30 September 2019
EMA/CHMP/486041/2019 Corr.1[1]
Inspections, Human Medicines Pharmacovigilance and Committees Division

# Committee for medicinal products for human use (CHMP)

## Final Minutes for the meeting on 24-27 June 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

**Disclaimers**

Some of the information contained in the minutes is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published in the CHMP meeting highlights once the procedures are finalised and start of referrals will also be available.

Of note, the minutes are a working document primarily designed for CHMP members and the work the Committee undertakes.

**Note on access to documents**

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

[1] Correction in section 3.1.2

**Temporary visiting address** Spark building ● Orlyplein 24 ● 1043 DP Amsterdam ● The Netherlands
**For deliveries** refer to www.ema.europa.eu/how-to-find-us
**Send us a question** via www.ema.europa.eu/contacts **Telephone** +31(0)88 781 6000 An agency of the European Union

© European Medicines Agency, 2019. Reproduction is authorised provided the source is acknowledged.

# Table of contents

# 1. Introduction

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

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some meeting participants in upcoming discussions as included in the pre-meeting list of participants and restrictions. See (current) June 2019 CHMP minutes for the list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session held 24-27 June 2019 (to be published post July 2019 CHMP meeting).

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

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

## 1.2. Adoption of agenda

CHMP agenda for 24-27 June 2019

The CHMP adopted the agenda.

## 1.3. Adoption of the minutes

CHMP minutes for 27-29 May 2019.

ORGAM minutes for 17 June 2019.

The CHMP minutes for 27-29 May 2019 were adopted.

The Minutes of the June 2019 CHMP ORGAM meeting held on 17 June 2019, together with all decisions taken at that meeting, were adopted.

# 2. Oral Explanations

## 2.1. Pre-authorisation procedure oral explanations

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

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

Scope: Oral explanation, SAG Report

**Action**: Oral explanation to be held on Tuesday, 25 June 2019 at time 14:00

List of Outstanding Issues adopted on 26.04.2019, 31.01.2019, 15.11.2018. List of Questions adopted on 31.05.2018.

An oral explanation was held on Tuesday, 25 June 2019. The presentation by the applicant focused on the clinical data in different subgroups.

### 2.1.2. larotrectinib - Orphan - EMEA/H/C/004919

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

Scope: Oral explanation

The list of questions to the BSWP was adopted via written procedure on 12.06.2019.

**Action**: Oral explanation to be held on Monday, 24 June 2019 at time 16:30

List of Outstanding Issues adopted on 29.05.2019, 28.03.2019. List of Questions adopted on 11.12.2018.

The CHMP was updated on the BSWP responses to the CHMP list of questions.

An oral explanation was held on Monday, 24 June 2019. The presentation by the applicant focused on the clinical data in different subgroups as well as post-approval commitments.

## 2.2. Re-examination procedure oral explanations

No items

## 2.3. Post-authorisation procedure oral explanations

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

Novartis Europharm Limited

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

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

Oral explanation

**Action**: Oral explanation to be held on Monday, 24 June 2019 at time 14:30

Request for Supplementary Information adopted on 28.02.2019, 15.11.2018, 26.07.2018.

An oral explanation was held on Monday, 24 June 2019. The presentation by the applicant focused on the clinical data and historical controls.

See 5.1

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

PTC Therapeutics International Limited

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

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

Oral explanation

Participation of patient representatives.

**Action**: Oral explanation to be held on Tuesday, 25 June 2019 at time 11:00

Request for Supplementary Information adopted on 28.02.2019, 13.12.2018.

An oral explanation was held on Tuesday, 25 June 2019. The presentation by the applicant focused on the clinical data in different subgroups.

See 5.1

## 2.4. Referral procedure oral explanations

No items

# 3. Initial applications

## 3.1. Initial applications; Opinions

### 3.1.1. Azacitidine Celgene - azacitidine - EMEA/H/C/005300

Celgene Europe BV; Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML)

Scope: Opinion

**Action**: For adoption

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

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.

### 3.1.2. Evenity - romosozumab - EMEA/H/C/004465

UCB Pharma S.A.; Treatment of osteoporosis

Scope: Opinion

**Action**: For adoption

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

List of Outstanding Issues adopted on 29.05.2019, 28.02.2019, 15.11.2018, 20.09.2018. List of Questions adopted on 26.04.2018.

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

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

The Icelandic and Norwegian Members were not in agreement with the CHMP recommendation.

The divergent position was appended to the opinion.

The refusal question and answers document was circulated for information.

### 3.1.3. Giapreza - angiotensin II - EMEA/H/C/004930

La Jolla Pharmaceutical II B.V.; treatment of hypotension in adults with distributive or vasodilatory shock who remain hypotensive despite fluid and vasopressor therapy

Scope: Opinion

**Action**: For adoption

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

List of Outstanding Issues adopted on 28.03.2019. List of Questions adopted on 18.10.2018.

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

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

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

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

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

The summary of opinion was circulated for information.

### 3.1.4. Lacosamide UCB - lacosamide - EMEA/H/C/005243

UCB Pharma S.A.; treatment of epilepsy

Scope: Opinion

**Action**: For adoption

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

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.

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

### 3.2.1. bortezomib - EMEA/H/C/005074

treatment of multiple myeloma

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 31.01.2019.

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.

### 3.2.2. clopidogrel / acetylsalicylic acid - EMEA/H/C/004996

indicated for the secondary prevention of atherothrombotic events

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 31.01.2019.

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

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

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

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

neoplasm (BPDCN)

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 24.04.2019.

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.

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

### 3.2.4. fostamatinib - EMEA/H/C/005012

indicated for the treatment of thrombocytopenia

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 31.01.2019.

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

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

### 3.2.5. emapalumab - Orphan - EMEA/H/C/004386

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

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 13.12.2018.

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

The Committee adopted a list of outstanding issues.

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

### 3.2.6. rituximab - EMEA/H/C/005387

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

Scope: List of outstanding issues

**Action**: For adoption

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. viable T-cells - Orphan - ATMP - EMEA/H/C/002397

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

Scope: List of outstanding issues

**Action**: For adoption

List of Outstanding Issues adopted on 14.09.2018, 25.05.2018. List of Questions adopted on 08.09.2017.

The CHMP was updated on discussions at the CAT. The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee agreed to the 3rd list of outstanding issues adopted by the CAT with a specific timetable.

The CHMP agreed to the CAT decision to consult an ad-hoc expert group and proposed amendments to the list of questions for the ad-hoc expert group, which was adopted.

### 3.2.8. omadacycline tosilate - EMEA/H/C/004715

treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI) in adults

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 31.01.2019.

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.

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

Accelerated assessment

Roche Registration GmbH; Treatment of mature B cell lymphomas

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 24.04.2019.

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.

### 3.2.10. rituximab - EMEA/H/C/004807

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

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 18.10.2018.

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

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

### 3.2.11. netarsudil - EMEA/H/C/004583

indicated for the reduction of elevated intraocular pressure (IOP) in adults with open-angle glaucoma or ocular hypertension.

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 31.01.2019.

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.

### 3.2.12. quizartinib - Orphan - EMEA/H/C/004468

Daiichi Sankyo Europe GmbH; treatment of acute myeloid leukaemia

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 29.01.2019.

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.

### 3.2.13. onasemnogene abeparvovec - Orphan - ATMP - EMEA/H/C/004750

Accelerated assessment

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

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 22.02.2019.

The CHMP was updated on discussions at the CAT. The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee agreed to the list of outstanding issues adopted by the CAT with a specific timetable.

The CHMP agreed to the CAT decision to consult the SAG Neurology and agreed to the list of questions for this expert group as adopted by the CAT.

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

### 3.3.1. brolucizumab - EMEA/H/C/004913

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

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

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

### 3.3.2. recombinant vesicular stomatitis virus - zaire ebola virus vaccine (live) - EMEA/H/C/004554

Accelerated assessment

Ebola Vaccine

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. cefiderocol - EMEA/H/C/004829

Accelerated assessment

treatment of infections due to aerobic Gram-negative bacteria

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. fenfluramine - Orphan - EMEA/H/C/003933

Zogenix GmbH; treatment of seizures associated with Dravet syndrome in children aged 2 years to 17 years and adults.

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

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

### 3.3.5. imlifidase - Orphan - EMEA/H/C/004849

Hansa Biopharma AB; indicated for desensitization treatment of highly sensitized adult kidney transplant patients with positive crossmatch against an available deceased donor.

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

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

### 3.3.6. methylthioninium chloride - EMEA/H/C/002776

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

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

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

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

treatment of primary hypercholesterolaemia or mixed dyslipidaemia

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.

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

treatment of primary hypercholesterolaemia or mixed dyslipidaemia

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.

### 3.3.9. treprostinil sodium - Orphan - EMEA/H/C/005207

SciPharm Sarl; treatment of thromboembolic pulmonary hypertension (CTEPH)

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. sodium oxybate - EMEA/H/C/004962

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

Scope: Letter from applicant dated 12 June 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted in April 2019

**Action**: For adoption

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

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 April 2019.

### 3.4.2. adalimumab - EMEA/H/C/004879

treatment of juvenile idiopathic arthritis, paediatric plaque psoriasis, paediatric Crohn's disease, paediatric uveitis

Scope: Letter from applicant dated 12 June 2019 requesting an extension of clock stop to respond to the list of questions adopted in March 2019

**Action**: For adoption

List of Question adopted on 28.03.2019.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the list of questions adopted in March 2019

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

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

Scope: Letter from applicant dated 24 May 2019 requesting an extension of clock stop to respond to the list of questions adopted in April 2019.

**Action**: For adoption

List of questions adopted on 26.04.2019.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the list of questions adopted in April 2019.

### 3.4.4. erlotinib - EMEA/H/C/005071

treatment of lung and pancreatic cancers

Scope: Letter from applicant dated 17 June 2019 requesting an extension of clock stop to

respond to the list of outstanding issues adopted in May 2019.

**Action**: For adoption

List of Outstanding Issues adopted on 29.05.2019. List of Questions adopted on 13.12.2018.

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 May 2019.

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

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

Scope: Letter from applicant dated 3 June 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted in December 2018.

**Action**: For adoption

List of Questions adopted on 13.12.2018.

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 December 2018.

### 3.4.6. crisaborole - EMEA/H/C/004863

treatment of mild to moderate atopic dermatitis

Scope: Letter from applicant dated 19 June 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted in May 2019.

**Action**: For adoption

List of Outstanding Issues adopted on 29.05.2019, 28.02.2019. List of Questions adopted on 20.09.2018.

The CHMP discussed the request by the applicant and did not agree with the requested additional extension to the clock stop, but to a shorter extension.

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

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

Scope: Letter from applicant requesting an extension to the clockstop to respond to the List of Questions adopted on 26.04.2019

**Action**: For adoption

List of Questions adopted on 26.04.2019.

The CHMP agreed to the request by the applicant for an extension to the clockstop to respond to the List of Questions adopted on 26.04.2019.

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

### 3.5.1. Xyndari - glutamine - Orphan - EMEA/H/C/004734

Emmaus Medical Europe Ltd; treatment of sickle cell disease

Scope: Appointment of re-examination rapporteurs, draft timetable

Letter from the applicant dated 11 June 2019 requesting a re-examination of the opinion adopted on 29 May 2019.

**Action**: For adoption

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

Opinion adopted on 29.05.2019. List of Outstanding Issues adopted on 31.01.2019. List of Questions adopted on 28.06.2018.

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

The CHMP noted the draft timetable.

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

No items

## 3.7. Withdrawals of initial marketing authorisation application

No items

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

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

### 4.1.1. Imraldi - adalimumab - EMEA/H/C/004279/X/0019/G

Samsung Bioepis NL B.V.

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Extension application to introduce a new strength of 40 mg/0.8 ml solution for injection in a vial, to allow the administration to paediatric patients requiring less than a full 40mg dose.
C.I.z - To update the Product Information for the pre-filled syringe (EU/1/17/1216/001-004) and pre-filled pen (EU/1/17/1216/005-008) presentations in line with the dosage regimen changes introduced with the extension application. Minor additional amendments to the SmPC and PL are also made to align the PI with Humira (the reference product).
The RMP (version 3.0) is updated in accordance.”

**Action**: For adoption

List of Questions adopted on 28.03.2019.

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

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

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

### 4.1.2. Tecentriq - atezolizumab - EMEA/H/C/004143/X/0017

Roche Registration GmbH

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

Scope: "Extension application to add a new strength of 840 mg (60 mg/ml) for Tecentriq concentrate for solution for infusion in a vial and a new indication (metastatic triple-negative breast cancer (TNBC)). The new indication applies only to the 840 mg strength."

**Action**: For adoption

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

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

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

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

The CHMP noted the letter of recommendations dated 19.06.2019

The CHMP agreed by consensus to the request for 1 year of market protection for a new indication.

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

Pfizer Europe MA EEIG

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

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

**Action**: For adoption

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

The Committee discussed the issues identified in this application, mainly relating to the comparability of the formulations.

The Committee adopted the CHMP recommendation and scientific discussion together with the 2nd 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. Emgality - galcanezumab - EMEA/H/C/004648/X/0004

Eli Lilly Nederland B.V.

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

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

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to the efficacy data and the proposed posology.

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

No items

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

No items

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

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

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

GlaxoSmithKline (Ireland) Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include patients aged 5 years and older in the current approved indication for Benlysta (belimumab powder for solution for infusion 120 mg/ml and 400 mg/ml) based on the results of the safety, efficacy and pharmacokinetics study in patients aged 5 years to 17 years (BEL114055). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated with safety and efficacy information.
Update of sections 4.2, 5.1 and 5.2 of the SmPC for Benlysta (belimumab, solution for

injection in pre-filled pen and pre-filled syringe, 200 mg) to reflect the paediatric data available for the intravenous formulation. The Package Leaflet is updated accordingly. The RMP version 28.0 is submitted to reflect the results of the study and to bring it in line with the GVP Module V RMP template version 2.0. In addition, the MAH took the opportunity to make some editorial changes in the product information and bring it in line with the latest QRD template version 10.0."

**Action**: For adoption

Request for Supplementary Information adopted on 28.02.2019.

The Committee discussed the issues identified in this application. The main issues discussed related the extrapolation of efficacy and safety data from adults to children aged 5-11 years old.

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

### 5.1.2. Cyramza - ramucirumab - EMEA/H/C/002829/II/0027

Eli Lilly Nederland B.V.

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Kolbeinn Gudmundsson (IS) (MNAT with FI for Non-Clinical, FI for Quality, LT for Clinical Pharmacology), PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include Cyramza indicated as monotherapy for the treatment of adult patients with hepatocellular carcinoma who have an alpha fetoprotein (AFP) of ≥ 400 ng/mL, after prior sorafenib therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in accordance. The Package Leaflet is updated in accordance. RMP version 8.1 has been submitted."

**Action**: For adoption

Request for Supplementary Information adopted on 28.03.2019, 15.11.2018.

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

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

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

The summary of opinion was circulated for information.

### 5.1.3. Dupixent - dupilumab - EMEA/H/C/004390/II/0012

sanofi-aventis groupe

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

Scope: "Extension of indication for Dupixent to extend the atopic dermatitis indication to the paediatric adolescent population 12 years to 17 years. This application is submitted in accordance with the requirement of Article 46. 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 accordingly."

**Action**: For adoption

Request for Supplementary Information adopted on 31.01.2019.

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

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

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

The summary of opinion was circulated for information.

