteur: Bjorg Bolstad  
Opinion adopted on 10.12.2020.

Positive Opinion adopted by consensus on  
10.12.2020. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**Privigen - human normal immunoglobulin -  
EMA/H/C/000831/II/0169**

CSL Behring GmbH, Rapporteur: Jan Mueller-  
Berghaus  
Request for Supplementary Information adopted  
on 10.12.2020.

Request for supplementary information adopted  
with a specific timetable.

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**ProQuad - measles, mumps, rubella and  
varicella vaccine (live) -  
EMA/H/C/000622/II/0143**

MSD Vaccins, Rapporteur: Jan Mueller-Berghaus  
Opinion adopted on 10.12.2020.

Positive Opinion adopted by consensus on  
10.12.2020. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**Puregon - follitropin beta -  
EMA/H/C/000086/II/0111/G**

Merck Sharp & Dohme B.V., Rapporteur: Peter  
Kiely  
Request for Supplementary Information adopted  
on 10.12.2020.

Request for supplementary information adopted  
with a specific timetable.

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**Puregon - follitropin beta -  
EMA/H/C/000086/II/0112/G**

Merck Sharp & Dohme B.V., Rapporteur: Peter  
Kiely  
Request for Supplementary Information adopted  
on 10.12.2020.

Request for supplementary information adopted  
with a specific timetable.

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**Reblozyl - luspatercept -  
EMA/H/C/004444/II/0001/G, Orphan**

Celgene Europe BV, Rapporteur: Milena Stain  
Opinion adopted on 26.11.2020.  
Request for Supplementary Information adopted  
on 15.10.2020.

Positive Opinion adopted by consensus on  
26.11.2020. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**Reblozyl - luspatercept -  
EMA/H/C/004444/II/0002/G, Orphan**

Celgene Europe BV, Rapporteur: Milena Stain  
Opinion adopted on 10.12.2020.

Positive Opinion adopted by consensus on  
10.12.2020. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**Riluzole Zentiva - riluzole -  
EMA/H/C/002622/II/0027**

Zentiva, k.s., Rapporteur: Kirstine Moll Harboe  
Opinion adopted on 26.11.2020.  
Request for Supplementary Information adopted

Positive Opinion adopted by consensus on  
26.11.2020. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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on 24.09.2020.

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**Sancuso - granisetron -  
EMA/H/C/002296/II/0058**

Kyowa Kirin Holdings B.V., Rapporteur: Simona Stankeviciute

Request for Supplementary Information adopted on 10.12.2020, 12.11.2020, 04.09.2020.

Request for supplementary information adopted with a specific timetable.

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**Simulect - basiliximab -  
EMA/H/C/000207/II/0107**

Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus

Opinion adopted on 03.12.2020.

Request for Supplementary Information adopted on 15.10.2020.

Positive Opinion adopted by consensus on 03.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Spectrila - asparaginase -  
EMA/H/C/002661/II/0021/G**

medac Gesellschaft für klinische Spezialpräparate mbH, Rapporteur: Andrea Laslop

Opinion adopted on 10.12.2020.

Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Strensiq - asfotase alfa -  
EMA/H/C/003794/II/0050, Orphan**

Alexion Europe SAS, Rapporteur: Armando Genazzani

Request for Supplementary Information adopted on 19.11.2020.

Request for supplementary information adopted with a specific timetable.

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**Thyrogen - thyrotropin alfa -  
EMA/H/C/000220/II/0106**

Genzyme Europe BV, Rapporteur: Peter Kiely

Opinion adopted on 19.11.2020.

Positive Opinion adopted by consensus on 19.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Trulicity - dulaglutide -  
EMA/H/C/002825/II/0054**

Eli Lilly Nederland B.V., Rapporteur: Martina Weise

Opinion adopted on 03.12.2020.

Request for Supplementary Information adopted on 29.10.2020.

Positive Opinion adopted by consensus on 03.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Voncento - human coagulation factor VIII / human von Willebrand factor -  
EMA/H/C/002493/II/0045**

CSL Behring GmbH, Rapporteur: Paula Boudewina van Hennik

Opinion adopted on 03.12.2020.

Positive Opinion adopted by consensus on 03.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Xadago - safinamide -  
EMA/H/C/002396/II/0034**

Zambon S.p.A., Rapporteur: Johann Lodewijk

Request for supplementary information adopted with a specific timetable.

<p>Hillegge Request for Supplementary Information adopted on 26.11.2020, 02.04.2020, 16.01.2020.</p>	
<p><b>Xolair - omalizumab -</b> <b>EMA/H/C/000606/II/0105/G</b> Novartis Europharm Limited, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 03.12.2020.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p><b>Yervoy - ipilimumab -</b> <b>EMA/H/C/002213/II/0086</b> Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 10.12.2020.</p>	<p>Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p><b>Zavicefta - ceftazidime / avibactam -</b> <b>EMA/H/C/004027/II/0023/G</b> Pfizer Ireland Pharmaceuticals, Rapporteur: Bjorg Bolstad Request for Supplementary Information adopted on 10.12.2020, 06.11.2020, 01.10.2020.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p><b>WS1906/G</b> <b>Hexacima-EMA/H/C/002702/WS1906/</b> <b>0108/G</b> <b>Hexaxim-EMA/H/W/002495/WS1906/</b> <b>0113/G</b> <b>Hexyon-EMA/H/C/002796/WS1906/</b> <b>0112/G</b> Sanofi Pasteur, Lead Rapporteur: Jan Mueller- Berghaus Opinion adopted on 10.12.2020.</p>	<p>Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p><b>WS1914/G</b> <b>Mircera-EMA/H/C/000739/WS1914/</b> <b>0080/G</b> <b>NeoRecormon-EMA/H/C/000116/</b> <b>WS1914/0109/G</b> Roche Registration GmbH, Lead Rapporteur: Martina Weise Opinion adopted on 19.11.2020.</p>	<p>Positive Opinion adopted by consensus on 19.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p><b>WS1924</b> <b>HyQvia-EMA/H/C/002491/WS1924/0064</b> <b>Kiovig-EMA/H/C/000628/WS1924/0105</b> Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 26.11.2020.</p>	<p>Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p><b>WS1982</b> <b>Aflunov-EMA/H/C/002094/WS1982/</b> <b>0065</b></p>	<p>Positive Opinion adopted by consensus on 03.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP</p>

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**Foclivia-EMA/H/C/001208/WS1982/0061**

Seqirus S.r.l., Lead Rapporteur: Armando Genazzani  
Opinion adopted on 03.12.2020.

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recommendation.

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

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**AUBAGIO - teriflunomide - EMA/H/C/002514/II/0033**

sanofi-aventis groupe, Rapporteur: Martina Weise, "To update sections 4.4 and 4.8 of the SmPC regarding skin reactions in particular to drug reaction with eosinophilia and systemic symptoms (DRESS) and to update the frequency of severe skin reactions from "Not known" to "Uncommon", following a review of the Sanofi global PV database. The Package Leaflet section 4 is updated as to add fever." Request for Supplementary Information adopted on 19.11.2020.

Request for supplementary information adopted with a specific timetable.

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**Caelyx pegylated liposomal - doxorubicin - EMA/H/C/000089/II/0094**

Janssen-Cilag International NV, Rapporteur: Ondřej Slanař, "Update of sections 4.2 and 4.8 of the SmPC in line with the SmPC guideline. In addition, the MAH took the opportunity to update the PI in line with the QRD template version 10.1 and with the EDQM standard terms. Furthermore, the list of local representatives in the Package Leaflet is updated." Opinion adopted on 10.12.2020. Request for Supplementary Information adopted on 03.09.2020, 14.05.2020.

Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Darzalex - daratumumab - EMA/H/C/004077/II/0041, Orphan**

Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "C.I.4 Update of section 4.8 of the SmPC in order to include CMV infections as a new adverse drug reaction (ADR) with frequency common following a comprehensive, cross-program evaluation of all potential cases of treatment-emergent cytomegalovirus (CMV) infections with use of daratumumab. The Package Leaflet is updated accordingly. Several minor linguistic improvements are also proposed." Opinion adopted on 03.12.2020.

Positive Opinion adopted by consensus on 03.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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<p><b>Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0013</b></p> <p>Sanofi Pasteur, Rapporteur: Christophe Focke, "To update sections 4.2, 4.8 and 5.1 of the SmPC in order to introduce a new posology regimen from 3 doses to 2 doses for individuals from 9 years of age based on interim results from study CYD65 listed as a category 3 study in the RMP; this is a Phase II, observer-blind, placebo-controlled trial in order to assess Immunogenicity and Safety of Tetravalent Dengue Vaccine Given in 1-, 2-, or 3-Dose Schedules Followed by a Single Booster; section 3 of the Package Leaflet is updated accordingly" Request for Supplementary Information adopted on 10.12.2020.</p>	<p>See agenda 9.1</p> <p>Request for supplementary information adopted with a specific timetable.</p>
<p><b>Foclivia - influenza virus surface antigens (inactivated) of strain A/Vietnam/1194/2004 (H5N1) - EMEA/H/C/001208/II/0058</b></p> <p>Seqirus S.r.l, Rapporteur: Armando Genazzani, "Update of sections 2, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 5.1, 6.4 and 6.5 of the SmPC based on data obtained from two clinical trials (V87_25 and V87_26) already assessed and approved for Aflunov, the corresponding H5N1 Zoonotic Influenza Vaccine (procedure EMEA/H/C/002094/II/0044/G approved in June 2019) in order to align both products. In addition, the MAH took the opportunity to also add in section 5.1 data from study V87P2 and study V87P11 (A/Turkey/turkey/1/2005) included for the RMP of both products and in the label of Aflunov for further alignment; the Package Leaflet and Labelling are updated accordingly. Finally, the marketing authorization holder (MAH) makes additional changes based on the most recent EU Guidelines and some additional minor editorial corrections." Opinion adopted on 26.11.2020.</p>	<p>Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p><b>Genvoya - elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004042/II/0070/G</b></p> <p>Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, "- C.I.4 (Type II): Update of section 4.5 of the SmPC to include data on the drug-drug interaction between Genvoya and the thienopyridine anti-platelet drugs clopidogrel</p>	<p>Request for supplementary information adopted with a specific timetable.</p>



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and prasugrel, based on a MAH cumulative safety review. The Package Leaflet is updated accordingly.

- C.I.4 (Type II): Update of section 4.5 of the SmPC to include data on the drug-drug interaction between Genvoya and medicinal products or oral supplements containing polyvalent cations, based on a MAH cumulative safety review. The Package Leaflet is updated accordingly.

In addition, the Marketing Authorisation Holder (MAH) took the opportunity to correct the amount of lactose stated in section 2 of the SmPC and make minor editorial changes throughout the PI."

Request for Supplementary Information adopted on 10.12.2020.

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**Imfinzi - durvalumab -  
EMA/H/C/004771/II/0024**

AstraZeneca AB, Rapporteur: Sinan B. Sarac, "Update of sections 4.4 and 4.8 of the SmPC in order to add immune thrombocytopenia to the list of adverse drug reactions (ADRs) with frequency (rare) following the MAH internal review; the Package Leaflet (PL) is updated accordingly. The MAH took the opportunity to correct information in the PL and to make editorial changes to the names of the manufacturer in Annex II and to units in Annex IIIA."

Opinion adopted on 10.12.2020.

Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Invanz - ertapenem -  
EMA/H/C/000389/II/0062**

Merck Sharp & Dohme B.V., Rapporteur: Fátima Ventura, "Update of section 4.8 of the SmPC in order to add 'hypersensitivity vasculitis' to the list of adverse drug reactions (ADRs) with frequency 'Rare', based on post-marketing reports; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, update the PI in line with the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017 Rev.1) regarding sodium content, and bring the PI in line with the latest QRD template version 10.1. The MAH also updated the Package leaflet to add the missing

Positive Opinion adopted by consensus on 03.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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adverse event "injection site induration" with frequency 'Rare'."

Opinion adopted on 03.12.2020.

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**Jinarc - tolvaptan -**

**EMA/H/C/002788/II/0031**

Otsuka Pharmaceutical Netherlands B.V.,  
Rapporteur: Armando Genazzani, "Update of sections 4.2 and 4.4 of the SmPC in order to include information on patients with CKD late stage 4 based on final results from study 156-12-211 listed as a category 3 study in the RMP; this is a Phase 3b, Multicenter, Open-label Trial to Evaluate the Long Term Safety of Immediate-release Tolvaptan (OPC-41061, 30 mg to 120 mg/day, Split dose) in Subjects with Autosomal Dominant Polycystic Kidney Disease."

Request for Supplementary Information adopted on 10.12.2020.

Request for supplementary information adopted with a specific timetable.

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**Keytruda - pembrolizumab -**

**EMA/H/C/003820/II/0094**

Merck Sharp & Dohme B.V., Rapporteur:  
Armando Genazzani, "Update of sections 4.4 and 5.1 of the SmPC in order to update efficacy information based on final results from study KEYNOTE-361 listed as a PAES in the Annex II; this is a Phase III Randomised, Controlled Clinical Trial of Pembrolizumab with or without Platinum-based Combination Chemotherapy versus Chemotherapy in Subjects with Advanced or Metastatic Urothelial Carcinoma; Annex IID is updated accordingly."

Request for Supplementary Information adopted on 10.12.2020.

Request for supplementary information adopted with a specific timetable.

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**Lorviqua - lorlatinib -**

**EMA/H/C/004646/II/0009/G**

Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, "Update of sections 4.2 and 5.2 of the SmPC in order to change the posology recommendations in patients with severe renal impairment based on the results from study B7461010 (a phase 1, single dose open-label study to evaluate the pharmacokinetics of lorlatinib in subjects with impaired renal function). The package leaflet has been updated accordingly."

Update of sections 4.4 and 4.5 of the SmPC in order to include information regarding drug-drug interaction with moderate CYP3A4/5 inducers based on study B7461026 (Phase 1,

Request for supplementary information adopted with a specific timetable.

open-label, fixed sequence, 2-period study to investigate the effect of multiple doses of modafinil on the pharmacokinetics of single dose lorlatinib in healthy participants). The MAH took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 10.12.2020.

**LUTATHERA - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123/II/0022, Orphan**  
Advanced Accelerator Applications, Rapporteur: Janet Koenig, "Update of sections 4.2, 4.4, 4.5, 4.6, 4.8 and 5.1 of the SmPC in order to introduce structural changes in the dosing and administration and warnings and precautions section, include clarifications in the pregnancy and overdose sections, update instructions for use based on end user feedback and update of amino acid solution information based on review and approval of LysaKare; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to include correction of typographical errors and editorial changes in the PI in line with the latest QRD template version 10.1." Opinion adopted on 10.12.2020. Request for Supplementary Information adopted on 12.11.2020.

Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Lyumjev - insulin lispro - EMEA/H/C/005037/II/0005**  
Eli Lilly Nederland B.V., Rapporteur: Outi Mäki-Ikola, "Update of sections 4.2 and 5.2 of the SmPC in order to update pharmacokinetic information based on final results from study I8B-MC-ITSA (submitted in accordance with Article 46 of regulation (EC) No 1901/2006). This study was conducted to evaluate the pharmacokinetics and glucodynamics of Lyumjev compared to Humalog in children, adolescents, and adults with Type 1 Diabetes Mellitus." Request for Supplementary Information adopted on 10.12.2020, 15.10.2020.

Request for supplementary information adopted with a specific timetable.

**Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0037**  
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, "Submission of

Request for supplementary information adopted with a specific timetable.

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the final clinical study report from study B16-439 (Phase 3b, a Multi-Center, Randomized, Open-Label, Pragmatic Study of Glecaprevir/Pibrentasvir (G/P) +/- Ribavirin for GT1 Subjects with Chronic Hepatitis C Previously Treated with an NS5A Inhibitor + Sofosbuvir Therapy)."

Request for Supplementary Information adopted on 19.11.2020.

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**Mekinist - trametinib -  
EMA/H/C/002643/II/0041**

Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.5, 4.6 and 5.2 of the SmPC in order to add drug-drug interaction information with hormonal contraceptives and to updated relevant part of the SmPC regarding this interaction; the Package Leaflet is updated accordingly. Furthermore the MAH took the occasion to include the information regarding the sodium content in the products in line with relevant guidelines and to bring the PI in line with the latest QRD template version 10.1. In addition, the MAH took the opportunity to introduce some editorial changes in the PI and to update the list of local representatives for The Netherlands in the Package Leaflet."

Request for Supplementary Information adopted on 03.12.2020.

Request for supplementary information adopted with a specific timetable.