### 5.1.4. Dupixent - dupilumab - EMEA/H/C/004390/II/0017

sanofi-aventis groupe

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

Scope: "Extension of indication to include a new indication in adult patients with chronic rhinosinusitis with nasal polyposis. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
An updated RMP is submitted (V 4.0)"

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly concerning the wording of the indication with regard to the target population.

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

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

Novo Nordisk A/S

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

Scope: "Extension of indication to include treatment of children and adolescents aged 1 year and above based on data from the phase 3b clinical trial NN1218-4101, supported by data from the Clinical Pharmacology trials NN1218-4371 and clinical study NN1218-3888 which was included in the initial MAA.
As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC and the corresponding sections of the Package Leaflet are updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make other non-related minor or editorial changes were implemented throughout the EU PI to increase readability/consistency.
An updated RMP version 3.1 was agreed during the procedure."

**Action**: For adoption

Request for Supplementary Information adopted on 26.04.2019.

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

The Committee adopted a positive opinion by consensus together with the CHMP Assessment

Report and translation timetable.

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

The summary of opinion was circulated for information.

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

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce

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

**Action**: For adoption

Request for Supplementary Information adopted on 28.02.2019.

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

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

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

The summary of opinion was circulated for information.

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

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include combination use with obinutuzumab for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL) for Imbruvica based on data from the phase 3 study PCYC-1130-CA; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the SmPC and Package Leaflet with minor editorial/administrative changes. An updated RMP (version 12) is agreed."

**Action**: For adoption

Request for Supplementary Information adopted on 28.02.2019.

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

addressed.

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

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

The summary of opinion was circulated for information.

### 5.1.8. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0065

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication to include, as monotherapy or in combination with platinum and 5-fluorouracil (5-FU) chemotherapy, first-line treatment of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) in adults for Keytruda; based on the results from KEYNOTE-048, a randomized, multi-center, open-label phase 3 study investigating pembrolizumab, or pembrolizumab plus platinum plus 5-FU chemotherapy versus platinum plus 5-FU plus cetuximab in subjects with first-line recurrent or metastatic HNSCC.
As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated version of the RMP (Version 22.1) is also being submitted."

**Action**: For adoption

Request for Supplementary Information adopted on 28.03.2019.

The Committee discussed the issues identified in this application, mainly relating to the wording of the indication with regard to the study population as well as concerning efficacy data in different subgroups.

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

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

Merck Sharp & Dohme B.V.

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

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

**Action**: For adoption

Request for Supplementary Information adopted on 26.04.2019.

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

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

### 5.1.10. Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0012

Les Laboratoires Servier

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin

Scope: "Extension of indication to include Lonsurf indicated for the treatment of adult patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction, who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, platinum-, and either a taxane- or irinotecan-based chemotherapy. 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.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. RMP version 6.1 has also been submitted and updated in accordance with Template Rev 2."

**Action**: For adoption

Request for Supplementary Information adopted on 31.01.2019.

The Committee discussed the issues identified in this application, mainly relating the wording of the indication to be consistent with other indication wordings in this therapeutic area.

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

### 5.1.11. Lucentis - ranibizumab - EMEA/H/C/000715/II/0076

Novartis Europharm Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

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

**Action**: For adoption

Request for Supplementary Information adopted on 28.02.2019.

The Committee discussed the issues identified in this application, mainly relating to the clinical efficacy data in different subgroup populations in relation to the extension of indication request.

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

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

Boehringer Ingelheim International GmbH

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

Scope: "Extension of indication to include new indication for OFEV for the treatment of Systemic Sclerosis associated Interstitial Lung Disease (SSc-ILD).
As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The MAH takes this opportunity to also introduce minor linguistic corrections to the Annexes for France and Sweden. The RMP version 7.0 has also been submitted."

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

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to the clinical efficacy data in different subgroup populations in relation to the extension of indication request.

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

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

Novartis Europharm Limited

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

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

Oral explanation

**Action**: For adoption

Request for Supplementary Information adopted on 28.02.2019, 15.11.2018, 26.07.2018.

See 2.3

An oral explanation was held on Monday, 24 June 2019.

The CHMP adopted a negative opinion by majority, recommending the refusal of the variation(s) to the terms of the marketing authorisation.

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

The divergent position was appended to the opinion.

The refusal question and answers document was circulated for information.

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

Janssen-Cilag International NV

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

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

**Action**: For adoption

Request for Supplementary Information adopted on 26.04.2019.

The Committee discussed the issues identified in this application, mainly relating to the wording in some sections of the SmPC as well as the risk management plan.

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

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

sanofi-aventis groupe

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

Scope: "Extension of indication to include "treatment of adults with insufficiently controlled type 2 diabetes mellitus to improve glycaemic control as an adjunct to diet and exercise in addition to other oral medicinal products for the treatment of diabetes" based on the phase 3 Study EFC13794; a 26-week randomized, open-label, active controlled, parallel-group, study assessing the efficacy and safety of the insulin glargine/lixisenatide fixed ratio combination in adults with Type 2 Diabetes inadequately controlled on GLP-1 receptor agonist and metformin (alone or with pioglitazone and/or SGLT2 inhibitors), followed by a fixed ratio combination single-arm 26-week extension period. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated and the Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to update the contact details of the local representatives in Denmark, the Netherlands and the UK in the Package Leaflet and to implement minor editorial changes in the annexes. An updated RMP version 4.0 was provided as part of the application."

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to the wording of the indication, especially whether the concomitant use with other oral medicinal products for the treatment of diabetes is sufficiently justified.

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

## 5.1.16. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0018

Roche Registration GmbH

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

Scope: "Extension of indication to include Tecentriq, in combination with carboplatin and etoposide, indicated for the first-line treatment of adult patients with extensive-stage small

cell lung cancer (ES-SCLC) for Tecentriq; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. RMP version 8.0 has been submitted"

**Action**: For adoption

Request for Supplementary Information adopted on 31.01.2019.

The Committee discussed the issues identified in this application, mainly relating to the wording in some sections of the SmPC as well as clarification on some clinical analyses.

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

## 5.1.17. Toujeo - insulin glargine - EMEA/H/C/000309/II/0108

Sanofi-Aventis Deutschland GmbH

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include new population for Toujeo. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance."

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to the clinical efficacy data in support of the extension variation as well as the wording in some sections of the SmPC.

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

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

PTC Therapeutics International Limited

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

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

Oral explanation

Participation of patient representatives.

**Action**: For adoption

Request for Supplementary Information adopted on 28.02.2019, 13.12.2018.

See 2.3

An oral explanation was held on Tuesday, 25 June 2019. The presentation by the applicant focused on the clinical data in different subgroups.

The CHMP adopted a negative opinion by consensus recommending the refusal of the

variation(s) to the terms of the marketing authorisation.

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

The refusal question and answers document was circulated for information.

## 5.1.19. Victoza - liraglutide - EMEA/H/C/001026/II/0049

Novo Nordisk A/S

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include treatment of children and adolescents aged 10 years and above with type 2 diabetes mellitus based on Study NN2211-1800; a Phase 1 clinical pharmacology, multi-centre, randomised, double-blind placebo controlled trial, and Study NN2211-3659; a Phase 3a efficacy and safety, multi-centre, randomised, parallel group, placebo controlled trial with a 26-week double blind period followed by a 26-week open label period (main part). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, and 5.2 of the SmPC are being updated and the Package Leaflet is updated accordingly.
Additionally, in accordance with the excipients guideline from 2017, the MAH took the opportunity to include sodium in SmPC section 4.4 and the Package Leaflet. Changes were also made to the PI to bring it in line with the current Agency/QRD template, SmPC guideline and other relevant guideline(s).
An updated RMP version 30.1 was agreed during the procedure."

**Action**: For adoption

Request for Supplementary Information adopted on 28.03.2019.

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

The Committee adopted a positive opinion 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. Zerbaxa - ceftolozane / tazobactam - EMEA/H/C/003772/II/0020

Merck Sharp & Dohme B.V.

Rapporteur: Bjorg Bolstad, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension of indication to include treatment of Nosocomial pneumonia, including ventilator associated pneumonia for Zerbaxa, based on results from the randomised, double-blind, multicentre clinical trial CXA-NP-11-04 (PN008).
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance (sections 1, 2, 3, 4 and 6).
The applicant also took the opportunity to implement editorial changes in section 5.2 of the SmPC and to bring section 4.4 of the SmPC and section 2 of the PL in line with the latest Annex to the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for

human use'.
Version 2.1 of the RMP was also submitted."

**Action**: For adoption

Request for Supplementary Information adopted on 29.05.2019, 28.03.2019.

The Committee discussed the issues identified in this application, mainly concerning the susceptibility breakpoints.

The Committee adopted a 3rd request for supplementary information with a specific timetable.

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

Pfizer Ireland Pharmaceuticals

Rapporteur: Alar Irs, PRAC Rapporteur: Maia Uusküla

Scope: "Extension of indication to include paediatric patients from birth to less than 2 months old for Zinforo; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated based on results from 2 new pharmacokinetic/clinical studies (studies D3720C00006 (P903-21) and D3720C00009 (C2661002)) and a population pharmacokinetic analysis (PMAR-EQDD-C266b-Other-809). The Package Leaflet is updated in accordance. The RMP version 18.1 has also been agreed upon."

**Action**: For adoption

Request for Supplementary Information adopted on 28.02.2019.

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

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

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

The summary of opinion was circulated for information.

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

AstraZeneca AB

Lead Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.1 , 4.2, 4.4, 4.8, and 5.1 of the SmPC of Forxiga, Edistride, Xigduo and Ebymect to modify the indication and to reflect new data based on final results from study D1693C00001 (DECLARE). This was 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 Package Leaflets (PL) are updated accordingly. The dapagliflozin Risk Management Plan (RMP) and dapagliflozin/metformin RMP have also been updated to version 17 and version 11 respectively. The worksharing applicant took the opportunity to make editorial changes and

bring the PI in line with the updated excipient guideline (lactose wording in SmPC section 4.4). The worksharing procedure leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan."

**Action**: For adoption

Request for Supplementary Information adopted on 26.04.2019.

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

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

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

The summary of opinion was circulated for information.

### 5.1.23. WS1550
### Docetaxel Zentiva - docetaxel - EMEA/H/C/000808/WS1550/0058
### Taxotere - docetaxel - EMEA/H/C/000073/WS1550/0131

Aventis Pharma S.A.

Lead Rapporteur: Alexandre Moreau, Lead Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension of indication to include in combination with androgen-deprivation therapy (ADT), with or without prednisone or prednisolone, for the treatment of patients with metastatic hormone-sensitive prostate cancer for Taxotere and Docetaxel Zentiva; as a consequence, sections 4.1, 4.2, 4.4 and 4.8 of the SmPC are updated. The Package Leaflet is updated accordingly. The RMP version 1.0 has also been submitted. In addition, the Worksharing applicant took the opportunity to update information impacting the local representatives in the packages leaflets."

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to the most appropriate patient population and the time of starting treatment.

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

No items

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

No items

# 6. Ancillary medicinal substances in medical devices

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

No items

## 6.2. Update of Ancillary medicinal substances in medical devices

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

## 8.2. Priority Medicines (PRIME)

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

### 8.2.1. List of applications received

**Action:** For information

The CHMP noted the list of applications received.

### 8.2.2. Recommendation for PRIME eligibility

**Action:** For adoption

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

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

# 9. Post-authorisation issues

## 9.1. Post-authorisation issues

### 9.1.1. Aflunov - prepandemic influenza vaccine (h5n1) (surface antigen, inactivated, adjuvanted) - EMEA/H/C/002094/II/0044/G

Seqirus S.r.l,

Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli

Scope: "Update of sections 4.4, 4.6, 4.8 and 5.1 of the SmPC following clinical study reports of studies V87_25 and V87_26 listed as post approval commitments; these are Phase 3, stratified, randomized, controlled, observer-blind, multicenter studies; the Package Leaflet and Labelling are updated accordingly.
The updated RMP version 3.0 has also been submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some amendments to the PI and make some additional minor editorial corrections."

**Action**: For discussion

Request for Supplementary Information adopted on 29.05.2019, 28.02.2019, 20.09.2018.

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

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

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

The summary of opinion was circulated for information.

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

Amgen Europe B.V.

Rapporteur: Jorge Camarero Jiménez

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

**Action:** For adoption

Request for Supplementary Information adopted on 28.02.2019, 15.11.2018.

The Committee discussed the issues identified in this application, mainly relating to efficacy data for the current and new dosing regimen.

The Committee adopted a 3$^{rd}$ request for supplementary information with a specific timetable.

### 9.1.3. OPDIVO - nivolumab - EMEA/H/C/003985/II/0065

Bristol-Myers Squibb Pharma EEIG

Co-Rapporteur: Paula Boudewina van Hennik

Scope: "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update posology and clinical related information based on interim results from Phase 3b/4 Study CA209384 (A Dose Frequency Optimization, Phase IIIB/IV Trial of Nivolumab 240 mg Every 2 Weeks vs Nivolumab 480 mg Every 4 weeks in Subjects with Advanced or Metastatic Non-small Cell Lung Cancer who Received Up to 12 Months of Nivolumab at 3 mg/kg or 240 mg Every 2 Weeks) and further supported by pharmacometric analyses in subjects with 2L+ NSCLC."

**Action:** For discussion

The Committee discussed the issues identified in this application, mainly concerning the dosing regimens in relation to efficacy results.

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

### 9.1.4. Optimark (withdrawn) – gadoversetamide - EMEA/H/C/000745/ANX/014.11

Guerbet

Lead Rapporteur: Greg Markey

Scope: Long-term effects study ALS-Gd64/001 on gadolinium accumulation in the bone for gadoversetamide, gadoteric acid, gadobutrol, gadoxetic acid, gadopentetic acid and gadodiamide containing medicinal products.

Request for PRAC advice was adopted via written procedure on 07.06.2019

**Action:** For adoption

The CHMP agreed to the PRAC advice.

## 10. Referral procedures

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

No items

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

No items

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

No items

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

### 10.4.1. Flurbiprofen Geiser – oromucosal spray – EMEA/H/A-29(4)/1487

Geiser Pharma S.L.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Johann Lodewijk Hillege

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

Action: For adoption

The applicant has submitted a hybrid application under Article 10(3) of Directive 2001/83/EC for Flurbiprofen Geiser 8.75mg oromucosal spray. NL is of the opinion that the therapeutic equivalence between the reference and test product has not been adequately demonstrated since no clinical trials have been submitted and the justification for the absence of clinical trials is not considered acceptable.

The CHMP appointed Jorge Camarero Jiménez as Rapporteur and Johann Lodewijk Hillege as Co-Rapporteur.

The CHMP adopted a list of questions with a specific timetable.

List of Questions: 27.06.2019

Submission of responses: 29.08.2019

Re-start of the procedure: 19.09.2019

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 27.09.2019

Comments: 04.10.2019

Updated Rapporteur/co-rapporteur ARs circulated to CHMP: 10.10.2019

CHMP list of outstanding issues / opinion: October 2019 CHMP

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

No items

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

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

MAH various

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

Scope: Opinion

**Action:** For adoption

Review of the benefit-risk balance following notification by AIFA in Italy on 8 June 2018 of a

referral under Article 31 of Directive 2001/83/EC.

The CHMP adopted an opinion by consensus, recommending that the marketing authorisations for bacterial lysates-containing medicinal products for respiratory conditions should be varied.

- The indications of bacterial lysate medicines are being restricted to prophylaxis of recurrent respiratory tract infections, with the exception of pneumonia. Bacterial lysate medicines should not be prescribed for treatment of existing respiratory infections or for prophylaxis of pneumonia due to lack of efficacy data.
- The prescribing information of the medicines will be updated accordingly.
- The use of the medicines for prevention can continue, but the MAHs must provide further data on safety and effectiveness from new clinical studies by 2026.

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

The CHMP agreed to the public health communication.

### 10.6.2. Fosfomycin containing medicinal products – EMEA/H/A-31/1476

MAH various

Rapporteur: Ondrej Slanar, Co-Rapporteur: Janet Koenig

Scope: List of outstanding issues

**Action:** For adoption

Need to re-evaluate the benefit-risk ratio of the approved indications considering the current scientific knowledge. Furthermore, the appropriate dose and duration of administration for both oral and intravenous formulations need to be discussed as well as the adequacy of safety relevant information and information about pharmacological properties.

The German National Competent Authority triggered a referral under Article 31 of Directive 2001/83 based on interest of the Union, requesting an opinion to CHMP on the benefit-risk of fosfomycin-containing products and on the need for regulatory measures to be taken.

List of Oustanding Issues adopted on 28. March 2019. List of questions adopted on 13 December 2018.

The members were updated on the responses to the list of questions and discussed the available data in the different indications and formulations.

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

Submission of responses: 01.08.2019

Re-start of the procedure: 22.08.2019

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 30.08.2019

Comments: 06.09.2019

Updated Rapporteur/co-rapporteur AR(s) circulated to CHMP: 12.09.2019

CHMP opinion/LoI: September 2019 CHMP

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

### 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

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

**Action**: For information

The CHMP noted the information.

## 12. Inspections

### 12.1. GMP inspections

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

### 12.2. GCP inspections

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

### 12.3. Pharmacovigilance inspections

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

## 12.4. GLP inspections

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

# 13. Innovation Task Force

## 13.1. Minutes of Innovation Task Force

No items

## 13.2. Innovation Task Force briefing meetings

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

No items

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

No items

## 13.4. Nanomedicines activities

No items

# 14. Organisational, regulatory and methodological matters

## 14.1. Mandate and organisation of the CHMP

### 14.1.1. Area of expertise of CHMP Co-opted Member

Discussion on area of expertise in light of the expiry of the mandate of co-opted member Sol Ruiz on 21/07/2019.

The area of expertise of Sol Ruiz is quality and safety (biological) in advanced therapies (gene, cell and tissue therapies).

**Action:** For discussion

Agreed area of expertise: Quality and safety (biological), with expertise in advanced therapies (gene, cell and tissue therapies)

Deadline for nominations 18 July EOB.

## 14.2. Coordination with EMA Scientific Committees

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

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

**Action:** For information

The CHMP noted the information.

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

**Action:** For adoption

The CHMP adopted the EURD list.

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

CAT draft minutes of meeting held on 19-21 June 2019

**Action:** For information

The CHMP noted the draft minutes.

### 14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at June 2019 PDCO

**Action:** For information

The CHMP noted the information.

Report from the PDCO meeting held on 25-28 June 2019

**Action:** For information

The CHMP noted the report.

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

Report from the COMP meeting held on 18-20 June 2019

**Action:** For information

The CHMP noted the report.

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 25-27 June 2019

**Action:** For information

The CHMP noted the report.

Questions to Pharmacokinetics Working Party on Bioequivalence for orally inhaled products containing beclomethasone diproprionate (BDP)

**Action:** For adoption

The CHMP agreed to the questions to the PKWP

Questions to Pharmacokinetics Working Party on need to measure both enantiomers as proof of bioequivalence

**Action:** For adoption

The CHMP agreed to the questions to the PKWP

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

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

Chair: Anja Schiel

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

**Action:** For information

Scientific advice letters

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

The CHMP noted the report.

### 14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 21-22 May 2019.

**Action:** For adoption

The CHMP adopted the table of decisions.

PRAC advice on liposomal formulations and non-liposomal formulations of doxorubicin

**Action:** For discussion

The CHMP noted the PRAC advice but did not agree to the proposed actions as the timelines were considered too long. More rapid risk mitigation was requested by the CHMP. Further discussion expected at the July Plenary.

### 14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz, Vice-Chair: Nanna Aaby Kruse

Reports from BWP June 2019 meeting to CHMP for adoption:

- 20 reports on products in scientific advice and protocol assistance
- 10 reports on products in pre-authorisation procedures
- 1 report on products in post-authorisation procedures
- 4 reports on products in plasma master file

**Action:** For adoption

The CHMP adopted the reports.

### 14.3.4. Blood Product Working Party (BPWP)

Chair: Jacqueline Kerr

Election of BPWP Vice-Chair

**Action:** For election

The CHMP elected Karri Pentilla as vice-chair for a second 3-year term.

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

Scope: Revised AMEG scientific advice for public consultation on the preliminary risk profiling and overview of comments received during the public consultation

**Action:** For adoption

The CHMP adopted the revised AMEG scientific advice.

## 14.4. Cooperation within the EU regulatory network

No items

## 14.5. Cooperation with International Regulators

No items

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

No items

## 14.7. CHMP work plan

No items

## 14.8. Planning and reporting

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

2019 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

## 15.1. AOB topic

### 15.1.1. Preparedness of the system and capacity increase

**Action:** For information

The CHMP noted the information.

## 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 June 2019 CHMP meeting

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

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Melinda Sobor | Member | Hungary | No part in discussions, final deliberations and voting as appropriate as regards the following procedures: | **Dupixent -** EMEA/H/C/004390/II/0012 **Dupixent** - EMEA/H/C/004390/II/0017 |
| Agnes Gyurasics | Alternate | Hungary | No interests declared | |
| Hrefna Gudmundsdottir | Alternate | Iceland | No interests declared | |
| Jayne Crowe | Member | Ireland | No interests declared | |
| Peter Kiely | Alternate | Ireland | No interests declared | |
| Daniela Melchiorri | Member | Italy | No restrictions applicable to this meeting | |
| Natalja Karpova | Member | Latvia | No interests declared | |
| Romaldas Mačiulaitis | Member | Lithuania | No participation in final deliberations and voting on: | **polatuzumab vedotin** - EMEA/H/C/004870 **Tecentriq** - EMEA/H/C/004143/X/0017 **Tecentriq** - EMEA/H/C/004143/II/0018 |
| 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 | |
| Simona Badoi | Member | Romania | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Francisek Drafi | Member | Slovakia | No interests declared | |
| Rajko Kenda | Member | Slovenia | No restrictions applicable to this meeting | |
| Maria Concepcion Prieto Yerro | Member | Spain | No interests declared | |
| Jorge Camarero Jiménez | Alternate | Spain | No participation in final deliberations and voting on: | **polatuzumab vedotin** - EMEA/H/C/004870 **Tecentriq** - EMEA/H/C/004143/X/0017 **Tecentriq** - EMEA/H/C/004143/II/0018 |
| Kristina Dunder | Member | Sweden | No interests declared | |
| Filip Josephson | Alternate | Sweden | No interests declared | |
| Greg Markey | Member | United Kingdom | No interests declared | |
| Nithyanandan Nagercoil | Alternate | United Kingdom | No restrictions applicable to this meeting | |
| Koenraad Norga | Co-opted member | Belgium | No participation in final deliberations and voting on: | **Benlysta** - EMEA/H/C/002015/II/0062 |
| 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 | |
| Christian Gartner | Co-opted member | Austria | No restrictions applicable to this meeting | |
| Sabine Mayrhofer | Expert - in person* | Germany - BfArM | No interests declared | |
| Anja Schiel | Expert - in person* | Norway - NOMA | No interests declared | |
| Anna Joo | Expert - in person* | Sweden - MPA | No restrictions applicable to meetings | |
| Fabienne Gaugazova | Expert - in person* | Sweden - MPA | No restrictions applicable to this meeting | |
| Sylvain Gueho | Expert - in person* | France | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Astrid Doutreluingne | Expert - in person* | France - ANSM | No part in discussions, final deliberations and voting as appropriate as regards the following procedures: | **Lucentis** - EMEA/H/C/000715/II/0076 **Revolade** - EMEA/H/C/001110/II/0049 **brolucizumab** - EMEA/H/C/004913 |
| Anne Hasle Buur | Expert - in person* | Denmark - DMA | No interests declared | |
| Tomas Radimersky | Expert - in person* | Czech Republic | No interests declared | |
| Nele Berthels | Expert - in person* | Belgium | No interests declared | |
| Rosalía Ruano Camps | Expert - in person* | Spain | No interests declared | |
| Frank Holtkamp | Expert - in person* | Netherlands | No interests declared | |
| Lisette Berm | Expert - in person* | Netherlands | No restrictions applicable to this meeting | |
| Kirstine Moll Harboe | Expert - in person* | Denmark | No interests declared | |
| Sara Galluzzo | Expert - in person* | Italy | No interests declared | |
| Helena Fonseca | Expert - in person* | Portugal | No interests declared | |
| Angeliki Siapkara | Expert - in person* | UK | No interests declared | |
| Maciej Kostrubiec | Expert - via telephone* | Poland - URPL | No interests declared | |
| Andrea Wallington | Expert - via telephone* | United Kingdom | No interests declared | |
| Andrew Exley | Expert - via telephone* | United Kingdom | No interests declared | |
| Koenraad Brusselmans | Expert - via telephone* | Belgium | No restrictions applicable to meetings | |
| Mair Powell | Expert - via telephone* | Ireland | No interests declared | |
| Geraldine O'Dea | Expert - via telephone* | Ireland | No interests declared | |
| Grant Munkwase | Expert - via telephone* | Uganda | No interests declared | |
| Shirley Hopper | Expert - via telephone* | United Kingdom | No interests declared | |
| Simona Stankeviciute | Expert - via telephone* | Lithuania | No interests declared | |
| Egbert Flory | Expert - via telephone* | Germany | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Carmen Rodriguez | Expert - via telephone | WHO | Confidentiality agreement | |
| Elisabeth Pluut | Expert - via telephone | WHO | Confidentiality agreement | |
| Agnieszka Przybyszewska | Expert - via telephone* | Ireland | No interests declared | |
| Eskild Colding-Jorgensen | Expert - via telephone* | Denmark | No restrictions applicable to this meetings | |
| Runa Vavia Fenger | Expert - via telephone* | Denmark | No restriction applicable to meetings | |
| Aldana Rosso | Expert - via telephone* | Denmark | No interests declared | |
| Camilla Aertebjerg Baek | Expert - via telephone* | Denmark | No part in discussions, final deliberations and voting as appropriate as regards: | **Fiasp -** EMEA/H/C/004046/II/0010 **Victoza** - EMEA/H/C/001026/II/0049 |
| Paolo Foggi | Expert - via telephone* | Italy | No interests declared | |
| Janneke van Leeuwen | Expert - via telephone* | Netherlands | No interests declared | |
| Peter Mol | Expert - via telephone* | Netherlands | No interests declared | |
| Macarena Rodriguez Mendizabal | Expert - via Adobe* | Spain | No interests declared | |
| Johannes Hendrikus Ovelgonne | Expert - via Adobe* | Netherlands | No interests declared | |
| Michal Zwiewka | Expert - via Adobe* | Germany | No interests declared | |
| Sylvia Kuehn | Expert - via Adobe* | Germany - BfArM | No restrictions applicable to meetings | |
| Thomas Stock | Expert - via Adobe* | Germany | No interests declared | |
| Bruna Dekic | Expert - via Adobe* | Germany | No restrictions applicable to this meeting | |
| Bettina Bücker | Expert - via Adobe* | Germany | No interests declared | |
| Mikael Andersson | Expert - via Adobe* | Sweden | No interests declared | |
| Marja van de Bovenkamp | Expert - via Adobe* | NL | No interests declared | |
| Martina Schussler-Lenz | Expert - via Adobe* | DE | No interests declared | |
| Meeting run with the help of EMA staff | | | | |

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

# 17. Explanatory notes

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

**Oral explanations** *(section 2)*

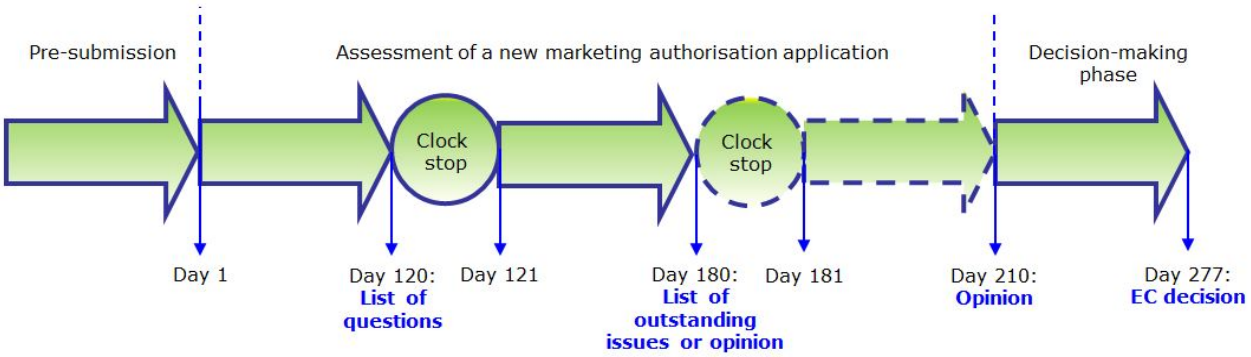
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

**Initial applications** *(section 3)*

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

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

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




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

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

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

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

Extensions of marketing authorisations are applications for the change or addition of new strengths, formulations or routes of administration to existing marketing authorisations. Extension applications

follow a 210-day evaluation process, similarly to applications for new medicines (see figure above).

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

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

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

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

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

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

**Re-examination procedures** *(section5.3)*

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

**Withdrawal of application** *(section 3.7)*

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

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

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

**Pre-submission issues** *(section 8)*

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

**Post-authorisation issues** *(section 9)*

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

**Referral procedures** *(section 10)*

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

found here.

**Pharmacovigilance issues** *(section 11)*

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

**Inspections Issues** *(section 12)*

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

**Innovation task force** *(section 13)*

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

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

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

**Satellite groups / other committees** *(section 14.2)*

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

**Invented name issues** *(section 14.3)*

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

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 September 2019
EMA/CHMP/487839/2019

# Annex to 24-27 June 2019 CHMP Minutes




**Temporary visiting address** Spark building ● Orlyplein 24 ● 1043 DP Amsterdam ● The Netherlands
**For deliveries** refer to www.ema.europa.eu/how-to-find-us
**Send us a question** via www.ema.europa.eu/contacts **Telephone** +31(0)88 781 6000


An agency of the European Union

© European Medicines Agency, 2019. Reproduction is authorised provided the source is acknowledged.