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**NINLARO - ixazomib -  
EMA/H/C/003844/II/0025, Orphan**

Takeda Pharma A/S, Rapporteur: Armando Genazzani, "Update of the SmPC section 4.9 with additional information on Ninlaro overdose. The Package leaflet is updated accordingly."

Request for Supplementary Information adopted on 26.11.2020.

Request for supplementary information adopted with a specific timetable.

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**Nplate - romiplostim -  
EMA/H/C/000942/II/0078**

Amgen Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of sections 4.8 and 5.1 of the SmPC to reflect the main results from study 20101221 following the assessment performed under Article 46 of Regulation 1901/2006. Study 20101221 is an open-label trial to evaluate safety in children from 1 year of age to less than 18 years of age with primary ITP regardless of splenectomy status, including a protocol supplement to implement bone

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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marrow evaluations.”

Opinion adopted on 26.11.2020.

Request for Supplementary Information adopted on 03.09.2020.

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**Ofev - nintedanib -**

**EMA/H/C/003821/II/0034**

Boehringer Ingelheim International GmbH, Rapporteur: Peter Kiely, “Update of section 5.1 of SmPC to include results of a double-blind, randomised, parallel-group trial to evaluate the efficacy and safety of Ofev co-administered with oral sildenafil, compared to treatment with Ofev alone, in patients with idiopathic pulmonary fibrosis (IPF) and advanced lung function impairment (INSTAGE clinical trial).”

Opinion adopted on 10.12.2020.

Request for Supplementary Information adopted on 22.10.2020, 16.07.2020.

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Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Ozempic - semaglutide -**

**EMA/H/C/004174/II/0014**

Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.2 and 5.1 of the SmPC in order to include information on the use of semaglutide once weekly in combination with a SGLT-2 inhibitor, based on the final results from the SUSTAIN 9 study (study NN9535-4269); this is a 30-week, randomised, double-blind, placebo-controlled phase 3 trial investigating the efficacy and safety of semaglutide as add-on to treatment with an SGLT-2 inhibitor ± metformin or sulphonylurea (SU) in subjects with T2DM; the Package Leaflet is updated accordingly.”

Opinion adopted on 03.12.2020.

Request for Supplementary Information adopted on 10.09.2020, 05.06.2020.

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Positive Opinion adopted by consensus on 03.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Palynziq - pegvaliase -**

**EMA/H/C/004744/II/0015, Orphan**

BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege, “Submission of the final report from the non-clinical study BMN-165-18-080 listed as a category 3 study in the RMP.”

Opinion adopted on 10.12.2020.

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Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Parsabiv - etelcalcetide -**

**EMA/H/C/003995/II/0015**

Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Andrea Laslop (AT) (MNAT with AT for Coordination, AT for

Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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Clinical Efficacy, AT for Non-Clinical, AT for Clinical , AT for Clinical Safety, AT for Coordination, DE-BfArM for Quality), "Update of the SmPC section 4.4 to remove anti-etelcalcetide antibodies testing, and update of the Product information in line with QRD template v10.1."

Opinion adopted on 10.12.2020.

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**Perjeta - pertuzumab -  
EMA/H/C/002547/II/0053**

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Submission of the final report from study MO27775 (PERTAIN). This is a randomized, two-arm, open-label, multicenter Phase II trial assessing the efficacy and safety of pertuzumab given in combination with trastuzumab plus an aromatase inhibitor in first line patients with HER2-positive and hormone receptor-positive advanced (metastatic or locally advanced) breast cancer."

Opinion adopted on 19.11.2020.

Positive Opinion adopted by consensus on 19.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Qutenza - capsaicin -  
EMA/H/C/000909/II/0051/G**

Grunenthal GmbH, Rapporteur: Bruno Sepodes, "Update of section 4.2 and 4.4 to delete the explicit reference to pre-treatments used in clinical trials and to opioids. Update of section 4.4 of the SmPC to include more detail on unintended exposure to capsaicin."

Request for Supplementary Information adopted on 03.12.2020.

Request for supplementary information adopted with a specific timetable.

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**Remsima - infliximab -  
EMA/H/C/002576/II/0095**

Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, "Addition of a new posology for the rheumatoid arthritis indication that does not include IV induction doses."

Request for Supplementary Information adopted on 10.12.2020.

See agenda 9.1

Request for supplementary information adopted with a specific timetable.

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**Rubraca - rucaparib -  
EMA/H/C/004272/II/0024/G**

Clovis Oncology Ireland Limited, Rapporteur: Blanca Garcia-Ochoa, "Submission of the final reports from four non-clinical studies (Report 181000, OPT-2018-074, 8388100 and CLO-P8799)."

Opinion adopted on 03.12.2020.

Positive Opinion adopted by consensus on 03.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Stelara - ustekinumab -  
EMA/H/C/000958/II/0083**

Janssen-Cilag International NV, Rapporteur: Jayne Crowe, "Update of section 4.8 of the SmPC in order to add hypersensitivity vasculitis to the list of adverse drug reactions (ADRs) with frequency rare based on cumulative review from the literature and post-marketing reporting; the Package Leaflet is updated accordingly."

Opinion adopted on 26.11.2020.

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Stivarga - regorafenib -  
EMA/H/C/002573/II/0031**

Bayer AG, Rapporteur: Paula Boudewina van Hennik, "Submission of final study report for study 15982, a randomized, double blind, placebo-controlled, multicenter Phase 3 study that investigated regorafenib in subjects with hepatocellular carcinoma (HCC) after progression on sorafenib treatment."

Request for Supplementary Information adopted on 26.11.2020.

Request for supplementary information adopted with a specific timetable.

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**Taltz - ixekizumab -  
EMA/H/C/003943/II/0038/G**

Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, "Clinical studies in adult plaque psoriasis:

Type II- C.I.4 -Update of section 5.1 of the SmPC regarding long-term data in the treatment of psoriasis: RHAZ, RHBA, RHBC (3 studies of the "UNCOVER" series) were the pivotal registration studies, with response data up to 60 weeks already included in the SmPC. The current update relates to the extension data available, covering a total of 5 years.

Section 5.1 of the SmPC has also been updated with information from study RHCR (known as "IXORA-R") which is a 24-week head-to-head comparison of Taltz vs guselkumab.

Clinical studies in adult psoriatic arthritis:

Type II- C.I.4 -Update of section 5.1 of the SmPC regarding long-term data in the treatment of psoriatic arthritis: RHAP and RHBE (also known as SPIRIT-P1 and P2) were pivotal registration studies, with response data at 24 weeks and up to 52 weeks (SPIRIT-P1) already included in the SmPC. The current update relates to extension data available covering a total of 3 years. Section 5.1 of the SmPC has also been updated with longer-term data from study RHCF ("SPIRIT-H2H" Taltz vs

Request for supplementary information adopted with a specific timetable.

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adalimumab). Response data of up to 24 weeks are already in the SmPC and the addition of 52-week data are being proposed.”  
Request for Supplementary Information adopted on 10.12.2020, 15.10.2020.

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**Tecentriq - atezolizumab -  
EMA/H/C/004143/II/0050**

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, “Update of section 5.1 of the SmPC in order to reflect efficacy results based on the final OS analysis from study WO29522 (IMpassion130) comparing atezolizumab in combination with nab-paclitaxel with placebo with nab-paclitaxel for patients with previously untreated metastatic triple-negative breast cancer.”  
Opinion adopted on 10.12.2020.

Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Uptravi - selexipag -  
EMA/H/C/003774/II/0029**

Janssen-Cilag International N.V., Rapporteur: Martina Weise, “Update of section 5.1 of the SmPC based on interim survival and safety data from study AC-065A303 a long-term single-arm, open-label study to evaluate the safety and tolerability of selexipag / ACT-293987 in patients with Pulmonary Arterial Hypertension. In addition, the MAH took the opportunity to implement minor editorial changes and update the list of local representatives in the Package Leaflet.”  
Opinion adopted on 10.12.2020.  
Request for Supplementary Information adopted on 03.09.2020.

Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Veklury - remdesivir -  
EMA/H/C/005622/II/0012**

Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, “Submission of the final D28 mortality data by ordinal scale categories of Study COUS-540-5776 (NIAID-ACTT1), listed as a Specific Obligation in the Annex II of the Product Information, in order to confirm the efficacy and safety of remdesivir in patients on Invasive Mechanical Ventilation and Extracorporeal Membrane Oxygenation (IMV/ECMO). In addition, the MAH discuss the potential imbalance in the use of corticosteroids and effect modification in Study CO-US-540-5776. As a consequence, Annex II is updated accordingly.”

See agenda 9.1

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.



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Opinion adopted on 26.11.2020.  
Request for Supplementary Information adopted  
on 12.11.2020.

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**Vyxeos liposomal - daunorubicin /  
cytarabine - EMEA/H/C/004282/II/0014,  
Orphan**

Jazz Pharmaceuticals Ireland Limited,  
Rapporteur: Johanna Lähtenvuo, "Update of  
section 5.1 of the SmPC to reflect the 5-years  
overall survival data from the Follow-Up Phase  
of the Phase 3 Study CPX310-301. Additionally,  
the MAH has introduced minor editorial changes  
in the PI."

Opinion adopted on 26.11.2020.

Positive Opinion adopted by consensus on  
26.11.2020. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**XOSPATA - gilteritinib -  
EMEA/H/C/004752/II/0001, Orphan**

Astellas Pharma Europe B.V., Rapporteur: Bjorg  
Bolstad, "Submission of a pooled analysis report  
from studies 2215-CL-0101 (Phase 1/2), 2215-  
CL-0102 (Phase 1), 2215-CL-0301, 2215-CL-  
9100 (phase 3) listed as "Other forms of routine  
pharmacovigilance activities in section III.1 of  
the RMP". This is a pooled analysis to  
characterise gilteritinib-related differentiation  
syndrome, specifically incidence, observed signs  
and symptoms, duration, and response to  
intervention based on patient-level data from  
on-going trials in patients with acute myeloid  
leukaemia."

Opinion adopted on 26.11.2020.

Request for Supplementary Information adopted  
on 08.10.2020.

Positive Opinion adopted by consensus on  
26.11.2020. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**XOSPATA - gilteritinib -  
EMEA/H/C/004752/II/0003, Orphan**

Astellas Pharma Europe B.V., Rapporteur: Bjorg  
Bolstad, "C.I.4 Update of sections 4.4, 4.5 and  
5.2 of the SmPC in order to update information  
about Transporter drug-drug interactions based  
on final results from in vitro transporter studies  
identified as recommendations by CHMP  
(REC003) during the initial approval. In  
addition, the MAH took the opportunity to  
perform minor corrections and editorial changes  
in the PI."

Opinion adopted on 03.12.2020.

Request for Supplementary Information adopted  
on 29.10.2020, 03.09.2020.

Positive Opinion adopted by consensus on  
03.12.2020. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**Xtandi - enzalutamide -  
EMEA/H/C/002639/II/0050**

Request for supplementary information adopted  
with a specific timetable.

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Astellas Pharma Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 4.8 of the SmPC in order to add severe skin reactions to the list of adverse drug reactions (ADRs) with frequency not known based on a safety review; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor corrections in the SmPC."

Request for Supplementary Information adopted on 26.11.2020.

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**Zerbaxa - ceftolozane / tazobactam - EMEA/H/C/003772/II/0032**

Merck Sharp & Dohme B.V., Rapporteur: Bjorg Bolstad, "Update of section 5.1 of the SmPC for Zerbaxa to implement the EUCAST MIC breakpoints of ceftolozanetazobactam for Enterobacterales according to the EUCAST Clinical breakpoints table v. 10.0, valid from January 2020.

In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet."

Opinion adopted on 03.12.2020.

Positive Opinion adopted by consensus on 03.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**WS1822  
Relvar Ellipta-EMA/H/C/002673/  
WS1822/0045  
Revinty Ellipta-EMA/H/C/002745/  
WS1822/0043**

GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 5.1 of the SmPC to include descriptive data from a study investigating bronchoprotective and HPA-axis effects of fluticasone furoate versus fluticasone propionate or budesonide in an escalating repeat-dose, placebo-controlled, crossover study (study 203162) in 54 adults with a history of asthma, characterised by airway hyperresponsiveness and FEV1  $\geq$ 65% predicted.

In addition, the MAH has taken the opportunity to add a text related to SUMMIT data to section 5.1 of the high strength label (184/22 mcg) for Relvar/Revinty Ellipta. The text was agreed in procedure EMA/H/C/2673/WS/0992, however the change was mistakenly not implemented to the SmPC during this procedure.

Furthermore, additional minor modifications are introduced in the product information to bring it in line with the QRD template. Consequently,

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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amendments to annex II, IIIA and IIIB are also introduced."

Opinion adopted on 26.11.2020.

Request for Supplementary Information adopted on 15.10.2020, 25.06.2020.

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**WS1877**

**Invega-EMA/H/C/000746/WS1877/0068**  
**Paliperidone Janssen-Cilag International-**  
**EMA/H/C/005486/WS1877/0001**  
**Trevicta-EMA/H/C/004066/WS1877/**  
**0026**  
**Xeplion-EMA/H/C/002105/WS1877/**  
**0051**

Request for supplementary information adopted with a specific timetable.

Janssen-Cilag International NV, Lead  
Rapporteur: Kristina Dunder, "to add a new post-marketing adverse drug reaction (ADR) " Stevens-Johnson syndrome/toxic epidermal necrolysis" to section 4.8 (Undesirable effects) of the Summary of Product Characteristics (SmPC) for 4 centrally authorised medicinal products (INVEGA/XEPLION/TREVICTA/Paliperidone Janssen-Cilag International) and 2 medicinal products authorised via MRP (Risperdal Oral and Risperdal Consta). Section 4 of the Package Leaflet (PL) for each medicinal product is also amended accordingly."  
Request for Supplementary Information adopted on 03.12.2020.

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**WS1917**

**Kivexa-EMA/H/C/000581/WS1917/0087**  
**Triumeq-EMA/H/C/002754/WS1917/**  
**0085**  
**Trizivir-EMA/H/C/000338/WS1917/0119**  
**Ziagen-EMA/H/C/000252/WS1917/0114**

Request for supplementary information adopted with a specific timetable.

ViiV Healthcare B.V., Lead Rapporteur: Jean-Michel Race, "Update of sections 4.4 of the SmPC (for Ziagen, Kivexa, Trizivir and Triumeq) and 5.2 (for Triumeq only) to add new information about the drug-drug interactions between abacavir and riociguat. The Package Leaflet is updated accordingly. Furthermore, the MAH took the opportunity to introduce an excipient update for Ziagen, Kivexa and Trizivir in line with the SmPC guideline, a syringe instruction update in the Package Leaflet of Ziagen and a revised statement in section 6.6 of the SmPC for Triumeq in line with the QRD template. Moreover, minor editorial updates have been introduced throughout the Product

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Information of all four products.”  
Request for Supplementary Information adopted  
on 19.11.2020.

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**WS1922**

**Lixiana-EMA/H/C/002629/WS1922/0028**

**Roteas-EMA/H/C/004339/WS1922/0016**

Daiichi Sankyo Europe GmbH, Lead Rapporteur:  
Maria Concepcion Prieto Yerro, “Update of  
sections 4.2 and 5.2 of the SmPC, based on  
data from the bioavailability study DU176b-A-  
U166, in order to add information about the  
bioavailability of edoxaban crushed tablet  
administered by nasogastric tube or in apple  
puree and ingested versus the current tablet  
formulation in healthy subjects. The Package  
Leaflet has been updated accordingly. In  
addition, the MAH took the opportunity to  
correct typos in Lithuanian, Slovakian and  
Portuguese versions of the SmPC, Labelling and  
Package Leaflet.”

Opinion adopted on 26.11.2020.

Positive Opinion adopted by consensus on  
26.11.2020. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**WS1939**

**Vfend-EMA/H/C/000387/WS1939/0139**

Pfizer Europe MA EEIG, Lead Rapporteur:  
Johann Lodewijk Hillege, “Update of sections 4.3  
and 4.5 of the SmPC in order to add a new  
contraindication with ivabradine to the  
contraindications, and add drug-drug interaction  
information between voriconazole and  
ivabradine and venetoclax to the Interactions  
section. The Package Leaflet is updated  
accordingly.

In addition, the WSA took the opportunity to  
align with the current Annex to the European  
Commission guideline on ‘Excipients in the  
labelling and package leaflet of medicinal  
products for human use’ (SANTE-2017-11668),  
22 November 2019, EMA/CHMP/302620/2017  
Rev. 1\*, for lactose, and to update the list of  
local representatives in the Package Leaflet.”

Request for Supplementary Information adopted  
on 10.12.2020.

Request for supplementary information adopted  
with a specific timetable.