## A. PRE SUBMISSION ISSUES

### A.1. ELIGIBILITY REQUESTS

| | |
|---|---|
| Report on Eligibility to Centralised Procedure for June 2019: **For adoption** | Adopted |

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

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

### A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

## B. POST-AUTHORISATION PROCEDURES OUTCOMES

### B.1. Annual re-assessment outcomes

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

| | |
|---|---|
| **Evoltra - clofarabine - EMEA/H/C/000613/S/0063**<br>Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni | Positive Opinion adopted by consensus together with the CHMP assessment report.<br>The Marketing Authorisation remains under exceptional circumstances.<br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion. |
| **Firdapse - amifampridine - EMEA/H/C/001032/S/0064, Orphan**<br>BioMarin International Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga | Positive Opinion adopted by consensus together with the CHMP assessment report.<br>The Marketing Authorisation remains under exceptional circumstances.<br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion. |
| **Kolbam - cholic acid - EMEA/H/C/002081/S/0029, Orphan**<br>Retrophin Europe Ltd, Rapporteur: Constantinos Markopoulos, PRAC Rapporteur: Agni Kapou<br>Request for Supplementary Information adopted on 27.06.2019, 26.04.2019. | Request for supplementary information adopted with a specific timetable. |
| **Lamzede - velmanase alfa - EMEA/H/C/003922/S/0004, Orphan**<br>Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jan Neuhauser | Positive Opinion adopted by consensus together with the CHMP assessment report.<br>The Marketing Authorisation remains under exceptional circumstances.<br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion. |

## B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

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

| | |
|---|---|
| **Brimica Genuair - aclidinium / formoterol fumarate dihydrate - EMEA/H/C/003969/R/0026**<br>AstraZeneca AB, Duplicate, Duplicate of Duaklir Genuair, Rapporteur: Ewa Balkowiec Iskra, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Adam Przybylkowski<br>Request for Supplementary Information adopted on 29.05.2019. | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.<br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |
| **Cosentyx - secukinumab - EMEA/H/C/003729/R/0050**<br>Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Eva A. Segovia | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.<br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |
| **Duaklir Genuair - aclidinium / formoterol fumarate dihydrate - EMEA/H/C/003745/R/0026**<br>AstraZeneca AB, Rapporteur: Ewa Balkowiec Iskra, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Adam Przybylkowski<br>Request for Supplementary Information adopted on 29.05.2019. | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.<br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |
| **Duavive - estrogens conjugated / bazedoxifene - EMEA/H/C/002314/R/0021**<br>Pfizer Europe MA EEIG, Rapporteur: Martina Weise, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber<br>Request for Supplementary Information adopted on 27.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Firdapse - amifampridine - EMEA/H/C/001032/R/0062, Orphan**<br>BioMarin International Limited, Rapporteur: Kristina Dunder, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Ulla Wändel Liminga | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with |

| | |
|---|---|
| | unlimited validity.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |
| **Lynparza - olaparib - EMEA/H/C/003726/R/0029**<br>AstraZeneca AB, Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli<br><br>Request for Supplementary Information adopted on 27.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Otezla - apremilast - EMEA/H/C/003746/R/0027**<br>Celgene Europe BV, Rapporteur: Peter Kiely, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Eva A. Segovia | Positive Opinion adopted by consensus together with the CHMP assessment report.<br><br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |
| **Rasagiline ratiopharm - rasagiline - EMEA/H/C/003957/R/0014**<br>Teva B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Ana Sofia Diniz Martins<br>Request for Supplementary Information adopted on 27.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Rixubis - nonacog gamma - EMEA/H/C/003771/R/0029**<br>Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski<br>Request for Supplementary Information adopted on 27.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Trevicta - paliperidone - EMEA/H/C/004066/R/0022**<br>Janssen-Cilag International NV, Informed Consent of Xeplion, Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga<br>Request for Supplementary Information adopted on 27.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Trulicity - dulaglutide - EMEA/H/C/002825/R/0036**<br>Eli Lilly Nederland B.V., Rapporteur: Martina Weise, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Amelia Cupelli | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that the renewal of |

| | |
|---|---|
| Request for Supplementary Information adopted on 26.04.2019. | the marketing authorisation can be granted with unlimited validity.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |
| **Vargatef - nintedanib - EMEA/H/C/002569/R/0025**<br>Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Agni Kapou<br>Request for Supplementary Information adopted on 26.04.2019. | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |

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

| | |
|---|---|
| **Zalmoxis - nalotimagene carmaleucel - EMEA/H/C/002801/R/0015, Orphan, ATMP**<br>MolMed S.p.A, Rapporteur: Carla Herberts, Co-Rapporteur: Sol Ruiz, CHMP Coordinators: Paula Boudewina van Hennik and Maria Concepcion Prieto Yerro, PRAC Rapporteur: Brigitte Keller-Stanislawski<br>Request for Supplementary Information adopted on 24.05.2019. | Positive Opinion adopted by consensus together with the CHMP assessment report ‹and translation timetable›.<br><br>The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.<br><br>The Marketing Authorisation remains conditional.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |

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

| | |
|---|---|
| **Signal detection**<br><br>PRAC recommendations on signals adopted at the PRAC meeting held on 11-14 June 2019 PRAC: | |
| Rivaroxaban – XARELTO, RUNAPLAX - Signal of premature ending of the GALILEO study in patients who have received an artificial heart valve through a transcatheter aortic valve replacement (TAVR)<br>PRAC recommendation on a variation: **For Adoption** | Adopted. |
| Secukinumab – COSENTYX – Signal of dermatitis exfoliative generalised<br>PRAC recommendation on a variation: **For Adoption** | Adopted. |

| | |
|---|---|
| Temozolomide – TEMODAL- Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)<br>PRAC recommendation on a variation: **For Adoption** | Adopted. |
| PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its June 2019 meeting: | |
| **EMEA/H/C/PSUSA/00001267/201810** (eslicarbazepine acetate)<br>CAPS:<br>**Zebinix** (EMEA/H/C/000988) (eslicarbazepine acetate), Bial - Portela & Cª, S.A., Rapporteur: Martina Weise<br>NAPS:<br>**ESLICARBAZEPINE ACETAAT G.L.** - G.L. PHARMA GMBH<br>PRAC Rapporteur: Martin Huber, "From: 21/10/2015 To: 21/10/2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following changes:<br>Update of section 4.9 of the SmPC and section 3 of the PIL to reflect new information from overdose cases.<br>Update of section 4.8 of the SmPC and section 4 of the PIL to include weight increased.<br>The Package leaflet is updated accordingly.<br><br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00002014/201810** (methotrexate)<br>CAPS:<br>**Jylamvo** (EMEA/H/C/003756) (methotrexate), Therakind (Europe) Limited, Rapporteur: Bruno Sepodes<br>**Nordimet** (EMEA/H/C/003983) (methotrexate), Nordic Group B.V., Rapporteur: Bruno Sepodes<br>NAPS:<br>**VELOS** - DIFA COOPER S.P.A<br>PRAC Rapporteur: Martin Huber, "01 Jul 2017 - 31 Oct 2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following changes:<br>Update of section 4.5 of the SmPC to revise existing wording for the interaction of methotrexate with nitrous oxide for products with at least one indication in oncology.<br>Update of section 4.8 of the SmPC of methotrexate-containing pre-filled syringes and pre-filled pens to include "injection site necrosis" for methotrexate-containing pre-filled syringes and pre-filled pens. The PIL should be updated accordingly.<br>Update of section 2 of the package leaflet to reflect that contraindication in pregnancy only |

| | |
|---|---|
| | relates to non-oncologic indications for products with at least one indication in oncology.<br>This recommendation is without prejudice to the final conclusions of the ongoing referral procedure under Article 31 of Directive 2001/83/EC for risk of dosing errors with methotrexate.<br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00002697/201810**<br>(sevelamer)<br>CAPS:<br>**Renagel** (EMEA/H/C/000254) (sevelamer), Genzyme Europe BV, Rapporteur: Outi Mäki-Ikola<br>**Renvela** (EMEA/H/C/000993) (sevelamer carbonate), Genzyme Europe BV, Rapporteur: Bart Van der Schueren<br>**Sevelamer carbonate Winthrop** (EMEA/H/C/003971) (sevelamer carbonate), Genzyme Europe BV, Rapporteur: Bart Van der Schueren<br>NAPS:<br>**NAPs** - EU<br>PRAC Rapporteur: Laurence de Fays, "31-Oct-2017 – 30-Oct-2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following change(s):<br>Update of section 4.8 of the SmPC to add the adverse reaction "Crystal deposite intestine", "Gastrointestinal haemorrhage", "Intestinal ulceration,", "Gastrointestinal necrosis", "Colitis", "intestinal mass" with a frequency unknown.<br>Update of section 4.4. of the SmPC to update the existing warning regarding sevelamer crystals.<br>The package leaflet is updated accordingly.<br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010134/201812**<br>(sofosbuvir)<br>CAPS:<br>**Sovaldi** (EMEA/H/C/002798) (sofosbuvir), Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "06 December 2017 to 05 December 2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br>Update of section 4.5 of the SmPC to add new information on the impact of direct-acting antiviral (DAA) therapy on drugs metabolized by the liver (e.g. immunosuppressive agents) and on the potential need for dose adjustment of those drugs when they are co-administered with DAA therapy. The Package leaflet is updated accordingly.<br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |

| | |
|---|---|
| **EMEA/H/C/PSUSA/00010180/201811** (cabozantinib) CAPS: **CABOMETYX** (EMEA/H/C/004163) (cabozantinib), Ipsen Pharma, Rapporteur: Bjorg Bolstad **Cometriq** (EMEA/H/C/002640) (cabozantinib), Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Period Covered From: 29/11/2017 to 28/11/2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the maintenance of the marketing authorisation for the centrally authorised medicinal product Cabometyx and the variation to the terms of the marketing authorisation for the centrally authorised medicinal product Cometriq, concerning the following change(s): Update of section 4.8 of the SmPC in order to include 'pain in extremity' as a very common adverse drug reaction. The Package Leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010301/201811** (ibrutinib) CAPS: **Imbruvica** (EMEA/H/C/003791) (ibrutinib), Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "11/11/2017 To: 11/11/2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of sections 4.4 and 4.8 of the SmPC to introduce a warning, to add the adverse reactions Aspergillus infection, Pneumocystis jirovecii infection, Disseminated cryptococcosis with a frequency uncommon and to revise the frequency for the adverse reaction hepatic failure from not known to uncommon. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010307/201811** (aclidinium bromide / formoterol fumarate dihydrate) CAPS: **Brimica Genuair** (EMEA/H/C/003969) (aclidinium / formoterol fumarate dihydrate), AstraZeneca AB, Rapporteur: Ewa Balkowiec Iskra **Duaklir Genuair** (EMEA/H/C/003745) (aclidinium / formoterol fumarate dihydrate), AstraZeneca AB, Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski, "Period Covered From: 20/11/2017 To: | 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 authorisations for the above mentioned medicinal products, concerning the following changes: Update of section 4.8 of the SmPC to remove 'peripheral oedema' from the list of adverse drug reactions. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members |

| | |
|---|---|
| 19/11/2018” | agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010595/201811** (nusinersen)<br>CAPS:<br>**Spinraza** (EMEA/H/C/004312) (nusinersen), Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga, “From: 30/05/2018 To: 30/11/2018” | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br>Update section 4.8 “post-marketing experience” of the SmPC to add the adverse reaction “hypersensitivity (e.g. angioedema, urticaria and rash)”. The Package leaflet should be updated accordingly.<br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010614/201812** (pentosan polysulfate sodium (for centrally authorised product))<br>CAPS:<br>**elmiron** (EMEA/H/C/004246) (pentosan polysulfate sodium), bene-Arzneimittel GmbH, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Ana Sofia Diniz Martins, “01/06/2018 To: 01/12/2018” | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br>Update of section 4.4 of the SmPC to add a warning on pigmentary maculopathy. The Package leaflet is updated accordingly.<br>The PRAC also recommends that a DHPC should be issued according to the Communication Plan, as detailed in section 8 of the Assessment report.<br>In addition, MAH(s) should address the issues, as detailed in section 2 of the Assessment report, in the next RMP update to be submitted within an upcoming regulatory procedure affecting the RMP, preferably within the next PSUR.<br>In addition, MAH(s) should address the issues, as detailed in section 2 of the Assessment report, in the next RMP update to be submitted within an upcoming regulatory procedure affecting the RMP.<br>The frequency of PSUR submission should be revised to 1 year. This new frequency will take effect after the next data lock point currently published in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC. The next PSUR, which will still maintain the previous frequency, should cover the period from the 02.12.2018 to |

| | |
|---|---|
| | 01.06.2019 and be submitted within 70 days of the data lock point in accordance with the updated EURD list. The following PSUR, taking into account the new frequency, should cover the period from 02.06.2019 to 01.06.2020 and be submitted within 70 days of the data lock point in accordance with the updated EURD list.<br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010644/201811**<br>(atezolizumab)<br>CAPS:<br>**Tecentriq** (EMEA/H/C/004143) (atezolizumab), Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Period Covered From: 17/05/2018 To: 17/11/2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change:<br>Update of section 4.8 of the SmPC to include the information that infusion related reactions also include cases of hypersensitivity and anaphylaxis.<br>The Package Leaflet is updated accordingly.<br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010699/201811**<br>(erenumab)<br>CAPS:<br>**Aimovig** (EMEA/H/C/004447) (erenumab), Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Kirsti Villikka, "Period Covered From: 17/05/2018 To: 16/11/2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br>Update of section 4.8 of the SmPC to add the adverse reaction Hypersensitivity reactions including rash, swelling/oedema and urticaria.<br>The Package leaflet is updated accordingly.<br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010472/201811**<br>(osimertinib)<br>CAPS:<br>**TAGRISSO** (EMEA/H/C/004124) (osimertinib), AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst, "13/11/2017 To: 12/11/2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change:<br>Update of sections 4.4 and 4.8 of the SmPC in |

| | |
|---|---|
| | order to introduce a new warning on Stevens-Johnson Syndrome (SJS) and amend existing warnings on Interstitial Lung Disease (ILD) and changes in cardiac contractility and to add SJS in the list of adverse drug reactions (ADRs) with a rare frequency, respectively. The Package Leaflet is updated accordingly.<br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |

**B.4. EPARs / WPARs**

| | |
|---|---|
| **Cufence - trientine dihydrochloride - EMEA/H/C/004111, Orphan**<br>Univar BV, treatment of Wilson's disease., Known active substance (Article 8(3) of Directive No 2001/83/EC) | For information only. Comments can be sent to the PL in case necessary. |
| **Doxolipad - doxorubicin hydrochloride - EMEA/H/C/004110**<br>TLC Biopharmaceuticals B.V., treatment of breast and ovarian cancer, Hybrid application (Article 10(3) of Directive No 2001/83/EC) | For information only. Comments can be sent to the PL in case necessary. |
| **LysaKare - l-lysine hydrochloride / l-arginine hydrochloride - EMEA/H/C/004541**<br>Advanced Accelerator Applications, reduction of renal radiation exposure during Peptide-Receptor Radionuclide Therapy (PRRT) with lutetium (177Lu) oxodotreotide, Well-established use application (Article 10a of Directive No 2001/83/EC) | For information only. Comments can be sent to the PL in case necessary. |
| **Posaconazole Accord - posaconazole - EMEA/H/C/005005**<br>Accord Healthcare S.L.U., treatment of fungal infections, Generic, Generic of Noxafil, Generic application (Article 10(1) of Directive No 2001/83/EC) | For information only. Comments can be sent to the PL in case necessary. |
| **Posaconazole AHCL - posaconazole - EMEA/H/C/005028**<br>Accord Healthcare S.L.U., treatment of fungal infections in adults, Generic, Generic of Noxafil, Generic application (Article 10(1) of Directive No 2001/83/EC) | For information only. Comments can be sent to the PL in case necessary. |
| **Xyndari - glutamine - EMEA/H/C/004734, Orphan**<br>Emmaus Medical Europe Ltd., treatment of sickle cell disease, Known active substance (Article 8(3) | For information only. Comments can be sent to the PL in case necessary. |

of Directive No 2001/83/EC)

### 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

| | |
|---|---|
| **Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0066, Orphan**<br>Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik<br>Request for Supplementary Information adopted on 20.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0160**<br>Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 06.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Benlysta - belimumab - EMEA/H/C/002015/II/0068**<br>GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder<br>Request for Supplementary Information adopted on 27.06.2019, 26.04.2019. | Request for supplementary information adopted with a specific timetable. |
| **Flixabi - infliximab - EMEA/H/C/004020/II/0038**<br>Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 20.06.2019.<br>Request for Supplementary Information adopted on 02.05.2019, 14.03.2019. | Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0003**<br>Seqirus Netherlands B.V., Rapporteur: Sol Ruiz<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 14.03.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Hemoblast - thrombin - EMEA/H/D/002769/II/0006/G**<br>BSI Group, Rapporteur: Daniela Melchiorri<br><br>Opinion adopted on 14.06.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Hulio - adalimumab - EMEA/H/C/004429/II/0010/G** | Request for supplementary information adopted with a specific timetable. |

| | |
|---|---|
| Mylan S.A.S, Rapporteur: Bart Van der Schueren<br>Request for Supplementary Information adopted on 06.06.2019. | |
| **Ilumetri - tildrakizumab - EMEA/H/C/004514/II/0005/G**<br>Almirall S.A, Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 26.04.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Keppra - levetiracetam - EMEA/H/C/000277/II/0178/G**<br>UCB Pharma S.A., Rapporteur: Koenraad Norga<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Keytruda - pembrolizumab - EMEA/H/C/003820/II/0073**<br>Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 29.05.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Kovaltry - octocog alfa - EMEA/H/C/003825/II/0023**<br>Bayer AG, Rapporteur: Kristina Dunder<br>Opinion adopted on 27.06.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Matever - levetiracetam - EMEA/H/C/002024/II/0032**<br>Pharmathen S.A., Generic, Generic of Keppra, Rapporteur: Ondřej Slanař<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 14.02.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Myalepta - metreleptin - EMEA/H/C/004218/II/0004, Orphan**<br>Aegerion Pharmaceuticals B.V., Rapporteur: Bart Van der Schueren<br>Opinion adopted on 20.06.2019.<br>Request for Supplementary Information adopted on 02.05.2019. | Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0106**<br>Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik<br>Request for Supplementary Information adopted on 06.06.2019, 07.03.2019, 20.09.2018. | Request for supplementary information adopted with a specific timetable. |
| **Nulojix - belatacept - EMEA/H/C/002098/II/0059/G** | Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP |

| | |
|---|---|
| Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson<br>Opinion adopted on 20.06.2019. | Members were in agreement with the CHMP recommendation. |
| **Ogivri - trastuzumab - EMEA/H/C/004916/II/0006/G**<br>Mylan S.A.S, Rapporteur: Koenraad Norga<br>Opinion adopted on 14.06.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Ovitrelle - choriogonadotropin alfa - EMEA/H/C/000320/II/0078**<br>Merck Europe B.V., Rapporteur: Paula Boudewina van Hennik<br>Opinion adopted on 06.06.2019. | Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0029/G**<br>CSL Behring GmbH, Rapporteur: Kristina Dunder<br>Opinion adopted on 06.06.2019.<br>Request for Supplementary Information adopted on 02.05.2019. | Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0104/G**<br>Genzyme Europe BV, Rapporteur: Peter Kiely<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Vizarsin - sildenafil - EMEA/H/C/001076/II/0029**<br>KRKA, d.d., Novo mesto, Generic, Generic of Viagra, Rapporteur: Alexandre Moreau<br>Request for Supplementary Information adopted on 27.06.2019, 28.02.2019, 22.11.2018. | Request for supplementary information adopted with a specific timetable. |
| **Zessly - infliximab - EMEA/H/C/004647/II/0007**<br>Sandoz GmbH, Rapporteur: Bjorg Bolstad<br>Opinion adopted on 14.06.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1519/G**<br>**HyQvia-EMEA/H/C/002491/WS1519/0047/G**<br>**Kiovig-EMEA/H/C/000628/WS1519/0089/G**<br>Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 14.02.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1600/G**<br>**Aflunov-EMEA/H/C/002094/WS1600/0049/G** | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

| | |
|---|---|
| **Foclivia-EMEA/H/C/001208/WS1600/0044/G**<br>Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 23.05.2019. | recommendation. |
| **WS1620**<br>**Humalog-EMEA/H/C/000088/WS1620/0175**<br>**Liprolog-EMEA/H/C/000393/WS1620/0136**<br>Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **WS1625/G**<br>**Blitzima-EMEA/H/C/004723/WS1625/0025/G**<br>**Ritemvia-EMEA/H/C/004725/WS1625/0025/G**<br>**Truxima-EMEA/H/C/004112/WS1625/0028/G**<br>Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz<br>Opinion adopted on 06.06.2019. | Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Hexacima-EMEA/H/C/002702/WS1592/0089/G**<br>**Hexaxim-EMEA/H/W/002495/WS1592/0094/G**<br>**Hexyon-EMEA/H/C/002796/WS1592/0093/G**<br>Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 14.06.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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

| | |
|---|---|
| **Aclasta - zoledronic acid - EMEA/H/C/000595/II/0072**<br>Novartis Europharm Limited, Rapporteur: Kristina Dunder, “Update of sections 4.2 and 5.1 upon request of the CHMP following assessment of P46/036 based on final results from study ZOL446H2337; this is a randomised, double-blind, placebo-controlled efficacy and safety study of intravenous zoledronic acid | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| administered twice yearly compared to placebo in children with glucocorticoid-induced osteoporosis (GIO) which was part of the main clinical measure of the Aclasta paediatric investigational plan (PIP).<br>In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 26.04.2019. | |
| **Adenuric - febuxostat - EMEA/H/C/000777/II/0051**<br>Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to include the results of the post authorisation safety study CARES (TMX-67_301) to compare the cardiovascular outcomes of febuxostat and allopurinol in subjects with gout and cardiovascular comorbidities. This was a Multicenter, Randomized, Active-Control, Phase IIIB Study conducted at the request of the FDA. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. At the CHMP request, the RMP has been updated (version 7.0) and a DHPC was agreed to inform prescribers of the findings of the CARES study."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 29.05.2019, 28.03.2019, 13.12.2018, 04.10.2018. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Advagraf - tacrolimus - EMEA/H/C/000712/II/0054**<br>Astellas Pharma Europe B.V., Rapporteur: Jayne Crowe, "Update of section 4.2 of the SmPC to include a more clear statement for physicians regarding the potential risk of uncontrolled substitution between different tacrolimus formulations, even with those where BE has been proven, in order to minimise the risk of under or over exposure to tacrolimus."<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0151**<br>Amgen Europe B.V., Rapporteur: Martina Weise, | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

| | |
|---|---|
| "Submission of the final analysis of clinical study report (CSR, 10 May 2018) for study 20110226 to fulfill the post-marketing authorization measure (category 3 pharmacovigilance activity in the Aranesp EU Risk Management Plan (RMP). Study 20110226 is a phase 3, multicenter, randomized, double-blind, parallel group study - START-CKD: Strategies Using Darbepoetin alfa to Avoid Transfusions in Chronic Kidney."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 04.04.2019. | recommendation. |
| **Biktarvy - bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449/II/0008/G**<br>Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC in order to remove the recommendation for caution when methadone is co-administered with Biktarvy based on final results from study AD-141-2321, an in vitro assessment of human Cytochrome P450 inhibition potential of GS-943389 (the sulfate metabolite, M20, of bictegravir). The Package Leaflet is updated accordingly.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to remove reference to boceprevir in sections 4.4 and 4.5 of the SmPC and in the Package Leaflet as it is no longer available in the EU; as well as to introduce some minor editorial corrections throughout the SmPC and the Package Leaflet.<br>Submission of the final report from study AD-141-2322, an in vitro assessment of the inhibition potential of GS-943389 against human P-gp and BCRP transporters."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 31.01.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Brintellix - vortioxetine - EMEA/H/C/002717/II/0022/G**<br>H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, "Update of sections 4.8 and 5.1 of the SmPC in order to describe effects of vortioxetine on treatment-emergent sexual dysfunction based on the outcome of 2 prospective clinical studies (Studies 318 and 4001).<br>Update of sections 4.4 and 5.2 of the SmPC in order to reflect the outcome of study 401 in subjects with severe hepatic impairment." | Request for supplementary information adopted with a specific timetable. |

| | |
|---|---|
| Request for Supplementary Information adopted on 27.06.2019. | |
| **Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0075**<br>UCB Pharma S.A., Rapporteur: Kristina Dunder, "Update of section 4.1 of the SmPC to add more clarity to the axial spondyloarthritis (axSpA) indication statement in particular with regard to the terms radiographic versus non-radiographic axSpA. Update of sections 4.8 and 5.1 of the SmPC to reflect the availability of additional safety information from the phase 3 clinical study designed to evaluate the safety and efficacy of certolizumab in subjects with active axSpA without X-ray evidence of ankylosing spondylitis and objective signs of inflammation (AS0006)."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 28.03.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Cinryze - C1 esterase inhibitor (human) - EMEA/H/C/001207/II/0069**<br>Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC following a company review of the safety data base. The frequencies listed in the ADR table have been updated accordingly. The PL is updated accordingly."<br>Opinion adopted on 20.06.2019.<br>Request for Supplementary Information adopted on 16.05.2019. | Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **CRYSVITA - burosumab - EMEA/H/C/004275/II/0004, Orphan**<br>Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC, to reflect the results of study UX023-CL301, a phase III study undertaken to further assess the efficacy, safety and pharmacodynamics in paediatric patients aged 1-12 years with X-linked Hypophosphataemia (XLH). The provision of the final CSR addresses Specific Obligation 2 (ANX 002) and the requirements of article 46 of the paediatric regulation. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC to increase readability."<br>Request for Supplementary Information adopted on 27.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Dengvaxia - dengue tetravalent vaccine** | Request for supplementary information adopted |

| | |
|---|---|
| **(live, attenuated) - EMEA/H/C/004171/II/0003/G**<br>Sanofi Pasteur, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Sonja Hrabcik, "C.I.13 grouping: Submission of the final report from studies CYD14 and CYD15 listed as category 3 studies in the RMP. These are the final results of the pivotal efficacy studies including amendments to long-term efficacy follow-up (to capture the full range of dengue disease in the study population prospectively i.e. return to active detection of all symptomatic dengue cases) and long-term safety monitoring. No changes to the PI or RMP identified are proposed at this stage. Minor updates of the RMP will follow."<br>Request for Supplementary Information adopted on 27.06.2019. | with a specific timetable. |
| **ELOCTA - efmoroctocog alfa - EMEA/H/C/003964/II/0030**<br>Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2 and 4.8 of the SmPC in order to remove the class wording that no data are available in previously untreated patients and update the frequency category for blood and lymphatic system disorders in previously untreated patients following interim results from study 997HA306, this is an ongoing open-label, single-arm, multicentre study evaluating the safety and efficacy of rFVIIIFc in paediatric previously untreated patients with severe haemophilia A when used according to local standard of care; the Package Leaflet is updated accordingly.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to delete the non-mandatory list of local representatives."<br>Opinion adopted on 06.06.2019.<br>Request for Supplementary Information adopted on 04.04.2019, 31.01.2019. | Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0046**<br>Merck Sharp & Dohme B.V., Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.3, 4.4 and 4.9 of the SmPC in order to revise the current text regarding Ovarian Hyperstimulation Syndrome (OHSS) to add clarity and remove clinical advice describing specific clinical interventions for reducing OHSS that have | Request for supplementary information adopted with a specific timetable. |

| | |
|---|---|
| become outdated, based on post-marketing data and literature review. The Package Leaflet is updated accordingly.<br>In addition, the Marketing authorisation holder to include some editorial changes to the Package Leaflet."<br>Request for Supplementary Information adopted on 14.06.2019. | |
| **EXJADE - deferasirox - EMEA/H/C/000670/II/0064**<br>Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "To update the Risk Management Plan (RMP) version 16.0 for Exjade (deferasirox, EMEA/H/C/000670), covering all formulations (dispersible tablets, film-coated tablets and granules).<br>With this update, the MAH introduces the alignment with requirements of the new RMP template (as per the revised Good Pharmacovigilance Practices (GVP) Module V Rev.2) and consequential removal of the food interaction and drug-drug interactions (DDI) from the list of important identified risks. In addition, "drug reaction with eosinophilia and systemic symptoms" (DRESS) has been reclassified from important potential risk to important identified risk. The reclassification of DRESS was agreed with the PRAC during a previous procedure (EMEA/H/C/PSUSA/00000939/201710).<br>Additional minor changes are have been also implemented in the RMP.<br>With this variation, the Health Care Professional (HCP) guide is also updated."<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 14.02.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Exviera - dasabuvir - EMEA/H/C/003837/II/0044**<br>AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Update of section 4.3 of the SmPC to contraindicate the concomitant use with apalutamide, a strong CYP3A inducer, as well as to update section 4.5 of the SmPC on the interaction with apalutamide. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes." | Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| Opinion adopted on 06.06.2019. | |
| **IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0027, Orphan**<br>CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.4 of the SmPC to update the warning with regards to inhibitor development. Section 4.8 of the SmPC and the PL have been updated accordingly."<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Keytruda - pembrolizumab - EMEA/H/C/003820/II/0071**<br>Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "To update sections 4.2, 4.8, 5.1 and 5.2 of the SmPC based on interim results from study KEYNOTE-051; this is an ongoing Phase I/II, single-arm study to evaluate the PK, pharmacodynamics, toxicity, safety, and anti-tumour activity of pembrolizumab in paediatric participants (Measure 2 of PIP01). Additionally, the results of study PD018 / PA-0064; evaluation of expression of PD-1, PD-L1, and PD-L2 in archival paediatric tumour tissues, were submitted (Measure 1 of PIP01)."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 02.05.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Keytruda - pembrolizumab - EMEA/H/C/003820/II/0074**<br>Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Submission of the final CSR version 03 for KEYNOTE-013 summarising final data from the rrcHL cohort."<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Keytruda - pembrolizumab - EMEA/H/C/003820/II/0075**<br>Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Update of section 5.1 of the SmPC in order to reflect the updated results from study KEYNOTE-010 listed as a category 3 study in the RMP with a data cut-off of 16 March 2018. Study KEYNOTE-010 is a controlled phase II/III trial that randomized a total of 1034 previously-treated subjects with advanced or metastatic NSCLC whose tumours express PD-L1 to receive pembrolizumab at 2 mg/kg Q3W or 10 mg/kg Q3W or docetaxel at 75 mg/m2 Q3W. In addition, the MAH took the opportunity of this | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| variation to include additional instructions in section 4.5 of the SmPC to clarify the use of corticosteroids in subjects treated with pembrolizumab in combination with other chemotherapeutic agents. The Package Leaflet is updated accordingly."<br>Opinion adopted on 27.06.2019. | |
| **Keytruda - pembrolizumab - EMEA/H/C/003820/II/0076**<br>Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "To update section 5.1 of the SmPC based on final results from study KEYNOTE-052 (KN052) listed as a PAES in Annex II; this is a single arm Phase II Clinical Trial of pembrolizumab in subjects with advanced/unresectable or metastatic urothelial cancer (1st line)."<br>Opinion adopted on 27.06.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Kyprolis - carfilzomib - EMEA/H/C/003790/II/0031, Orphan**<br>Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 to add a once-weekly dose regimen for carfilzomib (Kyprolis) at 20/70 mg/m$^2$ in combination with dexamethasone (Kd) for the treatment of the currently indicated patient population. The MAH took the opportunity to implement editorial changes to the SmPC and Patient Information Leaflet (PIL) due to the revised excipients guideline (EMA/CHMP/302620/2017). The PIL is updated accordingly."<br>Request for Supplementary Information adopted on 27.06.2019, 28.02.2019, 15.11.2018. | Request for supplementary information adopted with a specific timetable.<br><br>See agenda items 9.1 |
| **Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0024**<br>AbbVie Deutschland GmbH & Co. KG, Rapporteur: Joseph Emmerich, "Submission of the final clinical report from the Phase 3 study M16-126 (A Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir (GLE)/Pibrentasvir (PIB) in Adults with Chronic Hepatitis C Virus (HCV) Genotype 5 or 6 Infection)."<br>Request for Supplementary Information adopted on 27.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0025**<br>AbbVie Deutschland GmbH & Co. KG, | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