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

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**Imfinzi - durvalumab -**

**EMA/H/C/004771/II/0023**

AstraZeneca AB, Rapporteur: Sinan B. Sarac,  
PRAC Rapporteur: David Olsen, “Update of

Positive Opinion adopted by consensus on  
10.12.2020. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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sections 4.2 and 5.1 of the SmPC in order to introduce a new posology regimen of 1500 mg every 4 weeks (Q4W) for the approved indication of the treatment of patients with locally advanced, unresectable non-small cell lung cancer (NSCLC) whose tumours express PD-L1 on  $\geq 1\%$  of tumour cells and whose disease has not progressed following platinum based chemoradiation therapy. The RMP version 4.1 has also been submitted."

Opinion adopted on 10.12.2020.

Request for Supplementary Information adopted on 12.11.2020, 15.10.2020.

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**Lynparza - olaparib -**

**EMA/H/C/003726/II/0042**

AstraZeneca AB, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to add Myelodysplastic syndrome (MDS)/Acute myeloid leukaemia (AML) to the list of adverse drug reactions with the frequency uncommon, modify the existing warning on MDS/AML and update efficacy information based on final results from study SOLO-2 listed as a PAES in the Annex II; this is a phase III randomised, double blind, placebo controlled, multicentre study of olaparib maintenance monotherapy in platinum sensitive relapsed BRCA mutated ovarian cancer patients who are in complete or partial response following platinum based chemotherapy; the Package Leaflet and Annex II are updated accordingly. The RMP version 21 has also been submitted."

Request for Supplementary Information adopted on 26.11.2020.

Request for supplementary information adopted with a specific timetable.

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**Lyxumia - lixisenatide -**

**EMA/H/C/002445/II/0030**

sanofi-aventis groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Submission of the final report from study TDR14311 listed as a category 3 study in the RMP, and submitted in accordance with article 46. This is a Randomized, double-blind, placebo-controlled, dose escalation study on safety, pharmacokinetics and pharmacodynamics of lixisenatide in paediatric patients with Type 2 diabetes mellitus not adequately controlled with metformin and/or basal insulin. The RMP version 6.0 has also been submitted. Furthermore, the MAH took the

Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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opportunity to make editorial changes in the SmPC (sections 4.2 and 5.1)."  
Opinion adopted on 10.12.2020.

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**Natpar - parathyroid hormone -  
EMA/H/C/003861/II/0026, Orphan**  
Shire Pharmaceuticals Ireland Limited,  
Rapporteur: Karin Janssen van Doorn, PRAC  
Rapporteur: Rhea Fitzgerald, "Submission of the final results of study PAR-C10-008; a long-term open-label study investigating the safety and tolerability of a rhPTH[1-84] for the treatment of adults with hypoparathyroidism – a clinical extension study (RACE). Update of SmPC section 5.1 to reflect 72-month data from the study. Update of the RMP (version 3.0) with the completed study results, to remove this study as an additional pharmacovigilance activity and to align with the GVP module V Rev 2."  
Request for Supplementary Information adopted on 26.11.2020.

Request for supplementary information adopted with a specific timetable.

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**Ocrevus - ocrelizumab -  
EMA/H/C/004043/II/0020**  
Roche Registration GmbH, Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 5.3 of the SmPC in order to update information on embryo-fetal and pre- and postnatal development in cynomolgus monkeys based on final results from study 17-1133 listed as a category 3 study in the RMP (MEA 006). The RMP v. 5.0 has also been submitted."  
Opinion adopted on 26.11.2020.  
Request for Supplementary Information adopted on 01.10.2020.

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**OFEV - nintedanib -  
EMA/H/C/003821/II/0038**  
Boehringer Ingelheim International GmbH,  
Rapporteur: Peter Kiely, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of sections 4.5, 4.6 and 5.2 of the SmPC in order to add drug-drug interaction information with the oral contraceptive Microgynon, a combination of ethynilestradiol and levonorgestrel based on final results from clinical study N°1199-0340. This was a phase I, open-label, 2-period cross-over, fixed-sequence design trial, investigated the effect of multiple oral doses of nintedanib on the single dose kinetics of a combination of ethinylestradiol and levonorgestrel

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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(Microgynon). The Package Leaflet is updated accordingly. The RMP is likewise updated to version 10.”  
Opinion adopted on 26.11.2020.  
Request for Supplementary Information adopted on 01.10.2020.

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**Ondexxya - andexanet alfa -  
EMA/H/C/004108/II/0009/G**

Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, “C.I.4, C.I.3, C.I.6 (non-EoI)  
Update of section 5.2 of the SmPC in order to update pharmacokinetic information based on results from study CSR 19-514 (PK Comparability) and CSR 16-508 (Japanese Ethnicity Study) listed as a specific obligation in the Annex II. Annex II was proposed to be updated accordingly. The RMP version 2.1 has also been submitted.”  
Request for Supplementary Information adopted on 10.12.2020, 30.04.2020.

Request for supplementary information adopted with a specific timetable.

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**Orbactiv - oritavancin -  
EMA/H/C/003785/II/0030**

Menarini International Operations Luxembourg S.A., Rapporteur: Janet Koenig, PRAC Rapporteur: Adam Przybylkowski, “Submission of the final report from 14-TMC-01, a surveillance study investigation, listed as a category 3 study in the RMP, part of the global SENTRY Antimicrobial Surveillance Program platform to monitor the activity of oritavancin against gram-positive clinical isolates collected from Europe and the US.  
This application addresses PAM MEA 003.4, presenting the cumulative surveillance data from 2010 to 2019 (including the first 5-year post-approval period).  
The RMP version 3.1 is approved with this variation.”  
Opinion adopted on 26.11.2020.  
Request for Supplementary Information adopted on 03.09.2020.

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Rubraca - rucaparib -  
EMA/H/C/004272/II/0023**

Clovis Oncology Ireland Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Annika Folin, “Update of sections 4.5, 4.6 and 5.2 of the SmPC to add drug-drug interaction (DDI) information with rosuvastatin and oral

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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contraceptives based on the results of study CO-338-095 listed as a category 3 study in the RMP; Study CO-338-095 is a phase 1, open-label, DDI study to determine the effect of rucaparib on the pharmacokinetics of oral rosuvastatin (Arm A) and oral contraceptives (ethinylestradiol and levonorgestrel - Arm B) in patients with advanced solid tumours. The RMP version 6.0 has also been submitted."

Opinion adopted on 26.11.2020.

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**Rydapt - midostaurin -**

**EMA/H/C/004095/II/0014, Orphan**

Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "C.I.4

Update of sections 4.2 and 4.4 of the SmPC in order to change posology recommendations and add Special warnings and precautions for use in Paediatric population following the occurrence of severe dose limiting toxicities (DLTs) in the paediatric study CPKC412A2218 which is currently on clinical hold. The study is part of the agreed PIP (EMA-000780-PIP01-09-M05) for which a Request for Modification was submitted on 20-Apr-2020. Section 5.1 of the SmPC and the Package Leaflet are updated accordingly. The RMP version 5.0 has also been submitted. In addition, the MAH takes this opportunity to introduce minor editorial changes to align the PI to the updated QRD template version 10.1."

Opinion adopted on 10.12.2020.

Request for Supplementary Information adopted on 17.09.2020.

Positive Opinion adopted by consensus on 10.12.2020. 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/0037**

GlaxoSmithKline Biologicals SA, Rapporteur: Christophe Focke, PRAC Rapporteur: Sonja Hrabcik, "To update sections 4.4 and 5.1 of the SmPC following the final results from study ZOSTER-064, listed as a category 3 study in the RMP; this is an observational study to assess frailty and other prognostic factors for development of herpes zoster in adult subjects who participated in studies ZOSTER-006 and ZOSTER-022 and the HZ efficacy, immunogenicity and safety of Shingrix by frailty status, in order to fulfil the post-authorisation

Request for supplementary information adopted with a specific timetable.



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measure MEA/FSR 012. The updated RMP version 4.1 has also been submitted.

The MAH takes the opportunity to implement some editorial changes in sections 4.4 and 5.1. and correction of the abbreviation CHO cells from Chinese Hamster Ovarian cells to Chinese Hamster Ovary cells in the Annex A."

Request for Supplementary Information adopted on 26.11.2020.

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**Sivextro - tedizolid phosphate -  
EMA/H/C/002846/II/0037**

Request for supplementary information adopted with a specific timetable.

Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon, "Update of section 5.1 of the SmPC in order to update the description of the potential risk of emergence of drug resistance with tedizolid phosphate, based on final results from study Surveillance of Tedizolid Activity and Resistance (STAR) listed as a category 3 study in the RMP; this is a surveillance study established in January 2014 to monitor tedizolid susceptibility activity and emergence of resistance across the US, 11 European Union countries, Russia and Turkey.

The RMP version 6.2 has also been submitted." Request for Supplementary Information adopted on 26.11.2020, 03.09.2020.

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**Vizimpro - dacomitinib -  
EMA/H/C/004779/II/0003/G**

Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Pfizer Europe MA EEIG, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2 and 5.2 of the SmPC in order to revise the dosing recommendation for patients with hepatic impairment and include relevant pharmacokinetics data based on results of study A7471058, evaluating the effect of severe hepatic impairment on the plasma PK, safety and tolerability after a single dose of dacomitinib. As a consequence, the MAH is proposing to remove the missing information "Safety in Patient with Severe Hepatic Impairment" from the list of safety concerns in the RMP. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1.

The MAH has also taken the opportunity to update the EU RMP to include PASS study A7471064 "Single Arm Study to Evaluate the Safety of Dacomitinib for the First-Line

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Treatment of Participants in India with Metastatic NSCLC with Epidermal Growth Factor Receptor (EGFR)-Activating Mutations” as a “Category 3 required additional pharmacovigilance activity”. A revised RMP v1.1 (clean and tracked) has been submitted.”  
Opinion adopted on 10.12.2020.  
Request for Supplementary Information adopted on 15.10.2020.

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**Xeljanz - tofacitinib -  
EMA/H/C/004214/II/0027**

Pfizer Europe MA EEIG, Rapporteur: Armando Genazzani, PRAC Rapporteur: Liana Gross-Martirosyan, “Update of sections 4.1, 4.2, 4.4 , 4.8, 5.1 and 5.2 of Xeljanz 11 mg prolonged-release tablets SmPC in order to include the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior disease modifying antirheumatic drug therapy; as an alternative to the immediate release film-coated tablets; Section 4.2 of Xeljanz film-coated tablets is also updated to include switching with the prolonged-release tablet in the treatment of PsA. The Package Leaflet is updated accordingly. The RMP version 13.1 has also been submitted.”  
Request for Supplementary Information adopted on 10.12.2020.

See agenda 9.1

Request for supplementary information adopted with a specific timetable.

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**Xtandi - enzalutamide -  
EMA/H/C/002639/II/0049**

Astellas Pharma Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, “Update of sections 4.7, 4.8, 5.1 and 5.2 of the SmPC in order to update efficacy and safety information based on final results from study MDV3100-14 (PROSPER) listed as a PAES in the Annex II; this is a phase 3, randomized, double-blind, placebo-controlled, efficacy and safety study of enzalutamide in patients with nonmetastatic castration-resistant prostate cancer; the Package Leaflet and Annex II are updated accordingly. The RMP version 14.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, make few editorial updates and bring the PI in line with the latest QRD template version 10.1.”  
Request for Supplementary Information adopted

Request for supplementary information adopted with a specific timetable.

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on 26.11.2020, 03.09.2020.

**Zykadia - ceritinib -**

**EMA/H/C/003819/II/0034**

Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Annika Folin, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect the results of study CLDK378A2112 as recommended by the CHMP. The study assesses the steady-state PK of 450 mg or 600 mg ceritinib taken daily with a low-fat meal as compared with that of 750 mg ceritinib taken daily in the fasted state in patients with metastatic ALK-positive NSCLC. The Package Leaflet is updated accordingly. The RMP version 16 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1. Other editorial changes include the addition of the sodium content in the SmPCs and PLs and the removal of the black triangle." Request for Supplementary Information adopted on 26.11.2020.

Request for supplementary information adopted with a specific timetable.

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**WS1844**

**Edistrade-EMA/H/C/004161/WS1844/0039**

**Forxiga-EMA/H/C/002322/WS1844/0057**

AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin, "Re-categorisation of the Forxiga/Edistrade PASS (D169C00011): Retrospective Cohort Study on the Risk of Diabetic Ketoacidosis (DKA) to determine the effectiveness of additional risk minimisation measures in place for DKA by assessing the impact of the risk minimisation measures on the risk of DKA in T1DM patients who are treated with dapagliflozin in Europe, from a category 1 to category 3 PASS in the RMP Version 20 and removal of the following Annex IID of the PI: Obligation to conduct the following Non-interventional PASS: In order to estimate the incidence of DKA in T1DM dapagliflozin users following implementation of RMMs in Europe, the MAH should conduct and submit the results from an observational cohort study using existing data sources in European countries where dapagliflozin will be launched for T1DM"

Request for Supplementary Information adopted on 10.12.2020, 15.10.2020, 23.07.2020.

See agenda 9.1 and 2.3

Request for supplementary information adopted with a specific timetable.

#### **B.5.4. PRAC assessed procedures**

<p>PRAC Led <b>DaTSCAN - ioflupane (123I) - EMA/H/C/000266/II/0060</b> GE Healthcare B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the first RMP" Opinion adopted on 26.11.2020. Request for Supplementary Information adopted on 03.09.2020.</p>	<p>Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>PRAC Led <b>EXJADE - deferasirox - EMA/H/C/000670/II/0068</b> Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report related to the Physician Survey (NO6987) conducted for Exjade to assess the impact of educational materials on the prescribers' awareness of doses and biological monitoring recommendations and to assess the awareness and appropriate use of both formulations (Dispersible Tablets and Film-Coated tablets). The updated RMP version 17.1 is submitted as well." Opinion adopted on 26.11.2020. Request for Supplementary Information adopted on 03.09.2020, 17.04.2020, 16.01.2020, 03.10.2019.</p>	<p>Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>PRAC Led <b>Myozyme - alglucosidase alfa - EMA/H/C/000636/II/0079</b> Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report from study ALGMYC07390, Prevalence of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reactions (MEA 053 resulting from variation EMA/H/C/000636/II/0052 ) to test the effectiveness of the approved Safety Information Packet (SIP)."</p>	<p>Request for supplementary information adopted with a specific timetable.</p>

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Request for Supplementary Information adopted on 26.11.2020, 09.07.2020, 12.03.2020.

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PRAC Led

**Neulasta - pegfilgrastim -  
EMA/H/C/000420/II/0113**

Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from study 20160176 listed as a category 3 study in the RMP. This is a retrospective cohort study with primary outcome the time from index date to diagnosis of MDS or AML (safety). As a result, sections 4.4 and 4.8 of the SmPC is updated to add a new warning on Myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML), and to add them in the list of adverse drug reactions (ADRs) with frequency uncommon; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1."

Opinion adopted on 26.11.2020.

Request for Supplementary Information adopted on 09.07.2020.

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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PRAC Led

**Neuraceq - florbetaben (18F) -  
EMA/H/C/002553/II/0033**

Life Radiopharma Berlin GmbH, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from study FBB-01\_03\_13 (PASS-2) (listed as a category 3 study in the RMP): a non-interventional, cross-sectional, retrospective, multicentre, multi-country registry to observe usage pattern, safety and tolerability of the diagnostic agent NeuraCeq (florbetaben (18F)) in European clinical practice. The RMP (version 5.9) is updated accordingly"

Request for Supplementary Information adopted on 26.11.2020.

Request for supplementary information adopted with a specific timetable.

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PRAC Led

**Ontruzant - trastuzumab -  
EMA/H/C/004323/II/0026**

Samsung Bioepis NL B.V., Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the RMP

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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version 4.0 in order to propose the early termination of long-term observational follow-up study for cardiac safety (SB3-G31-BC-E).”  
Opinion adopted on 26.11.2020.

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PRAC Led

**Orfadin - nitisinone -**

**EMA/H/C/000555/II/0074**

Swedish Orphan Biovitrum International AB,  
PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP  
liaison: Armando Genazzani, “Submission of the final report from study Sobi.NTBC-005 listed as a category 3 study in the RMP. This is a non-interventional Post-Authorization Safety Study (PASS) to evaluate long-term safety of Orfadin treatment in hypertyrosinemia type 1 (HT-1) patients in standard clinical care. The RMP version 5.3 has also been submitted.”

Request for Supplementary Information adopted on 26.11.2020, 03.09.2020.

Request for supplementary information adopted with a specific timetable.

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PRAC Led

**Pioglitazone Accord - pioglitazone -**

**EMA/H/C/002277/II/0020**

Accord Healthcare S.L.U., Generic, Generic of Actos, Rapporteur: Peter Kiely, PRAC  
Rapporteur: Rhea Fitzgerald, PRAC-CHMP  
liaison: Peter Kiely, “Update of the Risk Management Plan (RMP) for the removal of safety concerns and additional risk minimisation measures (ARRM) as per summary of RMP of Glidipion (pioglitazone; published on 20-Jul-2020), and content adapted to the new GVP Module V (Rev.2).”

Opinion adopted on 26.11.2020.

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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PRAC Led

**Piqray - alpelisib -**

**EMA/H/C/004804/II/0001**

Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP version 2.0 in order to replace the category 3 studies CBYL719C2402 and CBYL719A0IC02 with a new non-interventional safety study (CBYL719C2404). Additionally, a separated Health Care Professional Survey (CBYL719A0IC02) is proposed as part of the pharmacovigilance plan.”

Request for Supplementary Information adopted on 26.11.2020.

Request for supplementary information adopted with a specific timetable.

<p>PRAC Led</p> <p><b>Replagal - agalsidase alfa - EMEA/H/C/000369/II/0106</b></p> <p>Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of sections 4.8 and 4.4 of the Summary of Product Characteristics (SmPC) in order to update the list of adverse drug reactions (ADRs) information based on the final results from study HGT-REP-081 " a Multicenter Open-label Treatment Protocol to Observe the Safety of Replagal (agalsidase alfa) Enzyme Replacement Therapy in Canadian Patients with Fabry Disease" and the safety information reported in clinical trials. In addition, the MAH took the opportunity to introduce editorial and QRD changes in sections throughout the Product Information according to the QRD templates and current guidelines, including new warnings related to sodium excipient and traceability of biological medicinal products. The Package Leaflet is updated accordingly."</p> <p>Opinion adopted on 26.11.2020.</p> <p>Request for Supplementary Information adopted on 14.05.2020.</p>	<p>Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>PRAC Led</p> <p><b>Stelara - ustekinumab - EMEA/H/C/000958/II/0082</b></p> <p>Janssen-Cilag International NV, Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "To submit the final safety registry report of CNT01275PSO4005 "Nordic Database Initiative for Exposure to Ustekinumab: a Review and Analysis of Adverse Events from the Swedish and Danish National Registry Systems" listed as a category 3 in the RMP. An updated RMP version (18.2) has also been submitted."</p> <p>Request for Supplementary Information adopted on 26.11.2020.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p>PRAC Led</p> <p><b>Trulicity - dulaglutide - EMEA/H/C/002825/II/0051</b></p> <p>Eli Lilly Nederland B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Ilaria Baldelli, PRAC-CHMP liaison: Armando Genazzani, "Submission of the final study report for the PASS category 3 dulaglutide drug utilisation study B009: a multi-</p>	<p>Request for supplementary information adopted with a specific timetable.</p>

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database collaborative research program of observational studies to monitor the utilisation and safety of dulaglutide in the EU (ref. PAM MEA 002-002.5). An updated RMP version 6.1 was provided as part of the application."

Request for Supplementary Information adopted on 26.11.2020, 09.07.2020.

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PRAC Led

**VPRIV - velaglucerase alfa -**

**EMA/H/C/001249/II/0049, Orphan**

Shire Pharmaceuticals Ireland Limited,

Rapporteur: Martina Weise, PRAC Rapporteur:

Martin Huber, PRAC-CHMP liaison: Martina

Weise, "Submission of final physician data study

results for PASS study "Evaluation of the

Effectiveness of Risk Minimisation Measures: A

Survey among Health Care Professionals and

Patient/Caregivers to Assess their Knowledge

and Attitudes on Prescribing and Home

Administration Conditions of Velaglucerase

Alpha (VPRIV) in 6 European Countries"

(EUPASS 14255)"

Request for Supplementary Information adopted

on 26.11.2020.

Request for supplementary information adopted with a specific timetable.

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PRAC Led

**Zinforo - ceftaroline fosamil -**

**EMA/H/C/002252/II/0055**

Pfizer Ireland Pharmaceuticals, Rapporteur: Alar

Irs, PRAC Rapporteur: Maia Uusküla, PRAC-

CHMP liaison: Alar Irs, "Update of sections 4.4

and 5.2 of the SmPC in order to include

information on the use of ceftaroline in patients

with cystic fibrosis, based on a pooled

population pharmacokinetic (Pop PK) analysis

that included data from cystic fibrosis patients

treated with ceftaroline fosamil. This submission

fulfils the post-authorisation measure LEG

016.1. In addition, the Marketing Authorisation

Holder (MAH) took the opportunity to make

minor editorial changes."

Request for Supplementary Information adopted

on 26.11.2020.

Request for supplementary information adopted with a specific timetable.

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PRAC Led

**WS1653**

**Enbrel-EMA/H/C/000262/WS1653/0230**

**LIFMIOR (EXP)-EMA/H/C/004167/**

**WS1653/0024**

Pfizer Europe MA EEIG, Lead Rapporteur: Maria

Concepcion Prieto Yerro, Lead PRAC Rapporteur:

Request for supplementary information adopted with a specific timetable.



Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of the second 5-year report from the British Society for Rheumatology Biologics Register (BSRBR, also referred as study B1801309) listed as a category 3 study in the RMP. This is a prospective observational cohort study which investigates the long-term outcomes of patients with rheumatoid arthritis treated with etanercept with particular reference to safety." Request for Supplementary Information adopted on 26.11.2020, 17.04.2020, 16.01.2020.

PRAC Led

**WS1760**

**Lixiana-EMA/H/C/002629/WS1760/0024**  
**Roteas-EMA/H/C/004339/WS1760/0011**

Daiichi Sankyo Europe GmbH, Lead Rapporteur:

Maria Concepcion Prieto Yerro, Lead PRAC

Rapporteur: Adrien Inoubli, PRAC-CHMP liaison:

Alexandre Moreau, "Submission of the final

study report from study ETNA-DUS: a

retrospective drug utilisation chart review study

listed as a category 3 study in the RMP. The

Edoxaban Treatment in Routine Clinical Practice

Drug Utilisation Study (ETNA-DUS) was

designed to gain insight on how edoxaban is

used in real practice. The ETNA-DUS intends to

help identify prescription patterns and the

effectiveness of the educational programs"

Opinion adopted on 26.11.2020.

Request for Supplementary Information adopted on 14.05.2020, 16.01.2020.

Positive Opinion adopted by consensus on

26.11.2020. The Icelandic and Norwegian CHMP

Members were in agreement with the CHMP recommendation.

PRAC Led

**WS1861/G**

**Kisplyx-EMA/H/C/004224/WS1861/0037/G**

**Lenvima-EMA/H/C/003727/WS1861/0037/G**

Eisai GmbH, Lead Rapporteur: Karin Janssen

van Doorn, Lead PRAC Rapporteur: Annika

Folin, PRAC-CHMP liaison: Kristina Dunder,

"Update of section 4.8 of the SmPC following

the submission of the final clinical study report

(CSR) for study E7080-G000-201 (Study 201) -

To evaluate the long-term safety of lenvatinib in

Medullary and Iodine-131 Refractory,

Unresectable differentiated thyroid carcinoma

(DTC), Stratified by Histology (MEA 001 for

Lenvima; from initial MAA for Kisplyx).

Submission of the final CSR for study E7080-

Positive Opinion adopted by consensus on

10.12.2020. The Icelandic and Norwegian CHMP

Members were in agreement with the CHMP recommendation.

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G000-303 (Study 303) - To evaluate long-term safety of lenvatinib in patients with RR-DTC (radioiodine refractory differentiated thyroid cancer) in a randomized, double-blind, placebo-controlled Phase 3 study (MEA 004 for Lenvima; MEA 002 for Kispilyx).

Submission of an updated integrated summary of safety (ISS) including data from DTC subjects in studies 201, 303 and E7080-J081-208 (study 208) - the latter study was to determine the long-term safety profile of lenvatinib in Japanese patients with advanced thyroid cancer (Kispilyx REC from Study 208 variation (procedure EMEA/H/C/003727/II/0008) for Lenvima).

The RMP version 12 has also been submitted.”  
Opinion adopted on 10.12.2020.

Request for Supplementary Information adopted on 03.09.2020.

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PRAC Led

**WS1944**

**Izba-EMA/H/C/002738/WS1944/0014**

**Travatan-EMA/H/C/000390/WS1944/0064**

Novartis Europharm Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Eva A. Segovia, “To submit and updated RMP for Travatan and Izba with the following proposed changes:

The following risks are proposed for removal in this RMP update:

important identified risks

- Macular oedema
- Hyperpigmentation
- Hypertrichoses
- Iris and uveal inflammations
- Cardiac and vascular disorders
- Respiratory disorders
- Hypersensitivity reactions

important potential risks:

- Melanoma
- Corneal damage due to use of preserved eye drops

- Use during pregnancy and lactation

removal of the following missing information topics:

- Long-term safety in the paediatric population
- Potential interactions

In addition, the format of the Risk management plan has been aligned with GVP Module V

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Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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Revision 2 requirements (EMA 2017).

The changes made to the RMP were performed following the PRAC recommendation dated 31-Oct-2019 for the recent PSUR with PSUR number PSUSA/003011/201902."

Opinion adopted on 26.11.2020.

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PRAC Led

**WS1972**

**Exviera-EMA/H/C/003837/WS1972/0049**

**Viekirax-EMA/H/C/003839/WS1972/0060**

AbbVie Deutschland GmbH & Co. KG, Lead

Rapporteur: Filip Josephson, Lead PRAC

Rapporteur: Maria del Pilar Rayon, "To provide an updated Risk Management Plans (RMP) for Viekirax and Exviera following the outcome of procedure EMA/H/C/PSA/J/0055 to change the due date for submission of the final study report for the HCC recurrence PASS study ."

Opinion adopted on 26.11.2020.

Positive Opinion adopted by consensus on

26.11.2020. 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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**Kymriah - tisagenlecleucel -**

**EMA/H/C/004090/II/0027, Orphan, ATMP**

Novartis Europharm Limited, Rapporteur: Rune Kjekken, Co-Rapporteur: Dariusz Sladowski, CHMP Coordinators: Ingrid Wang and Ewa Balkowiec Iskra

Opinion adopted on 10.12.2020, 04.12.2020.

Request for Supplementary Information adopted on 06.11.2020, 09.10.2020.

Positive Opinion adopted by consensus on

10.12.2020. The Icelandic and Norwegian CHMP

Members were in agreement with the CHMP recommendation.

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**Zolgensma - onasemnogene abeparvovec -**

**EMA/H/C/004750/II/0008, Orphan, ATMP**

Novartis Gene Therapies EU Limited,

Rapporteur: Johannes Hendrikus Ovelgonne,

Co-Rapporteur: Egbert Flory, CHMP

Coordinators: Johann Lodewijk Hillege and Jan

Mueller-Berghaus, , "Update to SmPC for

sections 4.4 (Special warnings and precautions for use), 4.8 (Undesirable Effects) and

corresponding sections in the Package Leaflet to

add a new safety signal of 'Thrombotic microangiopathy'."

Request for Supplementary Information adopted on 04.12.2020.

Request for supplementary information adopted with a specific timetable.

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**Zolgensma - onasemnogene abeparvovec -**

Request for supplementary information adopted

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<p><b>EMA/H/C/004750/II/0009/G, Orphan, ATMP</b></p> <p>Novartis Gene Therapies EU Limited,  Rapporteur: Johannes Hendrikus Ovelgonne,  Co-Rapporteur: Egbert Flory, CHMP  Coordinators: Johann Lodewijk Hillege and Jan Mueller-Berghaus  Request for Supplementary Information adopted on 04.12.2020.</p>	<p>with a specific timetable.</p>
<p><b>Zynteglo - betibeglogene autotemcel - EMA/H/C/003691/II/0017, Orphan, ATMP</b></p> <p>bluebird bio (Netherlands) B.V, Rapporteur: Carla Herberts, Co-Rapporteur: Violaine Closson Carella, CHMP Coordinators Paula Boudewina van Hennik and Alexandre Moreau  Opinion adopted on 10.12.2020, 04.12.2020.</p>	<p>Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>

#### **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**

<p><b>WS1834</b></p> <p><b>Aerius-EMA/H/C/000313/WS1834/0094</b></p> <p><b>Azomyr-EMA/H/C/000310/WS1834/0098</b></p> <p><b>Neoclarityn-EMA/H/C/000314/WS1834/0092</b></p> <p>Merck Sharp &amp; Dohme B.V., Duplicate, Duplicate of Allex (SRD), Azomyr, Opulis (SRD), Lead Rapporteur: Christophe Focke, "The scope of this variation is to update the product information to comply with the revised Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use". To update sections 2, 4.4 and 6.1 (6.1 only for oral solution) of the SmPC to reflect that the guidance on excipients has been changed. Section 2 of the Package Leaflet is updated accordingly. Additionally SmPC, PIL and Labelling were updated to the latest QRD version and some minor corrections of the text introduced also affecting other sections, which do not have impact on the content."</p> <p>Request for Supplementary Information adopted</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
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on 10.12.2020.

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**WS1878**

**Ambirix-EMA/H/C/000426/WS1878/0110**

**Fendrix-EMA/H/C/000550/WS1878/0073**

**Infanrix hexa-EMA/H/C/000296/WS1878/0284**

**Twinrix Adult-EMA/H/C/000112/WS1878/0145**

**Twinrix Paediatric-EMA/H/C/000129/WS1878/0146**

GlaxoSmithkline Biologicals SA, Lead  
Rapporteur: Christophe Focke  
Opinion adopted on 26.11.2020.

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**WS1890**

**Infanrix hexa-EMA/H/C/000296/WS1890/0286**

GlaxoSmithkline Biologicals SA, Lead  
Rapporteur: Christophe Focke  
Opinion adopted on 10.12.2020.

Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**WS1895/G**

**Lixiana-EMA/H/C/002629/WS1895/0029/G**

**Roteas-EMA/H/C/004339/WS1895/0017/G**

Daiichi Sankyo Europe GmbH, Lead Rapporteur:  
Maria Concepcion Prieto Yerro  
Opinion adopted on 26.11.2020.

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**WS1905**

**Infanrix hexa-EMA/H/C/000296/WS1905/0283**

GlaxoSmithkline Biologicals SA, Lead  
Rapporteur: Christophe Focke  
Opinion adopted on 26.11.2020.

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**WS1912**

**Ambirix-EMA/H/C/000426/WS1912/0111**

**Infanrix hexa-EMA/H/C/000296/WS1912/0285**

**Rotarix-EMA/H/C/000639/WS1912/0117**

**Twinrix Adult-EMA/H/C/000112/WS1912/0146**

**Twinrix Paediatric-EMA/H/C/000129/WS1912/0147**

GlaxoSmithkline Biologicals SA, Lead  
Rapporteur: Christophe Focke

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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Opinion adopted on 26.11.2020.

**WS1930**

**Hexacima-EMA/H/C/002702/WS1930/0107**

**Hexaxim-EMA/H/W/002495/WS1930/0112**

**Hexyon-EMA/H/C/002796/WS1930/0111**

Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

Request for Supplementary Information adopted on 03.12.2020.

Request for supplementary information adopted with a specific timetable.

**WS1931**

**Hirobriz Breezhaler-EMA/H/C/001211/WS1931/0060**

**Onbrez Breezhaler-EMA/H/C/001114/WS1931/0058**

**Oslif Breezhaler-EMA/H/C/001210/WS1931/0058**

Novartis Europharm Limited, Lead Rapporteur: Kirstine Moll Harboe, "To update SmPC sections 4.4 and 5.1 (indacaterol maleate) on LABA components and to make changes related to QT interval prolongation.

In addition the MAH has taken this opportunity to bring the annexes in line with QRD version 10.1 and to update the instruction for use in SmPC section 6.6 and package leaflet."

Opinion adopted on 10.12.2020.

Positive Opinion adopted by consensus on 10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**WS1940**

**Adcirca-EMA/H/C/001021/WS1940/0033**

**Cialis-EMA/H/C/000436/WS1940/0093**

**Tadalafil Lilly-EMA/H/C/004666/WS1940/0006**

Eli Lilly Nederland B.V., Lead Rapporteur: Maria Concepcion Prieto Yerro, "To include the excipient guidance in the labelling and package leaflet annex. In addition the QRD template has also been implemented. i.e. the MAH has updated the order of presentation in line with QRD for Cialis and Tadalafil Lilly.