| | |
|---|---|
| Rapporteur: Joseph Emmerich, “Update of sections 4.2, 4.8 and 5.1 of the SmPC to shorten the treatment duration in treatment-naïve subjects with compensated cirrhosis and Hepatitis C virus GT1, 2, 4, 5, or 6 infection, from 12 to 8 weeks, based on interim results from study M16-135 (EXPEDITION-8, A Single Arm, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir (GLE)/Pibrentasvir (PIB) in Treatment Naïve Adults with Chronic Hepatitis C Virus (HCV) Genotype 1 - 6 Infection and Compensated Cirrhosis). In addition, the marketing authorisation holder took the opportunity to revise the submission date of the final CSR for the hepatocellular carcinoma recurrence study in Annex IID, from Q2 2021 to Q2 2023.”<br>Opinion adopted on 27.06.2019. | recommendation. |
| **OPDIVO - nivolumab - EMEA/H/C/003985/II/0065**<br>Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Paula Boudewina van Hennik, “Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update posology and clinical related information based on interim results from Phase 3b/4 Study CA209384 (A Dose Frequency Optimization, Phase IIIB/IV Trial of Nivolumab 240 mg Every 2 Weeks vs Nivolumab 480 mg Every 4 weeks in Subjects with Advanced or Metastatic Non-small Cell Lung Cancer who Received Up to 12 Months of Nivolumab at 3 mg/kg or 240 mg Every 2 Weeks.) and further supported by pharmacometric analyses in subjects with 2L+ NSCLC.”<br>Request for Supplementary Information adopted on 27.06.2019. | Request for supplementary information adopted with a specific timetable.<br><br>See agenda item 9.1 |
| **Qtern - saxagliptin / dapagliflozin - EMEA/H/C/004057/II/0024**<br>AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, “Update of sections 4.2, 4.4 and 5.1 of the SmPC with information on the glycaemic efficacy and renal safety of dapagliflozin in patients with Type 2 diabetes mellitus and moderate renal impairment (CKD 3A) based on final results from study D1690C00024 (DERIVE) (dapagliflozin), and to reflect a change in renal cut-off value for saxagliptin. The package leaflet is updated accordingly.<br>The RMP version 4.1 has also been submitted. | Request for supplementary information adopted with a specific timetable. |

| | |
|---|---|
| In addition, the MAH took the opportunity to update SmPC sections 2, 4.8, 5.2 and Annex II to include the required excipient information in relation to sodium levels and lactose following the update to the Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use", as well as to bring the PI in line with EMA guidance ("Compilation of QRD decisions on stylistic matters in product information", EMA/25090/2002 Rev.18, published 08 December 2017)."<br>Request for Supplementary Information adopted on 27.06.2019. | |
| **Repatha - evolocumab - EMEA/H/C/003766/II/0031**<br>Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC based on the final results from study 20110271 (TAUSSIG) listed as a category 3 study in the RMP, submitted in order to fulfil MEA 003 and article 46 of Regulation EC No 1901/2006; this is a multicenter, open-label study to assess the long-term safety, tolerability and efficacy of AMG 145 (evolocumab) on LDL-C in adult and adolescent subjects with severe familial hypercholesterolemic (FH), including subjects with homozygous familial hypercholesterolemia (HoFH). In addition, the Marketing authorisation holder (MAH) took the opportunity to make a correction to the Labelling."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 28.03.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Saxenda - liraglutide - EMEA/H/C/003780/II/0023**<br>Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information regarding hypoglycaemia in patients with type 2 diabetes mellitus treated with insulin based on the final results from the Phase 3b clinical trial NN8022-4272 (SCALE Insulin), undertaken to investigate the effect and safety of liraglutide 3.0 mg in subjects with overweight or obesity and type 2 diabetes mellitus treated with basal insulin. The Package Leaflet is updated accordingly."<br>Opinion adopted on 14.06.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| **Sprycel - dasatinib - EMEA/H/C/000709/II/0064**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Sinan B. Sarac, "Update of section 5.2 of the SmPC based on results from existing and new pharmacokinetics (PK) analyses together with a review of literature data on the dasatinib PK profile in fasted conditions to assess implications arising for the recommendation for administration, as requested by the CHMP. In addition, the local representative's details for Germany have been updated. Minor editorial changes have been introduced throughout the Product Information."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 28.03.2019, 15.11.2018. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Sutent - sunitinib - EMEA/H/C/000687/II/0074**<br>Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, "Submission of the final analyses of the overall survival data, and the additional biomarker analyses collected from study A6181202 (multi-centre, single-arm, open-label, Phase 4 clinical trial of sunitinib in patients with progressive, advanced/metastatic, well-differentiated, unresectable pancreatic neuroendocrine tumours (pNET))."<br>Opinion adopted on 14.06.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Taltz - ixekizumab - EMEA/H/C/003943/II/0026/G**<br>Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, "Type II- C.I.4 -Update of section 5.1 of the SmPC based on results of study RHCF - a 52-Week Multicenter, Randomized, Open-Label, Parallel-Group Study Evaluating the Efficacy and Safety of ixekizumab versus adalimumab in Patients with Psoriatic Arthritis Who Are Biologic Disease-Modifying Anti-Rheumatic Drug Naïve. Type II- C.I.4 -Update of section 4.5 of the SmPC based on results of study RHBU – a study evaluating of the effect of ixekizumab on the pharmacokinetics of cytochrome P450 substrates in patients with moderate-to-severe plaque psoriasis."<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0102** | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP |

| | |
|---|---|
| Genzyme Europe BV, Rapporteur: Peter Kiely, "Update of sections 4.4 and 5.1 of the SmPC with long term follow-up results from studies HiLo and ESTIMABL1. Additionally, the sodium content provision wording in the Package Leaflet is aligned to the Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use" (SANTE-2017-11668). The MAH further made editorial changes throughout the Product Information."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 26.04.2019. | Members were in agreement with the CHMP recommendation. |
| **Tremfya - guselkumab - EMEA/H/C/004271/II/0010**<br>Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, "Update of sections 4.8 and 5.1 of the SmPC to add the long term 3-year clinical data from the two ongoing clinical studies CNTO1959PSO3001 (VOYAGE 1) and CNTO1959PSO3002 (VOYAGE 2) in subjects with plaque psoriasis."<br>Request for Supplementary Information adopted on 20.06.2019, 02.05.2019, 14.03.2019. | Request for supplementary information adopted with a specific timetable. |
| **Victoza - liraglutide - EMEA/H/C/001026/II/0050**<br>Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.1 of the SmPC, based on the phase 3b study NN2211-4315 (LIRA-ADD2SGLT2i), to include data on liraglutide vs placebo as add-on to SGLT2 inhibitors (+/- metformin) in subjects with type 2 diabetes mellitus. The Package Leaflet has been updated accordingly."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 26.04.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0053**<br>AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Update of section 4.3 of the SmPC to contraindicate the concomitant use with lomitapide, a CYP3A4 substrate, and apalutamide, a strong CYP3A inducer, as well as update of section 4.5 of the SmPC on the potential interactions with apalutamide, encorafenib, ibrutinib and lomitapide. The Package Leaflet is updated | Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| accordingly. In addition, the MAH took the opportunity to implement minor editorial changes."<br>Opinion adopted on 06.06.2019. | |
| **Xeloda - capecitabine - EMEA/H/C/000316/II/0083**<br>Roche Registration GmbH, Rapporteur: Janet Koenig, "Update of section 4.6 of the SmPC in order to add advice on post treatment contraception period and wash out period before initiation of breastfeeding. The package leaflet is updated accordingly."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 26.04.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **XGEVA - denosumab - EMEA/H/C/002173/II/0069**<br>Amgen Europe B.V., Rapporteur: Kristina Dunder, "Update of SmPC sections 4.2, 4.8, 5.1 and 5.2 based on the final analysis from study 20062004; a phase 2, open-label, single-group study to evaluate the safety and pharmacokinetics of denosumab in adult and adolescent subjects with giant cell tumour of bone (GCTB). The final CSR for study 20062004 was previously assessed by CHMP as part of procedure P46 027 and the finalisation of the study addresses the final PIP measure. Further, section 4.8 of the SmPC is being updated to include the new ADR 'alopecia' with a frequency of 'common', upon request by PRAC following the assessment of PSUSA/00009119/201809. In addition, the MAH took the opportunity to update the description of ONJ incidence in section 4.8 of the SmPC in order to express events per 100 patient years without a percentage sign. The Package Leaflet has been updated accordingly."<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **WS1511/G**<br>**Advagraf-EMEA/H/C/000712/WS1511/0052/G**<br>**Modigraf-EMEA/H/C/000954/WS1511/0031/G**<br>Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe, "Update of sections 4.5 and 4.8 of the SmPC to add the drug-drug interaction with letemovir and to add the febrile neutropenia with frequency unknown, based on the cumulative | Request for supplementary information adopted with a specific timetable. |

| | |
|---|---|
| review of the MAH safety database.<br>Update of section 4.6 of the SmPC to add the information on pregnancy and lactation following the cumulative review of the cases reported in the MAH global safety database, published literature and the transplantation pregnancy exposure registry.<br>The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor editorial changes throughout the PI and to implement the wording from the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'."<br>Request for Supplementary Information adopted on 14.06.2019, 14.03.2019. | |
| **WS1598**<br>**Cymbalta-EMEA/H/C/000572/WS1598/0079**<br>**Duloxetine Lilly-EMEA/H/C/004000/WS1598/0016**<br>**Xeristar-EMEA/H/C/000573/WS1598/0082**<br>**Yentreve-EMEA/H/C/000545/WS1598/0064**<br>Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim, Yentreve, Lead Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 5.1 to reflect on the data obtained from the paediatric study HMGW, submitted the final report for the paediatric study HMGW, a Phase 3b, Randomised, Double-Blind, Placebo-Controlled, Clinical Trial of Duloxetine in adolescent Juvenile Primary Fibromyalgia Syndrome (JPFS) population."<br>Opinion adopted on 14.06.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1607**<br>**Kisplyx-EMEA/H/C/004224/WS1607/0023**<br>**Lenvima-EMEA/H/C/003727/WS1607/0025**<br>Eisai GmbH, Lead Rapporteur: Bart Van der Schueren, "Update of section 5.2 of the SmPC based on the results of study E7080-A001- 010, a Multicenter Phase 0 Study in Healthy Subjects and Subjects with Either Hepatic or Renal Impairment to Obtain Plasma for Assessment of in Vitro Lenvatinib Protein Binding."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| on 23.05.2019. | |
| **WS1613**<br>**Epclusa-EMEA/H/C/004210/WS1613/0039**<br>**Vosevi-EMEA/H/C/004350/WS1613/0029**<br>Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to add new information regarding co-administration with atorvastatin, based on final results from study GS-US-342-4034.<br>Study GS-US-342-4034 was a phase 1 study to evaluate the effect of sofosbuvir/velpatasvir fixed dose combination on the pharmacokinetics of atorvastatin.<br>The Package Leaflet is updated accordingly.<br>In addition, the Worksharing Applicant took the opportunity to amend Annex II of the Product Information with regards to the due date for submission of study DAA-PASS. This study is designed to evaluate the recurrence of hepatocellular carcinoma and the date has been postponed from Q2 2021 to Q2 2023, as approved in the framework of WS1476.<br>Furthermore, the MAH implemented minor editorial updates throughout the Product Information."<br>Request for Supplementary Information adopted on 20.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **WS1617**<br>**Filgrastim**<br>**Hexal-EMEA/H/C/000918/WS1617/0050**<br>**Zarzio-EMEA/H/C/000917/WS1617/0051**<br>Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 6.6 of the SmPC in order to remove the latex warning based on company and post marketing data. The Package Leaflet is updated accordingly."<br>Opinion adopted on 14.06.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1627**<br>**Eviplera-EMEA/H/C/002312/WS1627/0099**<br>**Odefsey-EMEA/H/C/004156/WS1627/0042**<br>Gilead Sciences Ireland UC, Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 4.9 of the Eviplera and Odefsey SmPCs in order to remove the recommendation to use oral activated charcoal in the event of an overdose of rilpivirine and replace it with a general guidance | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| to contact poison control. In addition the MAH has taken the opportunity to update the lactose wording in section 4.4 of the SmPC and section 2 of the PL of Eviplera, according to the annex to the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use', as well as update section 5.1 of the Eviplera SmPC to reflect the full waiver for the Eviplera PIP. The MAH has also taken the opportunity to introduce minor administrative updates in the product information for both for Eviplera and Odefsey."<br>Opinion adopted on 27.06.2019. | |
| **WS1637**<br>**Ebymect-EMEA/H/C/004162/WS1637/0039**<br>**Edistride-EMEA/H/C/004161/WS1637/0032**<br>**Forxiga-EMEA/H/C/002322/WS1637/0051**<br>**Xigduo-EMEA/H/C/002672/WS1637/0050**<br>AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "Update of sections 4.4 (Special warnings and precautions for use) and 4.8 (Undesirable effects) of the SmPC of dapagliflozin-containing products with respect to the Fournier's gangrene class labelling language, following results from the DECLARE study (a Multicentre, Randomized, Double-Blind, Placebo-Controlled cardiovascular outcome trial in Patients with Type 2 Diabetes). The Package Leaflet is updated accordingly."<br>Request for Supplementary Information adopted on 27.06.2019. | Request for supplementary information adopted with a specific timetable. |