The details of the local representatives in Lithuania, Latvia, Estonia, France and Slovakia have been updated."

Request for Supplementary Information adopted on 26.11.2020.

Request for supplementary information adopted with a specific timetable.

**WS1950**

**Kinzalmono-EMA/H/C/000211/**

**WS1950/0116**

Positive Opinion adopted by consensus on 26.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

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**Micardis-EMA/H/C/000209/WS1950/0119**

recommendation.

**Pritor-EMA/H/C/000210/WS1950/0129**

Boehringer Ingelheim International GmbH, Lead Rapporteur: Armando Genazzani, "To update section 4.4 of the SmPC and section 2 of the PL in order to implement the wording 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' (SANTE-2017-11668), Revision 1 related to sorbitol and sodium content.

Furthermore, MAH took this opportunity to implement QRD template version 10.1.

Section 6 of the PL was updated to add 'K25' to povidone.

Finally, some editorial changes to correct the provided administrative information of the PI are included in the submission:

- For Kinzalmono/Pritor:

§ Correction of the date of latest renewal in section 9 of the SmPC.

§ Change of the phone number of local representative of MAH in Bulgaria in section 6 of PL.

- For Micardis:

§ Change of the phone number of local representative of MAH in Austria and Lithuania in section 6 of PL.

§ Removal of "D-" from the zip code of address of MAH and manufacturer in section 7 of the SmPC, section A of the Annex II, section 6 of the PL and section 11 of the Labelling.

- Addition of minor linguistic corrections to the PI of the following languages: LT, FI, SV and EL.

Further the MAH took the opportunity and include an editorial change ."

Opinion adopted on 26.11.2020.

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**WS1951**

**Combivir-EMA/H/C/000190/WS1951/0098**

**Telzir-EMA/H/C/000534/WS1951/0102**

ViiV Healthcare B.V., Lead Rapporteur: Jean-Michel Race, "To update section 4.4 of the SmPC and section 2 of the PL to update excipients labelling in alignment with excipients guideline (Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human

Positive Opinion adopted by consensus on 03.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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use' (SANTE-2017-11668) related to sodium content for:

- Telzir (fosamprenavir) 700 mg Film-coated tablets;
- Combivir (lamivudine/zidovudine) 150/300 mg Film-coated tablets.

In addition, the MAH took the opportunity to apply minor administrative changes in the following languages: LT, SL and FR.”

Opinion adopted on 03.12.2020.

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**WS1955**

**Exelon-EMA/H/C/000169/WS1955/0130**  
**Prometax-EMA/H/C/000255/WS1955/0130**

Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau, “To update sections 2 and 4.4 of the SmPC for Exelon 2mg/mL Oral Solution and Prometax 2mg/mL Oral Solution in line with the current excipients guideline (Annex to the European Commission guideline on ‘Excipients in the labelling and package leaflet of medicinal products for human use’ (SANTE-2017-11668)) with regards to sodium (from sodium benzoate and sodium citrate dihydrate) and sodium benzoate that are listed under the annex to the excipient guideline. Section 2 of package leaflet (PL) was updated accordingly. In addition, the MAH took this opportunity to bring the product information annexes for all presentations in line with the current QRD template.”

Opinion adopted on 19.11.2020.

Positive Opinion adopted by consensus on 19.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**WS1956**

**Zypadhera-EMA/H/C/000890/WS1956/0043**  
**Zyprexa-EMA/H/C/000115/WS1956/0130**

**Zyprexa Velotab-EMA/H/C/000287/WS1956/0098**

Eli Lilly Nederland B.V., Duplicate, Duplicate of Zyprexa, Lead Rapporteur: Outi Mäki-Ikola, “To include new wording on excipients in SmPC section 4.4 and in the package leaflet. The wording takes the new excipient guidance into account. In addition the MAH has also taken this opportunity to make minor changes in accordance with the QRD template.”

Opinion adopted on 19.11.2020.

Positive Opinion adopted by consensus on 19.11.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**WS1958/G**

Positive Opinion adopted by consensus on

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<b>Aflunov-EMEA/H/C/002094/WS1958/0063/G</b>	10.12.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<b>Foclivia-EMEA/H/C/001208/WS1958/0059/G</b>	
Seqirus S.r.l, Lead Rapporteur: Armando Genazzani	
Opinion adopted on 10.12.2020.	

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

<b>WS1884</b>	The MAH withdrew the procedure on 19.11.2020.
<b>Nuwiq-EMEA/H/C/002813/WS1884/0037</b>	
<b>Vihuma-EMEA/H/C/004459/WS1884/0019</b>	
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus	
Request for Supplementary Information adopted on 03.09.2020.	
Withdrawal request submitted on 19.11.2020.	
<b>Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0048</b>	The MAH withdrew the procedure on 30.11.2020.
Pfizer Ireland Pharmaceuticals, Rapporteur: Alar Irs, "Extension of the indication for the treatment of community acquired pneumonia (CAP) to include concurrent bacteraemia due to Streptococcus pneumoniae (SP) for all age groups, based on the results of previously submitted studies: FOCUS 1 (study P903-08) and FOCUS 2 (study P903-09), paediatric CAP study (study P903-31) and relevant post-marketing safety experience with ceftaroline for bacteraemic Streptococcus pneumoniae CAP. As a consequence, sections 4.1 and 5.1 of the SmPC are updated accordingly. No RMP has been provided within this application."	
Request for Supplementary Information adopted on 12.11.2020, 23.07.2020, 12.12.2019.	

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

PRAC Led	Request by the applicant for an extension of the clock-stop to respond to the RSI adopted on 26.11.2020.
<b>Brineura - cerliponase alfa - EMEA/H/C/004065/II/0027, Orphan</b>	
BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel	
Liminga, PRAC-CHMP liaison: Kristina Dunder, "An update to the RMP, to change the final date for the completion of the Post-authorisation efficacy study 190-203."	
The CHMP agreed to the request by the applicant.	

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Request for Supplementary Information adopted on 26.11.2020.

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**BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/II/0033/G**

Teva Pharma B.V., Rapporteur: John Joseph Borg, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Hans Christian Siersted, "Type II variation – C.I.6.a. - Extension of indication to include adolescents (12 years and older) for the regular treatment of asthma, where use of a combination (inhaled corticosteroid and long-acting  $\beta$ 2 adrenoceptor agonist) is appropriate: in patients not adequately controlled with inhaled corticosteroids and "as needed" inhaled short-acting  $\beta$ 2 adrenoceptor agonists; or in patients already adequately controlled on both inhaled corticosteroids and long-acting  $\beta$ 2 adrenoceptor agonists. The proposed extension to the indication is based upon data from the literature. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make an administrative update to the Greek, Islandic, Irish and Maltese local representatives phone numbers in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.1. An updated RMP version 3.0 was submitted as part of the application. Type IB variation - C.I.z other – updates of sections 4.2, 5.1 and 5.2 of the SmPC to update the information on paediatric data and section 4.4 of the SmPC to remove the warning regarding the risk of growth retardation in children and the guidance on how to address this risk as agreed during the assessment of the duplicate Budesonide/Formoterol Teva Pharma B.V. (EMA/H/C/004882), which was approved in Jan 2020."

Request by the applicant for an extension of the clock-stop to respond to the RSI adopted on 15.10.2020.

The CHMP agreed to the request by the applicant.

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**DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/II/0033/G,**

Teva Pharma B.V., Rapporteur: John Joseph Borg, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Hans Christian Siersted, "- Type II variation – C.I.6.a. - Extension of indication to include adolescents (12 years and older) for the regular treatment of asthma, where use of a

Request by the applicant for an extension of the clock-stop to respond to the RSI adopted on 15.10.2020.

The CHMP agreed to the request by the applicant.

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combination (inhaled corticosteroid and long-acting  $\beta_2$  adrenoceptor agonist) is appropriate: in patients not adequately controlled with inhaled corticosteroids and “as needed” inhaled short-acting  $\beta_2$  adrenoceptor agonists; or in patients already adequately controlled on both inhaled corticosteroids and long-acting  $\beta_2$  adrenoceptor agonists. The proposed extension to the indication is based upon data from the literature. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC have been updated and the package leaflet has been updated accordingly. In addition, the marketing authorisation holder took the opportunity to make an administrative update to the Greek, Islandic, Irish and Maltese local representatives phone numbers in the package leaflet. Furthermore, the product information is brought in line with the latest QRD template version 10.1. An updated RMP version 3.0 was submitted as part of the application.

- Type IB variation - C.I.z other – updates of sections 4.2, 5.1 and 5.2 of the SmPC to update the information on paediatric data and section 4.4 of the SmPC to remove the warning regarding the risk of growth retardation in children and the guidance on how to address this risk as agreed during the assessment of the duplicate, Budesonide/Formoterol Teva Pharma B.V. (EMA/H/C/004882), which was approved in January 2020.”

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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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<b>odevixibat - EMA/H/C/004691, Orphan</b>	<b>Accelerated review</b>
Albireo, treatment of progressive familial intrahepatic cholestasis (PFIC)	

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**COVID-19 mRNA vaccine (nucleoside-modified) - EMA/H/C/005735**  
Active immunization against COVID-19 disease

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**fingolimod - EMA/H/C/005661**  
treatment of multiple sclerosis

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**finerenone - EMA/H/C/005200**  
delay progression of kidney disease, reduce the risk of cardiovascular mortality and morbidity

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**maralixibat - EMA/H/C/005551, Orphan**

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FGK Representative Service GmbH, Treatment of Progressive Familial Intrahepatic Cholestasis Type 2 Treatment of Progressive Familial Intrahepatic Cholestasis Type 2

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**metformin hydrochloride / sitagliptin hydrochloride monohydrate - EMEA/H/C/005678**  
treatment of type 2 diabetes mellitus

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**arimoclomol - EMEA/H/C/005203, Orphan**  
Orphazyme A/S, treatment of Niemann-Pick disease type C (NPC)

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**COVID-19 mRNA Vaccine (nucleoside modified) - EMEA/H/C/005791**  
indicated for active immunization against coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus in adults aged 18 years and older.

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**adrenalin - EMEA/H/C/005584**  
For the emergency treatment of allergic reactions, including anaphylaxis.

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**lasmiditan - EMEA/H/C/005332**  
acute treatment of migraine with or without aura in adults

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**sitagliptin fumarate - EMEA/H/C/005741**  
treatment of type 2 diabetes mellitus

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**tepotinib - EMEA/H/C/005524**  
indicated for the treatment of adult patients with advanced non-small cell lung cancer.

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**teriparatide - EMEA/H/C/005543**  
treatment of osteoporosis

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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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**Noxafil - posaconazole - EMEA/H/C/000610/X/0063/G**  
Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, "Extension application to introduce a new pharmaceutical form (gastro-resistant powder and solvent for oral suspension), grouped with a type II variation (C.I.6.a) to extend the approved indications for Noxafil to the paediatric population. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC, as well as the package leaflet, are updated. The

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RMP (version 17.1) is updated in accordance.”

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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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#### **dexamethasone phosphate -**

##### **EMA/H/C/005740**

indicated for cerebral oedema, post-traumatic shock-lung syndrome, asthma, skin diseases, autoimmune diseases, rheumatoid arthritis, prophylaxis and treatment of post-operative or cytostatic-induced vomiting, treatment of COVID-19, eye inflammation and infection  
List of Questions adopted on 15.10.2020.

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#### **pralsetinib - EMA/H/C/005413**

treatment of non-small cell lung cancer (NSCLC)  
List of Questions adopted on 17.09.2020.

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#### **tanezumab - EMA/H/C/005189**

treatment of moderate to severe chronic pain associated with osteoarthritis (OA) in adult patients for whom treatment with non-steroidal anti-inflammatory drugs (NSAIDs) and/or an opioid is ineffective, not tolerated or inappropriate  
List of Questions adopted on 23.07.2020.

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#### **relugolix / estradiol / norethisterone acetate - EMA/H/C/005267**

treatment of uterine fibroids  
List of Questions adopted on 23.07.2020.

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#### **ponesimod - EMA/H/C/005163**

treatment of adult patients with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features  
List of Questions adopted on 23.07.2020.

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

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#### **Defitelio - defibrotide -**

##### **EMA/H/C/002393/S/0051, Orphan**

Gentium S.r.l., Rapporteur: Kristina Dunder,  
PRAC Rapporteur: Ulla Wändel Liminga

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#### **Orphacol - cholic acid -**

##### **EMA/H/C/001250/S/0038, Orphan**

Laboratoires CTRS, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Sofia Trantza

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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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**Atazanavir Mylan - atazanavir -  
EMA/H/C/004048/R/0016**

Mylan S.A.S, Generic, Generic of Reyataz,  
Rapporteur: Bjorg Bolstad, PRAC Rapporteur:  
Adrien Inoubli

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**Bortezomib Hospira - bortezomib -  
EMA/H/C/004207/R/0020**

Pfizer Europe MA EEIG, Generic, Generic of  
VELCADE, Rapporteur: Milena Stain, PRAC  
Rapporteur: Amelia Cupelli

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**Bortezomib SUN - bortezomib -  
EMA/H/C/004076/R/0015**

Sun Pharmaceutical Industries Europe B.V.,  
Generic, Generic of VELCADE, Rapporteur:  
Margareta Bego, PRAC Rapporteur: Amelia  
Cupelli

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**Cinqaero - reslizumab -  
EMA/H/C/003912/R/0038**

Teva B.V., Rapporteur: Johann Lodewijk Hillege,  
Co-Rapporteur: Jayne Crowe, PRAC Rapporteur:  
Brigitte Keller-Stanislowski

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**Lorviqua - lorlatinib -  
EMA/H/C/004646/R/0011**

Pfizer Europe MA EEIG, Rapporteur: Sinan B.  
Sarac, PRAC Rapporteur: Nikica Mirošević  
Skvrce

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**Nordimet - methotrexate -  
EMA/H/C/003983/R/0018**

Nordic Group B.V., Rapporteur: Bruno Sepodes,  
PRAC Rapporteur: Martin Huber

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**Pandemic influenza vaccine H5N1  
AstraZeneca - pandemic influenza vaccine  
(H5N1) (live attenuated, nasal) -  
EMA/H/C/003963/R/0040**

AstraZeneca AB, Rapporteur: Jan Mueller-  
Berghaus, PRAC Rapporteur: Sonja Hrabcik

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**Pemetrexed Fresenius Kabi - pemetrexed -  
EMA/H/C/003895/R/0023**

Fresenius Kabi Deutschland GmbH, Generic,  
Generic of Alimta, Rapporteur: Bjorg Bolstad,  
PRAC Rapporteur: Tiphaine Vaillant

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**Rubraca - rucaparib -  
EMA/H/C/004272/R/0025**

Clovis Oncology Ireland Limited, Rapporteur:

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Blanca Garcia-Ochoa, PRAC Rapporteur: Annika Folin

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**Zolgensma - onasemnogene abeparvovec -  
EMA/H/C/004750/R/0012, Orphan,  
ATMP**

Novartis Gene Therapies EU Limited,  
Rapporteur: Johannes Hendrikus Ovelgonne,  
Co-Rapporteur: Egbert Flory, PRAC Rapporteur:  
Ulla Wändel Liminga

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**Zynteglo - betibeglogene autotemcel -  
EMA/H/C/003691/R/0018, Orphan,  
ATMP**

bluebird bio (Netherlands) B.V, Rapporteur:  
Carla Herberts, PRAC Rapporteur: Brigitte  
Keller-Stanislowski

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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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**Darzalex - daratumumab -**

**EMA/H/C/004077/II/0043, Orphan**

Janssen-Cilag International NV, Rapporteur:  
Sinan B. Sarac, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Extension of indication to include treatment of adult patients with systemic light chain (AL) amyloidosis for Darzalex; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.2 of the RMP has also been submitted."

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**Darzalex - daratumumab -**

**EMA/H/C/004077/II/0044, Orphan**

Janssen-Cilag International NV, Rapporteur:  
Sinan B. Sarac, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Extension of indication for Darzalex subcutaneous formulation to include combination with pomalidomide and dexamethasone for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8,

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5.1 and 5.2 of the SmPC are updated. In addition, section 4.8 of the SmPC for the intravenous formulation is also updated based on the pooled safety analysis. The Package Leaflet is updated in accordance. Version 8.2 of the RMP has also been submitted.”

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**Keytruda - pembrolizumab -  
EMA/H/C/003820/II/0097**

Merck Sharp & Dohme B.V., Rapporteur:  
Armando Genazzani, Co-Rapporteur: Jan  
Mueller-Berghaus, PRAC Rapporteur: Menno van  
der Elst, “Extension of indication to include in  
combination with chemotherapy, first-line  
treatment of locally advanced unresectable or  
metastatic carcinoma of the oesophagus or  
HER-2 negative gastroesophageal junction  
adenocarcinoma in adults for Keytruda, based  
on the results from the pivotal KEYNOTE-590  
(KN590) trial. Phase 3, randomized, double-  
blind, placebo-controlled, multisite study to  
evaluate the efficacy and safety of  
pembrolizumab in combination with  
chemotherapy (cisplatin and 5-FU) versus  
chemotherapy (cisplatin with 5-FU) as first line  
treatment in participants with locally advanced  
unresectable metastatic adenocarcinoma or  
squamous cell carcinoma of the esophagus or  
advanced/metastatic Siewert type 1  
adenocarcinoma of the gastroesophageal  
junction; as a consequence sections 4.1, 4.8  
and 5.1 of the SmPC are updated. The Package  
Leaflet is updated in accordance. Version of the  
RMP (Version 30.1) has also been submitted.”

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**Tecentriq - atezolizumab -  
EMA/H/C/004143/II/0052**

Roche Registration GmbH, Rapporteur: Sinan B.  
Sarac, Co-Rapporteur: Jan Mueller-Berghaus,  
PRAC Rapporteur: Marcia Sofia Sanches de  
Castro Lopes Silva, “Extension of indication to  
include Tecentriq in combination with nab-  
paclitaxel and anthracycline-based  
chemotherapy for the neoadjuvant treatment of  
adult patients with locally advanced or early  
Triple Negative Breast Cancer (TNBC) based on  
the results of the pivotal study WO39392  
(IMpassion031); as a consequence, sections  
4.1, 4.2, 4.8 and 5.1 of the Tecentriq 840 mg  
concentrate for solution for infusion SmPC and  
section 4.8 of the Tecentriq 1,200 mg  
concentrate for solution for infusion SmPC are

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updated. The Package Leaflet is updated in accordance. Version 18 of the RMP has also been submitted.”

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**Verzenios - abemaciclib -**

**EMA/H/C/004302/II/0013**

Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Extension of indication to include Verzenios in combination with endocrine therapy for adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence; as a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted.”

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

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**WS1941**

**Edistride-EMA/H/C/004161/WS1941/0043**

**Forxiga-EMA/H/C/002322/WS1941/0062**

AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin, “Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for Forxiga and Edistride based on the results from the renal outcomes study D169AC00001 (DAPA-CKD). The Annex II.B and Package Leaflet of these products are updated accordingly. The DAPA-CKD study is a category 3, Post-Authorisation Safety Study (PASS) listed in the dapagliflozin RMP to evaluate the potential risk of lower limb amputation; it is a multicentre, event-driven, randomized, double-blind, parallel group, placebo-controlled study, evaluating the effect of dapagliflozin versus placebo, given once daily in addition to standard of care, to prevent the progression of chronic kidney disease (CKD) or cardiovascular (CV)/renal death.

In addition, the Risk Management Plan for dapagliflozin (version 22) has been updated.”

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**WS1953**

**Segluromet-EMA/H/C/004314/WS1953/**

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**0012**

**Steglatro-EMA/H/C/004315/WS1953/**

**0013**

Merck Sharp & Dohme B.V., Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Menno van der Elst, "Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC of Steglatro and Segluromet in order to modify the indication, update posology recommendations and include efficacy and safety information based on final results from the VERTIS CV study (protocol 8835-004/B1521021) listed as a category 3 study in the RMP. This is a multi-centre, multi-national, randomised, double-blind, placebo-controlled study to evaluate the effect of ertugliflozin on cardiovascular risk in adult patients with type 2 diabetes and established atherosclerotic cardiovascular disease. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted."

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

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**Abasaglar - insulin glargine -**

**EMA/H/C/002835/II/0035/G**

Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder

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**AYVAKYT - avapritinib -**

**EMA/H/C/005208/II/0002, Orphan**

Blueprint Medicines (Netherlands) B.V., Rapporteur: Blanca Garcia-Ochoa

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**AYVAKYT - avapritinib -**

**EMA/H/C/005208/II/0003/G, Orphan**

Blueprint Medicines (Netherlands) B.V., Rapporteur: Blanca Garcia-Ochoa

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**Benlysta - belimumab -**

**EMA/H/C/002015/II/0090**

GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder

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**Cystagon - mercaptamine bitartrate -**

**EMA/H/C/000125/II/0062**

Recordati Rare Diseases, Rapporteur: Maria Concepcion Prieto Yerro

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**Darunavir Mylan - darunavir -**

**EMA/H/C/004068/II/0012**

Mylan S.A.S, Generic, Generic of Prezista, Rapporteur: John Joseph Borg

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**Dupixent - dupilumab -****EMA/H/C/004390/II/0038/G**

sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

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**EVRA - ethinylestradiol / norelgestromin -****EMA/H/C/000410/II/0048/G**

Janssen-Cilag International NV, Rapporteur:  
Paula Boudewina van Hennik

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**Firmagon - degarelix -****EMA/H/C/000986/II/0038**

Ferring Pharmaceuticals A/S, Rapporteur:  
Alexandre Moreau

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**Gardasil 9 - human papillomavirus vaccine****[types 6, 11, 16, 18, 31, 33, 45, 52, 58]****(recombinant, adsorbed) -****EMA/H/C/003852/II/0044**

MSD Vaccins, Rapporteur: Kristina Dunder

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**Herceptin - trastuzumab -****EMA/H/C/000278/II/0166**

Roche Registration GmbH, Rapporteur: Jan  
Mueller-Berghaus

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**Herzuma - trastuzumab -****EMA/H/C/002575/II/0035/G**

Celltrion Healthcare Hungary Kft., Rapporteur:  
Jan Mueller-Berghaus

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**Hizentra - human normal immunoglobulin -****EMA/H/C/002127/II/0122**

CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

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**ILARIS - canakinumab -****EMA/H/C/001109/II/0072/G**

Novartis Europharm Limited, Rapporteur: Jan  
Mueller-Berghaus

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**Inflectra - infliximab -****EMA/H/C/002778/II/0094/G**

Pfizer Europe MA EEIG, Duplicate, Duplicate of  
Remsima, Rapporteur: Outi Mäki-Ikola

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**Inhixa - enoxaparin sodium -****EMA/H/C/004264/II/0073/G**

Techdow Pharma Netherlands B.V., Duplicate,  
Duplicate of Thorinane (EXP), Rapporteur:  
Andrea Laslop

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**Kadcyla - trastuzumab emtansine -****EMA/H/C/002389/II/0053**

Roche Registration GmbH, Rapporteur: Sinan B.

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Sarac

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**Kovaltry - octocog alfa -  
EMA/H/C/003825/II/0033**

Bayer AG, Rapporteur: Kristina Dunder

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**Lucentis - ranibizumab -  
EMA/H/C/000715/II/0090/G**

Novartis Europharm Limited, Rapporteur:  
Kristina Dunder

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**M-M-RVAXPRO - measles, mumps and  
rubella vaccine (live) -  
EMA/H/C/000604/II/0105**

MSD Vaccins, Rapporteur: Jan Mueller-Berghaus

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**MabThera - rituximab -  
EMA/H/C/000165/II/0179**

Roche Registration GmbH, Rapporteur: Sinan B.  
Sarac

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**Mepsevii - vestronidase alfa -  
EMA/H/C/004438/II/0019, Orphan**

Ultragenyx Germany GmbH, Rapporteur:  
Johann Lodewijk Hillege

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**MVASI - bevacizumab -  
EMA/H/C/004728/II/0017**

Amgen Technology (Ireland) Unlimited  
Company, Duplicate, Duplicate of KYOMARC,  
Rapporteur: Bjorg Bolstad

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**Myalepta - metreleptin -  
EMA/H/C/004218/II/0017/G, Orphan**

Amryt Pharmaceuticals DAC, Rapporteur: Karin  
Janssen van Doorn

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**Nucala - mepolizumab -  
EMA/H/C/003860/II/0038**

GlaxoSmithKline Trading Services Limited,  
Rapporteur: Peter Kiely

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**Orfadin - nitisinone -  
EMA/H/C/000555/II/0075**

Swedish Orphan Biovitrum International AB,  
Rapporteur: Armando Genazzani

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**Ozempic - semaglutide -  
EMA/H/C/004174/II/0019**

Novo Nordisk A/S, Rapporteur: Johann Lodewijk  
Hillege

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**POTELIGEO - mogamulizumab -  
EMA/H/C/004232/II/0008, Orphan**

Kyowa Kirin Holdings B.V., Rapporteur: Paula

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Boudewina van Hennik

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**Privigen - human normal immunoglobulin -  
EMA/H/C/000831/II/0170/G**

CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

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**ProQuad - measles, mumps, rubella and  
varicella vaccine (live) -  
EMA/H/C/000622/II/0144**

MSD Vaccins, Rapporteur: Jan Mueller-Berghaus

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**Puregon - follitropin beta -  
EMA/H/C/000086/II/0113**

Merck Sharp & Dohme B.V., Rapporteur: Peter Kiely

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**Quofenix - delafloxacin -  
EMA/H/C/004860/II/0007/G**

A. Menarini Industrie Farmaceutiche Riunite s.r.l., Rapporteur: Janet Koenig

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**Remsima - infliximab -  
EMA/H/C/002576/II/0096/G**

Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola

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**RoActemra - tocilizumab -  
EMA/H/C/000955/II/0098/G**

Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus

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**Ruconest - conestat alfa -  
EMA/H/C/001223/II/0058**

Pharming Group N.V, Rapporteur: Andrea Laslop

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**Soliris - eculizumab -  
EMA/H/C/000791/II/0115/G, Orphan**

Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa

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**Surgiflo Haemostatic Matrix Kit - human  
thrombin - EMA/H/D/002301/II/0021**

Presafe Denmark A/S, Rapporteur: Jan Mueller-Berghaus

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**Surgiflo Haemostatic Matrix Kit - human  
thrombin - EMA/H/D/002301/II/0022**

Presafe Denmark A/S, Rapporteur: Jan Mueller-Berghaus

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**Tecentriq - atezolizumab -  
EMA/H/C/004143/II/0051**

Roche Registration GmbH, Rapporteur: Sinan B. Sarac

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**Toujeo - insulin glargine -****EMA/H/C/000309/II/0117/G**

Sanofi-Aventis Deutschland GmbH, Duplicate,  
Duplicate of Lantus, Rapporteur: Johann  
Lodewijk Hillege

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**Vaxelis - diphtheria, tetanus, pertussis  
(acellular, component), hepatitis B (rDNA),  
poliomyelitis (inact.) and haemophilus type  
B conjugate vaccine (adsorbed) -****EMA/H/C/003982/II/0070**

MCM Vaccine B.V., Rapporteur: Christophe  
Focke

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**Votrient - pazopanib -****EMA/H/C/001141/II/0063/G**

Novartis Europharm Limited, Rapporteur: Sinan  
B. Sarac

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**VPRIV - velaglucerase alfa -****EMA/H/C/001249/II/0051, Orphan**

Shire Pharmaceuticals Ireland Limited,  
Rapporteur: Martina Weise

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**Zaltrap - aflibercept -****EMA/H/C/002532/II/0058/G**

sanofi-aventis groupe, Rapporteur: Filip  
Josephson

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**Zavicefta - ceftazidime / avibactam -****EMA/H/C/004027/II/0025/G**

Pfizer Ireland Pharmaceuticals, Rapporteur:  
Bjorg Bolstad

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**WS1935****Mircera-EMA/H/C/000739/WS1935/0083****NeoRecormon-EMA/H/C/000116/****WS1935/0110**

Roche Registration GmbH, Lead Rapporteur:  
Martina Weise

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**WS1942/G****Fluenz Tetra-EMA/H/C/002617/****WS1942/0103/G****Pandemic influenza vaccine H5N1****AstraZeneca-EMA/H/C/003963/****WS1942/0038/G**

AstraZeneca AB, Lead Rapporteur: Christophe  
Focke

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**WS1943/G****Fluenz Tetra-EMA/H/C/002617/****WS1943/0104/G****Pandemic influenza vaccine H5N1**

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**AstraZeneca-EMEA/H/C/003963/**

**WS1943/0039/G**

AstraZeneca AB, Lead Rapporteur: Christophe Focke

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**WS1954**

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

**WS1954/0289**

GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

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**WS1959**

**Hexacima-EMEA/H/C/002702/**

**WS1959/0109**

**Hexaxim-EMEA/H/W/002495/**

**WS1959/0114**

**Hexyon-EMEA/H/C/002796/**

**WS1959/0113**

Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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**WS1960**

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

**WS1960/0290**

GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

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**WS1974**

**Ratiograstim-EMEA/H/C/000825/**

**WS1974/0070**

**Tevagrastim-EMEA/H/C/000827/**

**WS1974/0078**

TEVA GmbH, Duplicate, Duplicate of Biograstim (SRD), Lead Rapporteur: Outi Mäki-Ikola

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

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**Adcetris - brentuximab vedotin -**

**EMEA/H/C/002455/II/0085, Orphan**

Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, "Update of the SmPC section 5.1 with the 5 year long-term follow up and final OS results for the C25007 study in HL. Editorial updates have been also implemented in the PI."

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**Adjupanrix - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) -**

**EMEA/H/C/001206/II/0072/G**

GlaxoSmithkline Biologicals SA, Informed Consent of Pandemrix (EXP), Rapporteur: Johann Lodewijk Hillege, "A grouped application"

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of 3 type II variations under category C.I.13:  
- Submission of a safety pharmacology study performed to assess the effect of AS03 alone and the adjuvanted influenza antigen on cardiovascular and respiratory of telemetered dogs (study MDS AA80120). - Submission of a biodistribution study (study GSK-CH-02-11) conducted in mice with the 3 components of the AS03 Adjuvant System radio-labelled ([<sup>14</sup>C]- $\alpha$ -tocopherol, [<sup>14</sup>C]-squalene, and [<sup>3</sup>H]-polysorbate) to support the understanding of mode of action of AS03. - Submission of a GLP reproductive and developmental toxicity study (study HLS GVB/007/063710) conducted to evaluate the effect of AS03 on embryo-fetal and peri- and post-natal development in CrI:CD (SD) IGS BR rats following intramuscular administration.”

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**Cosentyx - secukinumab -  
EMA/H/C/003729/II/0069**

Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola, “Update of section 5.1 of the SmPC based on final results from study CAIN457F3302; this is a randomised, double-blind, placebo-controlled study (MAXIMISE) which assessed the efficacy of secukinumab in PsA patients with axial manifestations who were naive to biologic treatment and responded inadequately to NSAIDs; the MAH took this opportunity to introduce minor editorial changes in section 5.1 of the SmPC.”

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**Cyramza - ramucirumab -  
EMA/H/C/002829/II/0039**

Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, “Update of section 4.8 of the SmPC in order to add hypothyroidism to the list of adverse reactions with a frequency of common based on the updated reference safety information for ramucirumab. The Package Leaflet is also updated. In addition, minor updates are included to the list of local representatives in the product information.”

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**Dapivirine Vaginal Ring 25 mg - dapivirine  
- EMA/H/W/002168/II/0003**

International Partnership for Microbicides Belgium AISBL, Rapporteur: Paula Boudewina van Hennik, “Submission of the final bioanalytical (sub)reports or annexes for the long-term stability experiments for the plasma

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and vaginal fluid samples of studies IPM 027 and IPM 035.”

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**Dupixent - dupilumab -**

**EMA/H/C/004390/II/0039**

sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, “To update section 4.8 of the SmPC to replace tables of adverse drug reactions per indication with a consolidated table of adverse drug reactions across all approved indications as agreed in the latest PSUR (EMA/H/C/PSUSA/00010645/ 202003). The Package Leaflets are updated accordingly.”

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**Enbrel - etanercept -**

**EMA/H/C/000262/II/0238**

Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, “Update of section 4.8 of the SmPC to add headache to the list of adverse drug reactions with a frequency very common; the package leaflet is updated accordingly. In addition, the MAH took the opportunity to remove text for inflammatory bowel disease and uveitis specific to the paediatric population from section 4.4 and 4.8 of the SmPC and the package leaflet for consistency as requested by PRAC in the latest PSUSA (PSUSA/00010795/202002).”

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**Epivir - lamivudine -**

**EMA/H/C/000107/II/0114**

ViiV Healthcare B.V., Rapporteur: Jean-Michel Race, “Update of sections 5.2 of the SmPC to add new information about the biotransformation of lamivudine. Furthermore, the MAH took the opportunity to introduce an excipient update in line with the SmPC guideline, a syringe and adapter instruction update in the Package Leaflet and a revision of Annex II in line with the QRD template. Moreover, minor editorial updates have been introduced throughout the Product Information.”