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

| | |
|---|---|
| **Aflunov - prepandemic influenza vaccine (h5n1) (surface antigen, inactivated, adjuvanted) - EMEA/H/C/002094/II/0044/G**<br>Seqirus S.r.l, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.4, 4.6, 4.8 and 5.1 of the SmPC following clinical study reports of studies V87_25 and V87_26 listed as post approval commitments; these are Phase 3, stratified, randomized, controlled, observer-blind, multicenter studies; the Package Leaflet and Labelling are updated accordingly. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.<br>See agenda item 9.1 |

| | |
|---|---|
| The updated RMP version 3.0 has also been submitted.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some amendments to the PI and make some additional minor editorial corrections."<br>Request for Supplementary Information adopted on 29.05.2019, 28.02.2019, 20.09.2018. | |
| **Benlysta - belimumab - EMEA/H/C/002015/II/0067**<br>GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 5.1 of the SmPC for Benlysta 120 mg and 400mg powder for concentrate for solution for infusion based on final results from study BEL115471/ HGS1006-C1112 listed as a category 3 study in the RMP; this is a Phase 3/4, multicenter, randomized, double-blind, placebo-controlled, 52-week study to evaluate the efficacy and safety of belimumab in African-American/Black subjects with systemic lupus erythematosus. Section 5.1 of the SmPC for Benlsyta 200 mg solution for injection was updated to cross refer to those results. Editorial changes were also brought to the section 5.2 of the SmPC for Benlsyta 200 mg solution for injection and the section 5.1 of the SmPC for Benlysta 120 mg and 400mg powder for concentrate for solution for infusion. The RMP was updated to version 31 with the results from study BEL115471/ HGS1006-C1112."<br>Opinion adopted on 27.06.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Brinavess - vernakalant - EMEA/H/C/001215/II/0035**<br>Correvio, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information following updates to the Company Core Safety Datasheet (CCDS) based on the results of an integrated safety analysis performed on data of existing clinical studies with a stronger emphasis on treatment-related ADRs and an incidence rate above one percent. The Package Leaflet was updated accordingly.<br>The RMP version 7.0 has also been submitted and incorporates the results from the new safety analysis. In addition the results from completed observational Cohort SPECTRUM study (A Prospective Observational Registry Study to | Request for supplementary information adopted with a specific timetable. |

| | |
|---|---|
| Characterise Normal Conditions of Use, Dosing and Safety Following Administration of Vernakalant IV Sterile Concentrate: PASS Protocol 6621-049) currently under assessment within Brinavess II/34 were included in the updated RMP.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to update sections 4.2, 4.4, 4.6, 4.7, 4.8, 5.1, 5.2, 5.3, 6.4 of the SmPC, Annex II, Labelling sections 3 and 5, Package Leaflet sections 2, 4, 5 and 6 to include editorial changes, to correct typographical errors and to bring the PI in line with the latest QRD template version 10 and well as to update statements related to the excipients in the SmPC and Package Leaflet in line with the EC Guideline on "Excipients in the Labelling and Package Leaflet of medicinal products for human use" of March 2018 and the EMA Annex to the EC Guideline of October 2017 (SANTE-2017-11668)."<br>Request for Supplementary Information adopted on 14.06.2019. | |
| **Fasenra - benralizumab - EMEA/H/C/004433/II/0014/G**<br>AstraZeneca AB, Rapporteur: Fátima Ventura, PRAC Rapporteur: David Olsen "B.IV.1.c – To add an autoinjector delivery device, Fasenra 30 mg solution for injection in pre-filled pen.<br>C.I.4 – Update of sections 4.2, 4.4, 6.4, 6.5, 6.6 of the SmPC in order to update the information for self-administration for Fasenra 30 mg solution for injection in pre-filled syringe. Furthermore, minor changes in section 4.4 are introduced as clarification.<br>Section 6.4 of the SmPC is also amended to include an update of the storage precautions in particularly to increase the room temperature storage time for Fasenra from 24 hours to 14 days.<br>In addition, the RMP (version 2.0) is updated to reflect the additional information about completed studies (ALIZE, GREGALE, AMES, GRECO), (Pregnancy registry (D3250R00026) and Malignancy Post Authorization Safety Study (D3250R00042). Furthermore, the RMP is revised in line with the RMP template (GVP Module V rev.2).<br>The requested group of variations proposed amendments to the Summary of Product | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| Characteristics, Labelling and Package Leaflet and to the Risk Management Plan (RMP).”<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 29.05.2019, 28.02.2019. | |
| **Flebogamma DIF - human normal immunoglobulin - EMEA/H/C/000781/II/0059/G**<br>Instituto Grifols, S.A., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, “C.I.z - Update of SmPC according to the Guideline on core SmPC for human normal immunoglobulin for intravenous administration (IVIg) which came into effect on 01 January 2019 to mainly:<br>- Include chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN) as new therapeutic indications<br>- Modify the Secondary immunodeficiencies (SID) therapeutic indication definition.<br>Other changes were made across sections 4.2, 4.3, 4.4, 4.5, 4.6, 4.8, 4.9 and 6.2 of the SmPC. The Package Leaflet is updated accordingly.<br>C.I.4 - Update of section 4.8 of the SmPC for Flebogamma DIF 100 mg/ml in order to update the safety information based on the final results from study IG0601: a multi-center, prospective, open-label, clinical trial to assess the safety and the efficacy of a new intravenous immune globulin (IGIV3I Grifols 10%) in patients with idiopathic (immune) thrombocytopenic purpura. The Package Leaflet is updated accordingly.<br>C.I.4 - Update of section 4.8 of the SmPC to revise the adverse drug reactions for both strengths based on all completed studies previously submitted. The Package Leaflet is updated accordingly.<br>The RMP version 7.2 has also been submitted to add the CIPD and MMN therapeutic indications and to convert to the RMP template Revision 2.”<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 26.04.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **IBRANCE - palbociclib - EMEA/H/C/003853/II/0019/G**<br>Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark, “Update of section 4.8 of the SmPC in order to include ILD/pneumonitis as ADRs based on a safety cumulative review together with | Request for supplementary information adopted with a specific timetable. |

| | |
|---|---|
| reclassification of the risk from potential to identified in the RMP (version 1.6). The Package Leaflet is updated accordingly. The MAH has also submitted the updated RMP version 1.6 in order to remove long term use from missing information in the list of safety concerns. In addition, the MAH is proposing to change the due date for submission of the final CSR of study A5481027 listed as a Category 3 study in the RMP."<br>Request for Supplementary Information adopted on 14.06.2019. | |
| **Iclusig - ponatinib - EMEA/H/C/002695/II/0051, Orphan**<br>Incyte Biosciences Distribution B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of the RMP to version 19, including deletion of previously agreed safety concerns. These deletions are proposed in line with the guideline on Good Pharmacovigilance Practices (GVP) Module V on RMP (revision 2 - dated on 31 March 2017). Other updates include: review of the categorisation of the posterior reversible encephalopathy syndrome (PRES) risk in the RMP in line with the request from PSUSA/00010128/201712; correction of the category (from Category 3 to 1) of the study AP24534-14-203, an imposed Annex II condition; revision of the due date for the submission of this study report to August 2021, as described in the Iclusig PI, and as agreed as part of procedure EMEA/H/C/002695/ANX/016."<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Inovelon - rufinamide - EMEA/H/C/000660/II/0052, Orphan**<br>Eisai GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of section 4.2 of the SmPC in order to include an additional method of administration via feeding tube for Inovelon oral suspension. This fulfills the CHMP recommendation to evaluate the feasibility of administrating the rufinamide oral suspension via an enteral feeding tube adopted with variation II/45.<br>The RMP version 11 has been submitted."<br>Opinion adopted on 14.06.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Intuniv - guanfacine - EMEA/H/C/003759/II/0015** | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP |

| | |
|---|---|
| Shire Pharmaceuticals Ireland Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Maria del Pilar Rayon, "Update of section 4.5 of the SmPC in order to remove the statement on potential drug interactions with drugs that inhibit OCT1 based on final results from study V8953M-SPD503; this is a non-clinical study (Transporter Interaction - OCT1 inhibition);<br>The RMP version 3.0 has also been submitted."<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 11.04.2019, 14.02.2019. | Members were in agreement with the CHMP recommendation. |
| **Kisqali - ribociclib - EMEA/H/C/004213/II/0003/G**<br>Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark, "C.I.4: Update of sections 4.2 and 5.2 of the SmPC in order to reflect the results of study CLEE011A2109: A Phase I, open label, multi-centre, parallel cohort, single dose study to evaluate the pharmacokinetics of LEE011 in healthy subjects with normal hepatic function and subjects with impaired hepatic function; C.I.4: Update of sections 4.2 and 5.2 of the SmPC in order to include a recommendation for a starting dose of 400 mg for patients with severe renal impairment and to reflect the results from study CLEE011A2116-Part I: A phase I, open label, multicentre, parallel-group, single dose two-staged study to evaluate the pharmacokinetics and safety of a single 400 mg oral dose of LEE011 in subjects with varying degrees of impaired renal function compared to matched healthy volunteers with normal renal function.<br>The updated RMP version 2.0 was agreed."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 17.01.2019, 06.09.2018. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0068**<br>Roche Registration GmbH, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "Submission of the final report from study BH21260 listed as a category 3 study in the RMP (MEA008.5). This is a randomized, controlled, open-label, multicenter, parallel-group study to assess all-cause mortality and | Request for supplementary information adopted with a specific timetable. |

| | |
|---|---|
| cardiovascular morbidity in patients with chronic kidney disease on dialysis and those not on renal replacement therapy under treatment with Mircera or reference ESAs. The RMP (version 12.0) is updated accordingly and transitioned to the new EU RMP template in line with the revised Good Pharmacovigilance Practice (GVP) Module V (Revision 2) guideline."<br>Request for Supplementary Information adopted on 14.06.2019, 17.01.2019, 04.10.2018. | |
| **Movymia - teriparatide - EMEA/H/C/004368/II/0010**<br>STADA Arzneimittel AG, Duplicate, Duplicate of Terrosa, Rapporteur: Milena Stain, PRAC Rapporteur: Ronan Grimes, "Submission of the final clinical study report from Study RGB1023O31; a Phase III, multi-centre, randomised, active-controlled, parallel-group, comparative efficacy/safety study. An updated RMP version 1.4 was agreed during the procedure."<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 11.04.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Signifor - pasireotide - EMEA/H/C/002052/II/0041/G, Orphan**<br>Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of section 4.8 of the SmPC based on the final CSR from study CSOM230B2219; a multi-center, randomized, open-label, Phase IV study to investigate the management of pasireotide-induced hyperglycemia with incretin based therapy or insulin in adult patients with Cushing's disease or acromegaly (listed as a category 3 study in the RMP).<br>A revised RMP version 7.0, updated in line with the revised GVP Module V, including changes to the safety concerns, was provided as part of the application."<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Spinraza - nusinersen - EMEA/H/C/004312/II/0014, Orphan**<br>Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga, "C.I.13: Submission of the final report from Phase 2 Study SM202 (EMBRACE or CS7) listed as a category 3 study in the RMP. This is a Phase | Request for supplementary information adopted with a specific timetable. |

| | |
|---|---|
| 2, randomized, double-blind, sham-procedure-controlled study to assess the safety and tolerability and explore the efficacy of ISIS 396443 (BIIB058) administered intrathecally in subjects with spinal muscular atrophy who are not eligible to participate in the clinical studies ISIS 396443-CS3B or ISIS 396443-CS4 due to age at screening and/or SMN2 copy number.<br>An updated RMP version 10.1 has also been submitted."<br>Request for Supplementary Information adopted on 14.06.2019. | |
| **TAGRISSO - osimertinib - EMEA/H/C/004124/II/0029**<br>AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2 and 5.2 of the SmPC in order to reflect the outcome of study D5160C00035, an open-label, Phase I study to assess the pharmacokinetics, safety and tolerability of osimertinib following a single oral 80 mg dose to patients with advanced solid tumours and normal renal function or severe renal impairment. This study was a Category 3 study in the EU-RMP. The RMP version 13 has also been submitted."<br>Request for Supplementary Information adopted on 27.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **Tecentriq - atezolizumab - EMEA/H/C/004143/II/0022**<br>Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.2 and 5.2 of the SmPC in order to add 2 dosing regimens, 840 mg every 2 weeks and 1680 mg every 4 weeks administered as an IV infusion for the approved indications, based on results of population pharmacokinetics modelling and simulation analyses (report No. 1085557) and supported by exposure-response analyses (report No. 1087176). The package leaflet is updated accordingly.<br>An updated RMP is also provided in order to reflect the proposed new dosing regimens, and to align the indication statement for metastatic urothelial carcinoma with the SmPC.<br>Moreover, the due date for submission of RMP commitments and an Annex II condition are proposed to be updated."<br>Request for Supplementary Information adopted | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| on 26.04.2019. | |
| **Terrosa - teriparatide - EMEA/H/C/003916/II/0009**<br>Gedeon Richter Plc., Rapporteur: Milena Stain, PRAC Rapporteur: Ronan Grimes, "Submission of the final clinical study report from study RGB1023O31; a Phase III, multi-centre, randomised, active-controlled, parallel-group, comparative efficacy/safety study. An updated RMP version 1.4 was agreed during the procedure."<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 11.04.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Truberzi - eluxadoline - EMEA/H/C/004098/II/0009/G**<br>Allergan Pharmaceuticals International Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update the safety information based on results from PK study ELX-PK-01 listed as a category 3 study in the RMP; this is a Single-dose, Open-label, Pharmacokinetic study of Eluxadoline in Healthy Subjects with normal Renal Function and Patients with Renal Impairment.<br>Update of sections 4.4 and 4.8 of the SmPC following Company Core Data Sheet (CCDS) update based on review of clinical safety data and post- marketing safety data. Section 4.3 has been updated to add clarification in line with section 4.4. and section 5.1 has been updated to add Pharmacotherapeutic Group and ATC code.<br>The RMP version 3.0 has also been submitted.<br>The Package Leaflet is updated accordingly.<br>In addition, the MAH also took the opportunity to change "eluxadoline" to "Truberzi" when referring to the medicinal product throughout the SmPC."<br>Request for Supplementary Information adopted on 27.06.2019, 28.03.2019. | Request for supplementary information adopted with a specific timetable. |
| **Uptravi - selexipag - EMEA/H/C/003774/II/0022**<br>Janssen-Cilag International N.V., Rapporteur: Martina Weise, PRAC Rapporteur: Adrien Inoubli, "Update of sections 4.2, 4.4 and 4.5 of the SmPC in order to update the safety information based on the final results from study AC-065-117 a listed category 3 study in the RMP which is a clinical pharmacology drug-drug interaction | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| (DDI) study, evaluating the effect of clopidogrel a moderate inhibitor of CYP2C8, on the pharmacokinetics of selexipag and its active metabolite ACT-333679. The package leaflet is updated accordingly.<br>The RMP version 6.1 has also been submitted.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to correct minor discrepancies in the SmPC."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 11.04.2019, 14.02.2019. | |
| **Vimpat - lacosamide - EMEA/H/C/000863/II/0073/G**<br>UCB Pharma S.A., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2, 4.4, 4.5 and 4.8 of the SmPC in order to include new safety information on cardiac arrhythmias based on safety signal assessment report (SSAR). In addition, the MAH took the opportunity to correct the frequency of the adverse event 'coordination abnormal' in section 4.8 of the SmPC from 'common' to 'uncommon' as the frequency of this ADR was erroneously classified as 'common' due to rounded ADR percentages in the initial SmPC. The Package Leaflet is updated accordingly. The RMP version 13.1 has also been submitted."<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 11.04.2019, 14.02.2019, 04.10.2018. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Xolair - omalizumab - EMEA/H/C/000606/II/0093**<br>Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of section 4.6 of the SmPC based on the data from the final study report of the category 3 Post-Authorisation Safety Study (PASS) Q2952g (EXPECT); this is an observational study to evaluate pregnancy outcomes and estimate the incidence of spontaneous foetal loss in pregnant women exposed to omalizumab prenatally and to explore the potential risk to newborn infants exposed via breast milk. The Package Leaflet has been updated accordingly. The RMP is updated to version 15.0."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 28.03.2019, 13.12.2018. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| **Yervoy - ipilimumab - EMEA/H/C/002213/II/0064**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of section 4.8 of the SmPC in order to update the safety information following final results from study CA184143 (A Multi-National, Prospective, Observational Study in Patients with Unresectable or Metastatic Melanoma) listed as a category 3 study in the RMP (MEA017.11); The RMP has been updated accordingly (submitted version 26.0). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the RMP in regards to already assessed MEA 036.1 concerning protocol synopsis on the extension of the Dutch Melanoma Treatment Registry (DMTR) to paediatric melanoma patients treated with ipilimumab. Furthermore the MAH took the opportunity to request a 6-month shift in the dates associated to the next implementation steps of the DMTR extension (Registration of paediatric patients in the DMTR register and final CSR submission). Editorial changes have also been included in section 5.1 of the SmPC to provide more clarity on whether studies relate to melanoma or RCC and to monotherapy or combination therapy with nivolumab."<br>Request for Supplementary Information adopted on 14.06.2019, 14.03.2019. | Request for supplementary information adopted with a specific timetable. |
| **Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0043**<br>Pfizer Ireland Pharmaceuticals, Rapporteur: Alar Irs, PRAC Rapporteur: Maia Uusküla, "Update of section 4.2 of the SmPC in order to provide dosing recommendations for a high-dose regimen of ceftaroline fosamil in paediatric patients for the treatment of complicated skin and soft tissue infections (cSSTI) for which Staphylococcus aureus is known or suspected of having minimum inhibitory concentrations (MIC) of 2 or 4 mg/L based on the final population modelling analysis report (PMAR) of extrapolation study PMAR-EQDD-C266b-DP4-826. In addition, the MAH made minor editorial changes to the SmPC. The RMP version 18.1 has also been submitted."<br>Opinion adopted on 27.06.2019.<br>Request for Supplementary Information adopted on 28.03.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| **WS1518**<br>**Epclusa-EMEA/H/C/004210/WS1518/0034**<br>**Harvoni-EMEA/H/C/003850/WS1518/0077**<br>**Sovaldi-EMEA/H/C/002798/WS1518/0055**<br>**Vosevi-EMEA/H/C/004350/WS1518/0025**<br>Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC (Epclusa, Harvoni), sections 4.2, 4.4, 5.1 and 5.2 (Sovaldi) and 4.2, 4.8 and 5.2 (Vosevi) in order to add new information regarding the use of the sofosbuvir-containing products in patients with renal impairment, based on final results from studies GS-US-342-4062, GS-US-337-4063 and GS-US-334-0154, listed as a category 3 study in the RMP and study GS-US-338-1125.<br>Study GS-US-342-4062 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of sofosbuvir/velpatasvir for 12 Weeks in subjects with chronic HCV infection who are on dialysis for end stage renal disease.<br>Study GS-US-337-4063 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of ledipasvir/sofosbuvir in subjects with genotype 1, 4, 5 and 6 chronic HCV infection who are on dialysis for end stage renal disease.<br>Study GS-US-334-0154 was a phase 2b, open label study of 200 mg or 400 mg sofosbuvir+ribavirin for 24 Weeks in Genotype 1 or 3 HCV infected subjects with renal insufficiency.<br>Study GS-US-338-1125 was a phase 1, open-label, parallel-group, single-dose study to evaluate the pharmacokinetics of voxilaprevir in subjects with normal renal function and severe renal impairment.<br>The Package Leaflet is updated accordingly. The RMPs have also been submitted for each of the products in this work-sharing procedure."<br>Request for Supplementary Information adopted on 14.06.2019, 11.04.2019. | Request for supplementary information adopted with a specific timetable. |