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**Eylea - aflibercept -**

**EMA/H/C/002392/II/0067**

Bayer AG, Rapporteur: Alexandre Moreau

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**Fabrazyme - agalsidase beta -**

**EMA/H/C/000370/II/0119**

Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, “Submission of the final report following CHMP conclusions on the related post-authorisation measure (MEA 57.12) from the

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Fabry registry, a global, observational and voluntary program designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Fabry disease. This is a long-term effectiveness study to enhance the understanding of long-term severe events and clinical continuous outcomes of Fabrazyme among 5 subgroups identified by modified Arends criteria, estimate the disease progression after Fabrazyme treatment among Classic male patients with sustained anti-agalsidase beta immunoglobulin G (IgG) antibodies (ADA); and compare the long-term effectiveness of Fabrazyme between Classic patients with lower-dose regimen and those with standard-dose regimen.”

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PRAC Led

**Fluad Tetra - influenza vaccine (surface antigen, inactivated, adjuvanted) - EMEA/H/C/004993/II/0008**

Seqirus Netherlands B.V., Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Karin Janssen van Doorn, “C.I.11.b: Submission of an updated RMP version 1.9 in order to provide a consolidated RMP for adjuvanted trivalent influenza vaccine (aTIV) and adjuvanted quadrivalent influenza vaccine (aQIV), including an alignment of safety concerns for aTIV and aQIV.”

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**Imbruvica - ibrutinib -**

**EMA/H/C/003791/II/0064, Orphan**

Janssen-Cilag International NV, Rapporteur: Filip Josephson, “Update of the SmPC section 5.1 to include PFS2 and data from the final analysis with long-term follow-up relevant to the Waldenström’s macroglobulinaemia (WM) indication and section 4.8, to include the long-term safety cumulative data - following the submission of the addendum to the final clinical study report from study PCYC-1127-CA. In addition, an amendment to section 4.4 of the SmPC to add adequate language regarding excipients with known effect and an amendment to Table 1 of the SmPC to include a footnote by cardiac failure to reflect inclusion of events with fatal outcomes were implemented. The Package Leaflet was revised accordingly.”

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**Invokana - canagliflozin -**

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**EMA/H/C/002649/II/0055**

Janssen-Cilag International NV, Rapporteur:  
Martina Weise, "Update to sections 4.2 and 5.1 of the Invokana SmPC to amend posology information concerning the treatment of patients with eGFR between  $\geq 30$  and  $< 45$  mL/min/1.73 m<sup>2</sup>, whether or not albuminuria is present; the update is based on further analysis of previously submitted CANVAS data (studies DIA3008 and DIA4003).  
The Applicant has also taken the opportunity to make minor editorial changes to section 4.5."

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**Iressa - gefitinib -****EMA/H/C/001016/II/0034**

AstraZeneca AB, Rapporteur: Filip Josephson,  
"Update of section 4.8 of the SmPC in order to add Palmar-plantar erythrodysesthesia syndrome to the list of adverse drug reactions (ADRs) with frequency uncommon; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1."

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**Kisplyx - lenvatinib -****EMA/H/C/004224/II/0039/G**

Eisai GmbH, Rapporteur: Karin Janssen van Doorn, "C.I.13. Submission of a nonclinical (primary pharmacodynamics) study report-M14014 on the Antiproliferative Activities of Lenvatinib Mesilate and Sorafenib Tosylate in VEGF-Stimulated Growth of HUVECs.  
C.I.13. Submission of a nonclinical (primary pharmacodynamics) study report-W-20140845 on the Antiangiogenic Activity of Lenvatinib Mesilate and Sorafenib Tosylate in bFGF-Induced Matrigel Plug Assay in Athymic Mice."

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**Mavenclad - cladribine -****EMA/H/C/004230/II/0016**

Merck Europe B.V., Rapporteur: Kirstine Moll Harboe, "C.I.4 Update of section 4.8 of the SmPC in order to add hypersensitivity to the list of adverse drug reactions (ADRs) with frequency "common" based on a review of cumulative clinical and post-marketing data. The Package Leaflet is updated accordingly."

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**Nilemdo - bempedoic acid -****EMA/H/C/004958/II/0007**

Daiichi Sankyo Europe GmbH, Rapporteur:  
Johann Lodewijk Hillege, "C.I.13: Submission of the final report from clinical study 1002-050"

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listed as a category 3 study in the RMP (MEA). This is a multicenter open-label extension (OLE) study to assess the long-term safety and efficacy of bempedoic acid 180 mg. Study 1002-050 was a roll-over extension study of a long-term (52 weeks), randomized, double-blind, controlled study (Study 1002-040, referred to as the parent study) of bempedoic acid 180 mg once daily versus placebo with a 2:1 randomization.”

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**Nustendi - bempedoic acid / ezetimibe -  
EMA/H/C/004959/II/0007**

Daiichi Sankyo Europe GmbH, Rapporteur: Johann Lodewijk Hillege, “C.I.13: Submission of the final report from clinical study 1002-050 listed as a category 3 study in the RMP (MEA). This is a multicenter open-label extension (OLE) study to assess the long-term safety and efficacy of bempedoic acid 180 mg. Study 1002-050 was a roll-over extension study of a long-term (52 weeks), randomized, double-blind, controlled study (Study 1002-040, referred to as the parent study) of bempedoic acid 180 mg once daily versus placebo with a 2:1 randomization.”

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**Ocrevus - ocrelizumab -  
EMA/H/C/004043/II/0023**

Roche Registration GmbH, Rapporteur: Kirstine Moll Harboe, “To update SmPC (section 5.1) with the newly available post-hoc analysis results related to the time-to-wheelchair data performed on clinical study WA25046 (ORATORIO) in the PPMS population.”

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**Opsumit - macitentan -  
EMA/H/C/002697/II/0039, Orphan**

Janssen-Cilag International N.V., Rapporteur: Maria Concepcion Prieto Yerro, “Update of sections 4.4, 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information of macitentan with moderate dual inhibitors of CYP3A4 and CYP2C9 based on results from a non-clinical study and a physiologically based pharmacokinetic study in healthy subjects and CYP2C9 poor metabolizers; the Package Leaflet is updated accordingly. A direct healthcare professional communication (DHPC) for this new safety information is being proposed. In addition, the MAH took the opportunity to update the list of local representatives in the

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Package Leaflet.”

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**Orgalutran - ganirelix -**

**EMA/H/C/000274/II/0046**

Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, “Update of section 4.2 of the SmPC in order to include information on handling air bubbles in the pre-filled syringes. The MAH aligned the Package Leaflet accordingly and took the opportunity to update the list of local representatives and to implement minor editorial changes in the PI.”

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**Perjeta - pertuzumab -**

**EMA/H/C/002547/II/0055**

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, “Submission of the final report from study BO25114 (JACOB). This is a double-blind, placebo-controlled, randomized, multicenter phase III study evaluating the efficacy and safety of pertuzumab in combination with trastuzumab and chemotherapy in patients with HER2-positive metastatic gastroesophageal junction and gastric cancer.”

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**Pravafenix - fenofibrate / pravastatin**

**sodium - EMA/H/C/001243/II/0030**

Laboratoires SMB s.a., Rapporteur: Jean-Michel Race, “Update of section 4.5 of the SmPC in order to add drug-drug interaction information with glitazones resulting in HDL cholesterol decrease, as already mentioned in the Product Information of other products containing fenofibrate 160 mg; update of sections 2 and 4.4 of the SmPC to correct the warning on lactose and to implement the wording on sodium, in line with the latest revision of the Excipients guideline. The Package Leaflet and the Labelling are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.1.”

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**Taltz - ixekizumab -**

**EMA/H/C/003943/II/0040**

Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, “Update of section 5.1 of the SmPC with long-term efficacy and safety data in axial spondyloarthritis from study RHBV - A multicenter, long-term extension study of 104 weeks, including a double-blind, placebo-controlled 40-week

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randomized withdrawal–retreatment period, to evaluate the maintenance of treatment effect of ixekizumab in patients with axial spondyloarthritis.”

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**Thalidomide Celgene - thalidomide -  
EMA/H/C/000823/II/0066**

Celgene Europe BV, Rapporteur: Alexandre Moreau, “Update of section 4.8 to include PML. This change is being introduced following the approval of version 11 of the Company Core Data Sheet (CCDS) for thalidomide. The PIL is updated accordingly.”

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**Xydalba - dalbavancin -  
EMA/H/C/002840/II/0037**

Allergan Pharmaceuticals International Limited, Rapporteur: Filip Josephson, “Submission of the final report from the microbial surveillance study 14-DUR-01, listed as a category 3 study in the RMP. This is a microbial surveillance study of dalbavancin activity tested against clinical isolates collected in Europe and United States. This submission addresses the post-authorisation measure MEA 002.3.”

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**WS1963**

**Leganto-EMA/H/C/002380/WS1963/  
0033**

**Neupro-EMA/H/C/000626/WS1963/0087**

UCB Pharma S.A., Lead Rapporteur: Bruno Sepodes, “To update section 4.4 of the SmPC to add a warning following the update of the Company Core Data Sheet (CCDS) for rotigotine. The CCDS update consists in the addition of 2 warnings related to dopamine dysregulation syndrome and dopamine agonist withdrawal syndrome; Section 2 of the Package Leaflet is updated accordingly.”

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**WS1976**

**Kisplyx-EMA/H/C/004224/WS1976/0040**

**Lenvima-EMA/H/C/003727/WS1976/  
0039**

Eisai GmbH, Lead Rapporteur: Karin Janssen van Doorn, “C.I.13-Submission of the final nonclinical (pharmacokinetic) study report-XT205008 on the Inhibitory potential on UDP-glucuronosyltransferase 2B17 by E7080 in human liver microsomes.”

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

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##### **ADYNOVI - ruriotocog alfa pegol - EMA/H/C/004195/II/0017**

Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst, ,  
"Update of sections 4.8 and 5.1 of the SmPC to provide results from the further analysis of the continuation study 261302 and the pharmacokinetics-guided dosing study 261303. The MAH took the opportunity to update the "sodium statement" in section 4.4 of the SmPC per the EU Excipient Guidelines. The Package Leaflet has been updated accordingly. The RMP version 2 has also been submitted."

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##### **Erleada - apalutamide - EMA/H/C/004452/II/0009**

Janssen-Cilag International N.V., Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Tiphaine Vaillant, "Update of section 5.3 of the SmPC in order to include non-clinical information based on final results from a 26-week carcinogenicity study (TOX13540) listed as a category 3 study in the RMP. The RMP version 3.2 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.1."

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##### **EXJADE - deferasirox - EMA/H/C/000670/II/0075**

Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, "The PI has been updated to remove discrepancies between SmPC and PL in sections 'Pregnancy and breast-feeding' and section 'Other medicines and EXJADE'. Furthermore, the Exjade SmPC and PL have been updated according to the Guidelines on excipients in the labelling and package leaflet of medicinal products for human use, Rev. 2. The MAH took also the opportunity to align the PI with the latest QRD template v. 10.1 and update the details of local representatives in EE, LV and NL. The Annex IID has been updated to reflect the new milestone for study C1670E2422. In addition, the EU RMP version 18.0 for Exjade has been revised to introduce following changes:

- Removal of the important identified risk,
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"Severe cutaneous adverse reactions (including Stevens-Johnson syndrome, Toxic epidermal necrolysis and Drug reaction with eosinophilia and systemic symptoms)"

- Change to the milestone for study CICAL670E2422 (category 1) and change to RMP commitment deliverable and milestone for study CICAL670F2202 (category 3)
- Removal of the study CICAL670F2429 (category 1) due to fulfilment of the corresponding Post-Authorisation Measure
- Removal of the expedited reporting requirement for the serious Adverse Drug Reactions (ADRs), 'Increase in hepatic enzymes >10 x upper limit of normal (ULN)', 'Serious rise in creatinine', 'results of renal biopsies', 'cataracts', 'hearing loss', gallstones' as agreed during PRAC PSUR Assessment (Procedure no.: EMEA/H/C/PSUSA/00000939/201910)."

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**Isentress - raltegravir -  
EMEA/H/C/000860/II/0093**

Merck Sharp & Dohme B.V., Rapporteur:  
Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, "Update of section 4.6 of the SmPC in order to update safety information following pregnancy outcome data for raltegravir 400 mg film-coated tablet from prospective reports of pregnancy data with known outcome and time of raltegravir exposure. The updated RMP version 15.1 has also been submitted. In addition, the MAH took the opportunity to correct an inconsistency in the text describing the possibility to divide the scored 100 mg chewable tablet by harmonising the text of the footer of Tables 1 and 2 of the chewable tablets' SmPC. This was already identified in the procedure EMEA/H/C/000860/IB/0087 and is in line with the assessment done in the extension application for the chewable tablets EMEA/H/C/000860/X/0024/G. Finally, the contact details of Germany have been updated in the List of local Representatives and the PI is being brought in line with the latest QRD template (version 10.1)"

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**Jakavi - ruxolitinib -  
EMEA/H/C/002464/II/0050**

Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Update of sections 4.2 and 5.1 of the SmPC in

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order to update the posology and the method of administration as well as to include the A2201/EXPAND study CINC424A2201 (referred to as A2201 or "EXPAND" study). The changes are based on final results of a category 3 clinical study, phase Ib study to fulfil an RMP post approval commitment. This is a dose-finding study intended to establish the maximum safe starting dose (MSSD) of ruxolitinib tablets administered orally to patients with MF in the previous unstudied population of patients who had baseline platelet counts  $\geq 50 \times 10^9/L$  and  $< 100 \times 10^9/L$ . The Package Leaflet is updated accordingly.

The RMP version 12 has also been submitted based on the results of study A2201 (category 3, additional pharmacovigilance activity), the review of safety concerns in compliance with the Good Pharmacovigilance Practices Module V, Revision 2, as well as recent PRAC outcome on PSUR (Procedure no.: EMEA/H/C/PSUSA/00010015/202002, CHMP Opinion dated 15-Oct-2020)."

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**Perjeta - pertuzumab -  
EMA/H/C/002547/II/0054**

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, "Submission of the final report from study MO28047 (PERUSE) listed as an obligation in the Annex II of the Product Information. This is a multicenter, open-label, single-arm study of pertuzumab in combination with trastuzumab and a taxane in first line treatment of patients with HER2- positive advanced (metastatic or locally recurrent) breast cancer. The RMP (version 13.0) is proposed to be updated accordingly."

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**Pyramax - pyronaridine / artesunate -  
EMA/H/W/002319/II/0023/G**

Shin Poong Pharmaceutical Co., Ltd., Rapporteur: Jean-Michel Race, PRAC Rapporteur: Adrien Inoubli, "Grouping of variations providing the final clinical study reports (CSR) of two completed studies:  
- Study SP-C-021-15: A Phase IIIb/IV cohort event monitoring study conducted in Central Africa to evaluate the safety in patients after the local registration of Pyramax (CANTAM study). This study is a Category 3 Required Additional Pharmacovigilance Activity described in the RMP

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(MEA 013).

- SP-C-026-18: A Randomized Open-Label Exploratory Study to Determine The Efficacy of Different Treatment Regimens of Pyramax (Pyronaridine-Artesunate) In Asymptomatic Carriers Of Plasmodium Falciparum Monoinfections. This non-imposed study was conducted in Gambia and Zambia and compared asymptomatic subjects with parasitaemia dosed according to the approved label of 3-day dosing with 2-day and 1-day dosing. There have been no new safety findings from the study but the RMP has been updated to reflect its details. As a result of the additional clinical data, corresponding changes to the Product Information (SmPC and PL) are proposed with the Grouping.

RMP version 17 has also been submitted, updated to reflect the results of both above-mentioned CSRs, and converted to the new RMP integrated template format (Rev 2.0.1)."

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**Qtern - saxagliptin / dapagliflozin -  
EMA/H/C/004057/II/0031**

AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ilaria Baldelli, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect new data based on final results from study D1693C00001 (DECLARE). This is a multi-centre, randomised, double-blind, placebo-controlled study to evaluate the effect of dapagliflozin on cardiovascular (CV) and renal outcomes in patients with T2DM with or without established CV disease. The labelling and Package Leaflet (PL) are updated accordingly. The Risk Management Plan (RMP) v5.1 has also been updated. The MAH took the opportunity to make additional editorial changes to the PI."

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**Revolade - eltrombopag -  
EMA/H/C/001110/II/0063**

Novartis Europharm Limited, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "Update of sections 4.2, 4.8 and 5.2 of SmPC to clarify dosing recommendations to ensure accurate treatment of patients of 'East-/Southeast-Asian' ancestry and to correct the ADR list based on currently available data, which was previously submitted and reviewed. Update of section 4.4 of the SmPC in line with the 'Excipients in the labelling and package leaflet of medicinal products for human use'.

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The Package leaflet has been updated accordingly.

An updated RMP has been submitted to update the final due date i.e. the date for the provision of the primary study report of CETB115E2201 (category 3) in the RMP and removal of important safety concerns, already endorsed by PRAC in the PSUSA procedure (EMA/H/C/PSUSA/00001205/201809)."

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**Steglujan - ertugliflozin / sitagliptin -  
EMA/H/C/004313/II/0015**

Merck Sharp & Dohme B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC for Steglujan in order to update clinical information following final results from the VERTIS CV study (protocol 8835-004/B1521021) listed as a category 3 study in the RMP. This is a multi-centre, multi-national, randomised, double-blind, placebo-controlled study to evaluate the effect of ertugliflozin on cardiovascular risk in adult patients with type 2 diabetes and established atherosclerotic cardiovascular disease. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity include an editorial change in section 4.1 of the SmPC."

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**Tasigna - nilotinib -  
EMA/H/C/000798/II/0107**

Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, "Submission of the 5-year data including data on late relapses from the ongoing studies ENESTfreedom (CAMN107I2201): A Phase II, single-arm, open-label, multicenter nilotinib TFR study in patients with BCR-ABL1 positive CML-CP, who had achieved durable minimal residual disease (MRD) status on first-line nilotinib treatment and ENESTop (CAMN107A2408): A Phase II, single-arm, open-label, multicenter study, evaluating TFR in patients with BCR-ABL1-positive CML-CP who achieved a sustained molecular response of MR4.5 on nilotinib treatment after switching from imatinib to nilotinib.

Consequently, the RMP version 23 is being updated to remove the additional pharmacovigilance activity 'collection and submission of data on late relapses from the

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ongoing studies ENESTfreedom (CAMN107I2201) and ENESTop (CAMN107A2408)' and the safety concern 'risk of resistance (in TFR)'."

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**TECFIDERA - dimethyl fumarate -  
EMA/H/C/002601/II/0069/G**

Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "C.I.4 type II variation: Update of section 4.8 of the SmPC in order to add rhinorrhoea to the list of adverse drug reactions (ADRs) with frequency unknown based on a systematic review of information from clinical and non-clinical studies, post-marketing data and scientific literature. The Package Leaflet has been updated accordingly.

C.I.4 type II variation: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study 109MS303 (ENDORSE) listed as a category 3 study in the RMP. This is a dose-blind, multicenter, extension study to determine the long-term safety and efficacy of two doses of BG00012 monotherapy in subjects with Relapsing-Remitting Multiple Sclerosis. The RMP version 11.1 has also been submitted."

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**Trumenba - meningococcal group B vaccine  
(recombinant, adsorbed) -  
EMA/H/C/004051/II/0032**

Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné, "C.I.4 To update sections 4.8 and 5.1 of the SmPC following the interim data from the primary vaccination phase (Stage 1) of study B1971057; this is a Phase 3, randomised, active-controlled, observer-blinded study to assess the immunogenicity, safety, and tolerability of bivalent rLP2086 when administered as a 2-dose regimen and a first-in-human study to describe the immunogenicity, safety, and tolerability of a bivalent rLP2086 containing pentavalent vaccine (MenABCWY) in healthy subjects  $\geq 10$  to  $< 26$  years of age. The MAH takes the opportunity to implement some editorial changes in section 4.4 of the SmPC and sections 2, 3 and 6 of the Package Leaflet in order to comply with the excipients guideline for Sodium Chloride."

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**Vargatef - nintedanib -**

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**EMA/H/C/002569/II/0037**

Boehringer Ingelheim International GmbH,  
Rapporteur: Sinan B. Sarac, PRAC Rapporteur:  
Agni Kapou, "Submission of the final report from  
study LUME BioNIS listed as an obligation in the  
Annex II of the Product Information. This is a  
non-interventional study in patients eligible for  
treatment with Vargatef to explore whether  
genetic or genomic markers (alone or combined  
with clinical covariates) could be used to predict  
overall survival. The Annex II and the RMP  
version 8.0 are updated accordingly."

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**Vimizim - elosulfase alfa -****EMA/H/C/002779/II/0034, Orphan**

BioMarin International Limited, PRAC  
Rapporteur: Rhea Fitzgerald, "Submission of an  
updated RMP version 5 in order to update the  
safety specifications (epidemiology of indication  
and target populations, exposures in clinical  
trials and post-marketing) and the  
pharmacovigilance plan (routine and additional  
pharmacovigilance activities). Deletion of a  
training material in section V.1 and addition of  
healthcare provider educational materials and  
process indicator to evaluate the distribution of  
the educational materials. Part VI and VII have  
been updated accordingly. The RMP has also  
been updated in line with EU RMP template  
(revision 2.0.1)."

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**Xeljanz - tofacitinib -****EMA/H/C/004214/II/0028**

Pfizer Europe MA EEIG, Rapporteur: Armando  
Genazzani, PRAC Rapporteur: Liana Gross-  
Martirosyan, "Submission of the final report on  
Biospecimen testing study, listed as a category  
3 study in the RMP. This is an exploratory study  
to assess biomarkers related to VTE events in  
study A3921133. The RMP version 14.1 has also  
been submitted."

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**WS1965/G****Hexacima-EMA/H/C/002702/WS1965/  
0110/G****Hexaxim-EMA/H/W/002495/WS1965/  
0115/G****Hexyon-EMA/H/C/002796/WS1965/  
0114/G**

Sanofi Pasteur, Lead Rapporteur: Jan Mueller-  
Berghaus, Lead PRAC Rapporteur: Brigitte  
Keller-Stanislawski, "C.I.4 (type II): Update of

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section 5.1 of the SmPC in order to describe the persistence of anti-HBs antibodies in subjects 6 years of age having received a hexavalent vaccine based on the final results from study A3L00052; this is a phase IV, open-label, multi-centre study in children previously vaccinated in study A3L38a with 3 doses of either Hexacima/Hexyon/Hexaxim (Group 1) or Infanrix Hexa (Group 2).

C.I.4 (type II): Update of sections 4.4 and 5.1 of the SmPC in order to reword safety and immunogenicity information regarding individuals with immunodeficiency based on the final results from study A3L44; this is a Phase III, single centre, open-label, two-arm study including HIV-exposed infected and uninfected infants vaccinated with a 3-dose infant primary series (at 6, 10, and 14 weeks of age) and a booster dose (at 15 to 18 months of age) with Hexacima/Hexyon/Hexaxim in Republic of South Africa. The updates to the SmPC were requested following assessment of these data by Article 46, EMEA/H/C/002702/P46/036 (Hexacima), EMEA/H/C/002796/P46/034 (Hexyon) and EMEA/H/W/002495/P46/036 (Hexaxim).

C.I.z (type IB): Updated of section 4.4 of the SmPC in order to include syncope within the precautions for use. The package leaflet is updated accordingly. In addition, the WSA took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 13.0 has also been submitted.”

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#### **B.6.11. PRAC assessed procedures**

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PRAC Led

##### **Adasuve - loxapine -**

##### **EMEA/H/C/002400/II/0032**

Ferrer Internacional s.a., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, “To submit the final clinical study report (CSR) for Study AMDC- 204-401 EU PASS: Post-authorisation Observational Study to Evaluate the Safety of ADASUVE - Staccato

loxapine for inhalation- in Agitated Persons in Routine Clinical Care.”

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PRAC Led

##### **Cetrotide - cetrorelix -**

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**EMA/H/C/000233/II/0075**

Merck Europe B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of an updated RMP (version 5.2), in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' including consequential removal of a number of important identified risks and important potential risk of congenital anomalies, as well as removal of missing information on infertile premenopausal women; information in the RMP has been revised based on the most recent data and the post-marketing exposure was updated."

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PRAC Led

**Conbriza - bazedoxifene -****EMA/H/C/000913/II/0054**

Pfizer Europe MA EEIG, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Update of Risk Management Plan (RMP) to include updated study milestones and to revise the RMP format in line with latest Good Pharmacovigilance Practices Guidance Module V, revision 2 guidelines."

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PRAC Led

**Eylea - aflibercept -****EMA/H/C/002392/II/0068**

Bayer AG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "The submission contains the study report of the PASS study Evaluation of Physician Knowledge of Safety and Safe Use Information for Aflibercept in Europe: A Follow-up Physician survey. The study was requested as a category 3 study. RMP has been updated accordingly (version 27.1)."

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PRAC Led

**Fabrazyme - agalsidase beta -****EMA/H/C/000370/II/0120**

Genzyme Europe BV, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report following CHMP conclusions on the related post-authorisation measure (FU2 57.4) from the MAH Fabry Pregnancy Sub-registry, a multicenter, international, longitudinal, observational study on pregnancy outcomes for any pregnant

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woman enrolled in the MAH Fabry Registry who also consented to participate in the Sub-registry, regardless of whether she was receiving disease therapy (such as ERT with agalsidase beta) and irrespective of the commercial product with which she may have been treated. This study is listed as a category 3 in the RMP.”

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PRAC Led

**Mavenclad - cladribine -**

**EMA/H/C/004230/II/0015**

Merck Europe B.V., Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, PRAC-CHMP liaison: Bruno Sepodes, “C.I.11.b type II submission of an updated RMP version 1.4 in order to align to the RMP template Rev. 2. In addition, the MAH took the opportunity to include long-term safety data from the completed PREMIERE registry and remove the completed study from the pharmacovigilance plan, update of the status of the post-approval safety studies CLARION and CLEAR and update the RMP with the most recent post-approval safety data from the PBRER.”

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PRAC Led

**Ovaleap - follitropin alfa -**

**EMA/H/C/002608/II/0034**

Theramex Ireland Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of the final study report for SOFIA (Safety of Ovaleap (Follitropin alfa) in Infertile Women Undergoing Superovulation for Assisted Reproductive Technologies, XM17-WH-5005) listed as a category 3 study in the RMP. This is a multi-national, comparative, prospective, non-interventional, observational cohort study. The RMP version 3.3 has also been submitted.”

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PRAC Led

**Revatio - sildenafil -**

**EMA/H/C/000638/II/0091**

Upjohn EESV, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP version 7.0 in order to update the summary of safety concerns in line with GVP module V rev 2 guidelines. Consequently, the educational programme for

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the risk of hypotension is proposed to be terminated.”

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PRAC Led

**WS1970**

**Eucreas-EMA/H/C/000807/WS1970/0081**

**Galvus-EMA/H/C/000771/WS1970/0067**

**Icandra-EMA/H/C/001050/WS1970/0084**

**Jalra-EMA/H/C/001048/WS1970/0069**

**Xiliarx-EMA/H/C/001051/WS1970/0067**

**Zomarist-EMA/H/C/001049/WS1970/0083**

Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, “RMP (Risk Management Plan) update to version 15.0 and amendment to Annex II of SmPC. The RMP update includes removal of RMP topics as per EMA GVP Module V, rev 2 guidelines and to align with the recommendations in the Galvus/Eucreas EMA/H/C/PSUSA/00003113/201802.”

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

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**Alofisel - darvadstrocel -**

**EMA/H/C/004258/II/0021, Orphan, ATMP**

Takeda Pharma A/S, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder

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**Kymriah - tisagenlecleucel -**

**EMA/H/C/004090/II/0030, Orphan, ATMP**

Novartis Europharm Limited, Rapporteur: Rune Kjekken, CHMP Coordinator: Ingrid Wang, “Update of section 5.1 of the SmPC to include the complete data set (updated overall survival analysis) of study CCTL019B2205J, a Phase II, single arm, multicenter study to determine the efficacy and safety of Kymriah in paediatric subjects with relapsed or refractory B-cell ALL. The clinical results have already been assessed in procedure EMA/H/C/004090/P46/011. In addition, the final ATC code for tisagenlecleucel (L01XX71) has been added as an editorial change.”

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**Yescarta - axicabtagene ciloleucel -**

**EMA/H/C/004480/II/0030, Orphan,**

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**ATMP**

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

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**Yescarta - axicabtagene ciloleucel -  
EMA/H/C/004480/II/0031, Orphan,  
ATMP**

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

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**Yescarta - axicabtagene ciloleucel -  
EMA/H/C/004480/II/0033, Orphan,  
ATMP**

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

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**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**

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**WS1946**

**Copalia-EMA/H/C/000774/WS1946/0113**

**Dafiro-EMA/H/C/000776/WS1946/0117**

**Exforge-EMA/H/C/000716/WS1946/  
0112**

Novartis Europharm Limited, Lead Rapporteur:  
Kirstine Moll Harboe

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**WS1949/G**

**Mosquirix-EMA/H/W/002300/WS1949/  
0050/G**

**Shingrix-EMA/H/C/004336/WS1949/  
0038/G**

GlaxoSmithkline Biologicals SA, Lead  
Rapporteur: Christophe Focke

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**WS1957/G**

**Hexacima-EMA/H/C/002702/WS1957/  
0111/G**

**Hexaxim-EMA/H/W/002495/WS1957/  
0116/G**

**Hexyon-EMA/H/C/002796/WS1957/  
0115/G**

Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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**WS1966**

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**Incresync-EMEA/H/C/002178/WS1966/0035**  
**Vipdomet-EMEA/H/C/002654/WS1966/0030**  
**Vipidia-EMEA/H/C/002182/WS1966/0025**  
Takeda Pharma A/S, Lead Rapporteur: Johann Lodewijk Hillege

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**WS1968**  
**Anoro Ellipta-EMEA/H/C/002751/WS1968/0033**  
**Laventair Ellipta-EMEA/H/C/003754/WS1968/0036**  
**Relvar Ellipta-EMEA/H/C/002673/WS1968/0047**  
**Revinty Ellipta-EMEA/H/C/002745/WS1968/0045**  
GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro

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**WS1973**  
**Infanrix hexa-EMEA/H/C/000296/WS1973/0291**  
GlaxoSmithKline Biologicals SA, Lead Rapporteur: Christophe Focke

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**WS1977**  
**Enurev Breezhaler-EMEA/H/C/002691/WS1977/0033**  
**Seebri Breezhaler-EMEA/H/C/002430/WS1977/0033**  
**Tovanor Breezhaler-EMEA/H/C/002690/WS1977/0037**  
Novartis Europharm Limited, Lead Rapporteur: Kirstine Moll Harboe

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**WS1980**  
**Axura-EMEA/H/C/000378/WS1980/0082**  
**Memantine Merz-EMEA/H/C/002711/WS1980/0018**  
Merz Pharmaceuticals GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro

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**WS1983/G**  
**Delstrigo-EMEA/H/C/004746/WS1983/0021/G**  
**Pifeltro-EMEA/H/C/004747/WS1983/0015/G**  
Merck Sharp & Dohme B.V., Lead Rapporteur: Filip Josephson

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**WS1985**

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**Aflunov-EMEA/H/C/002094/WS1985/  
0067**

**Foclivia-EMEA/H/C/001208/WS1985/  
0063**

Seqirus S.r.l, Lead Rapporteur: Armando  
Genazzani

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**WS1992/G**

**Nuwiq-EMEA/H/C/002813/WS1992/  
0038/G**

**Vihuma-EMEA/H/C/004459/WS1992/  
0020/G**

Octapharma AB, Lead Rapporteur: Jan Mueller-  
Berghaus

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**WS1996**

**Rixathon-EMEA/H/C/003903/WS1996/  
0046**

**Riximyo-EMEA/H/C/004729/WS1996/  
0046**

Sandoz GmbH, Lead Rapporteur: Jan Mueller-  
Berghaus

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**WS1999**

**Nuwiq-EMEA/H/C/002813/WS1999/0040**

**Vihuma-EMEA/H/C/004459/WS1999/  
0022**

Octapharma AB, Lead Rapporteur: Jan Mueller-  
Berghaus

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## **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. Timetables – 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).

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

**F.1. 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 07-10 December 2020 CHMP plenary:**

<b>Endocrinology-Gynaecology-Fertility-Metabolism</b>	
treatment of Hypoparathyroidism (SME)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
<b>Oncology</b>	
treatment of NRG1+ cancers (histology-independent), (SME)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
<b>ECT-001-CB</b> urgent allogeneic haematopoietic stem cell transplantations, (SME)	The CHMP granted eligibility to PRIME and adopted the critical summary report.

#### **G.3.2. List of procedures starting in December 2020 for January 2021 CHMP adoption of outcomes**

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