### B.5.4. PRAC assessed procedures

| | |
|---|---|
| PRAC Led<br>**Adasuve - loxapine - EMEA/H/C/002400/II/0030** | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

| | |
|---|---|
| Ferrer Internacional s.a., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of the category 3 final report from Drug Utilization study AMDC-204-403 EU (A Multinational Retrospective Medical Record Review to Evaluate Utilization Patterns of Adasuve-Staccato loxapine for inhalation in agitated persons in routine clinical care). In addition, the MAH also submitted the second report with results of the healthcare professional survey on the effectiveness of the additional risk minimisation measures in Annex 7 of the RMP submitted with this variation.”<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 11.04.2019. | recommendation. |
| PRAC Led<br>**Betmiga - mirabegron - EMEA/H/C/002388/II/0030**<br>Astellas Pharma Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, “Submission of the final report of the Drug Utilization Study of mirabegron using real-word healthcare databases from the NL, ES, UK and FI (study 178-PV-002), as agreed via MEA 009.2.”<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 17.01.2019, 04.10.2018. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Cerdelga - eliglustat - EMEA/H/C/003724/II/0020, Orphan**<br>Genzyme Europe BV, PRAC Rapporteur: Eva A. Segovia, “Submission of the final report from study ELIGLC06912 listed as a category 3 study in the RMP (MEA006). This is a Drug Utilization Study of Eliglustat in the United States (US) Population Using MarketScan Database and the International Collaborative Gaucher Group Registry. Consequently, submission of an updated RMP version 6 in order to reflect the submission of the final data for study ELIGLC06912. In addition, RMP version 6.0 has been aligned with the Guideline on GVP - Module V, revision 2 and the related new EU RMP template has been implemented.”<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| on 14.03.2019. | |
| PRAC Led<br>**Cotellic - cobimetinib -**<br>**EMEA/H/C/003960/II/0016**<br>Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP version 4 in order to align with the current GVP Rev 2. Additionally, in line with the request from PRAC in the AR dated 31 Oct 2018, the agreed wording is implemented.”<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Edurant - rilpivirine -**<br>**EMEA/H/C/002264/II/0034**<br>Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP version 8.1 in order to remove ‘bleeding disorders' as an important potential risk as agreed by PRAC during procedure PSUSA/00009282/201805. In addition, the MAH took the opportunity to remove some of the safety concerns and remove/reclassify additional pharmacovigilance activities (Category 4) in line with the revision 2 of the RMP template.”<br>Opinion adopted on 14.06.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Hulio - adalimumab -**<br>**EMEA/H/C/004429/II/0009**<br>Mylan S.A.S, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “Submission of an updated RMP version 3.0 in order to do the following changes:<br>As part of Post-Authorization Measures (category 3 according to the RMP), the applicant has to submit the study protocol on a longitudinal observational study of patients with rheumatoid arthritis treated with biologic and other new advanced targeted therapies by 31 March 2019 (Ref No.MEA/PRO 002). The applicant now proposes to use a different registry (RABBIT) than the previously agreed BSRBR-RA and to update the study milestones in the pharmacovigilance plan. Furthermore, the | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| submitted RMP consolidates updates approved in two other variations (procedures EMEA/H/C/004429/II/0004 and EMEA/H/C/004429/IB/0007)."<br>Opinion adopted on 14.06.2019. | |
| PRAC Led<br>**Kiovig - human normal immunoglobulin - EMEA/H/C/000628/II/0091**<br>Baxter AG, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 9.0 in order to include the new indication chronic inflammatory demyelinating polyradiculoneuropathy [CIDP] and update the list of safety concerns (implementation of new specifications from GCP Module V (Rev 2)."<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Kisplyx - lenvatinib - EMEA/H/C/004224/II/0024**<br>Eisai GmbH, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Bjorg Bolstad, "Submission of an updated RMP version 11.1 in order to update the study design for study E7080-G000-218 (MEA 007) from double-blind to open label as requested by the CHMP from post authorisation measure MEA 06.1. In addition the MAH is taking the opportunity to introduce minor administrative changes to the RMP."<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Otezla - apremilast - EMEA/H/C/003746/II/0023**<br>Celgene Europe BV, Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of an updated RMP version 11.4 in order to reclassify and/or rename the known safety concerns associated with the use of apremilast in accordance with the new Guideline on GVP Module V. In addition, the RMP is converted to the RMP template Revision 2. The MAH also took the opportunity to update the milestones of the pharmacovigilance plan of ongoing category 3 studies included in the RMP." | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 14.03.2019, 31.10.2018. | |
| PRAC Led<br>**Ozurdex - dexamethasone - EMEA/H/C/001140/II/0035**<br>Allergan Pharmaceuticals Ireland, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "C.I.13: Submission of the final report from study CMO-EPI-EYE-0522 listed as a category 3 study in the RMP. This is an observational, cross-sectional study conducted in France, Germany, Spain, and the UK having as primary objective the assessment of the effectiveness of the educational material provided to the treating physicians."<br>Request for Supplementary Information adopted on 14.06.2019. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Remicade - infliximab - EMEA/H/C/000240/II/0218**<br>Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder,<br>"Submission of the final study report on Remicade for the RABBIT Cohort 2 portion of the registry.<br>Rheumatoide Arthritis - Beobachtung der Biologika-Therapie (RABBIT) is a German RA registry established as a prospective observational cohort study on the long-term safety and effectiveness of biologic disease-modifying anti-rheumatic drugs in patients with RA.<br>RMP (v19) was updated with the conclusion of the study. The MAH also revised the list of safety concerns in the RMP as requested in the assessment of LEG 156."<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 11.04.2019, 17.01.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Revlimid - lenalidomide - EMEA/H/C/000717/II/0110, Orphan**<br>Celgene Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau,<br>"Submission of the final results of the | Request for supplementary information adopted with a specific timetable. |

| | |
|---|---|
| CC-5013-PASS-001 study report dated 2 Nov 2018, for the non-interventional post-authorisation safety study (PASS) of patients treated with lenalidomide."<br>Request for Supplementary Information adopted on 14.06.2019. | |
| PRAC Led<br>**Simponi - golimumab - EMEA/H/C/000992/II/0085**<br>Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study (CNTO148ART4002) listed as a category 3 study in the RMP. This is an observational phase 4 study using the Optum Research Database (ORD) to estimate the long-term safety profile in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) who are initiating Simponi treatment and/or other types of biologic and non-biologic treatments. In addition, the RMP (version 20.0) is updated to reflect the final study report from study CNTO148ART4002 and to revise the list of safety concerns in accordance with the GVP Module V guideline (rev. 2). The Annexes II and IIIA of the product information are updated to remove congestive heart failure and to add breakthrough infection after administration of live vaccine in infants exposed to golimumab in utero from the patient reminder card and labelling. In addition, the MAH took the opportunity to make some editorial changes in the SmPC."<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 11.04.2019, 17.01.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Tremfya - guselkumab - EMEA/H/C/004271/II/0013**<br>Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of RMP to remove exposure during lactation as missing information." | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Xadago - safinamide - EMEA/H/C/002396/II/0031**<br>Zambon S.p.A., Rapporteur: Johann Lodewijk | Request for supplementary information adopted with a specific timetable. |

| | |
|---|---|
| Hillege, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, “Submission of an updated RMP version 6.0 in order to implement RMP rev 2 template and introduce changes to pre-clinical, clinical and post-marketing exposure information and update the due date of DUS Z7219N02 from July 2019 to 28 February 2020.”<br>Request for Supplementary Information adopted on 14.06.2019. | |
| PRAC Led<br>**Zaltrap - aflibercept - EMEA/H/C/002532/II/0051**<br>sanofi-aventis groupe, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Filip Josephson, “Submission of the final report from study OBS13597 / OZONE listed as a category 3 study in the RMP. This is a prospective international observational cohort non-comparative study describing the safety and effectiveness of Zaltrap administered in combination with Folfiri for the treatment of patients with metastatic colorectal cancer in current clinical practice: A Post-Authorisation Safety Study (PASS). The RMP (final version 4.1) is updated accordingly and also adapted to revision 2 of the RMP template including revision of the List of Safety Concerns according to GVP module V Rev 2”<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 14.03.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**WS1568**<br>**Relvar Ellipta-EMEA/H/C/002673/WS1568/0043**<br>**Revinty Ellipta-EMEA/H/C/002745/WS1568/0041**<br>GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, “Submission of the final report from study HZC102972 listed as a category 3 study in the RMP. This is a post-authorisation safety study to further characterise the important potential risk of decreased bone mineral density (BMD) and associated fractures with FF/VI in the treatment of chronic obstructive pulmonary disease (COPD) by evaluating the effect of the inhaled | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| corticosteroid fluticasone furoate (FF) on bone mineral density by comparing fluticasone furoate (FF)/vilanterol (VI) treatment with VI treatment in subjects with moderate COPD."<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 11.04.2019. | |
| PRAC Led<br>**WS1596**<br>**Humalog-EMEA/H/C/000088/WS1596/0172**<br>**Liprolog-EMEA/H/C/000393/WS1596/0133**<br>Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin, "Submission of the final report from on-going review of adverse drug events related to Humalog MEA/028 and Liprolog MEA/021, listed as a category 3 study in the RMP. This is a post approval safety surveillance programme for lot-specific adverse event review to evaluate any potential change in frequency of hypersensitivity, immunogenicity, and lack of drug effect (LODE) events for insulin lispro synthesized via new manufacturing process."<br>Opinion adopted on 14.06.2019.<br>Request for Supplementary Information adopted on 16.05.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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

| | |
|---|---|
| **Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0005/G, ATMP**<br>CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder , "Update of the product information to reflect the study results of the 36-month follow up data for trial cod 16 HS 13 and the final study report with 60-month follow-up data for trial cod 16 HS 14.<br>Study cod 16 HS 13, is a Prospective, randomised, open label, multicentre Phase-III clinical trial to compare the efficacy and safety of the treatment with the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) with microfracture in subjects with cartilage defects of the knee with a defect size between 1 and 4 $cm^2$.<br>Study cod 16 HS 14, is a Prospective, randomised, open label, multicentre Phase-II | Request for supplementary information adopted with a specific timetable. |

| | |
|---|---|
| clinical trial to investigate the efficacy and safety of the treatment of large defects (4-10 $cm^2$) with three different doses of the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) in subjects with cartilage defects of the knee."<br>Request for Supplementary Information adopted on 21.06.2019, 24.05.2019. | |
| **Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0008, ATMP**<br>CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder<br>Request for Supplementary Information adopted on 21.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0006, Orphan, ATMP**<br>Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus<br>Opinion adopted on 27.06.2019, 21.06.2019.<br>Request for Supplementary Information adopted on 17.04.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0008, Orphan, ATMP**<br>Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 21.06.2019. | Request for supplementary information adopted with a specific timetable. |

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

### B.5.7. PRAC assessed ATMP procedures

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

| | |
|---|---|
| **WS1541**<br>**Abasaglar-EMEA/H/C/002835/WS1541/0025**<br>**Humalog-EMEA/H/C/000088/WS1541/0173**<br>**Liprolog-EMEA/H/C/000393/WS1541/0134**<br>Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder<br>Opinion adopted on 27.06.2019. | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| Request for Supplementary Information adopted on 23.05.2019. | |
| **WS1571**<br>**Keppra-EMEA/H/C/000277/WS1571/0174**<br>UCB Pharma S.A., Lead Rapporteur: Koenraad Norga<br>Opinion adopted on 20.06.2019.<br>Request for Supplementary Information adopted on 26.04.2019. | Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1584**<br>**Nuwiq-EMEA/H/C/002813/WS1584/0029**<br>**Vihuma-EMEA/H/C/004459/WS1584/0011**<br>Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 20.06.2019.<br>Request for Supplementary Information adopted on 26.04.2019. | Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1594**<br>**Infanrix hexa-EMEA/H/C/000296/WS1594/0257**<br>GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren<br>Opinion adopted on 20.06.2019. | Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1610/G**<br>**Silodyx-EMEA/H/C/001209/WS1610/0034/G**<br>**Urorec-EMEA/H/C/001092/WS1610/0037/G**<br>Recordati Ireland Ltd, Lead Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur: Amelia Cupelli, “To align the annexes and RMP of Urorec and Silodyx with the changes approved for the new, recently authorised product Silodosin Recordati, as listed below:<br>• combined SmPC for both strengths 4mg and 8mg hard capsules<br>• updates to QRD template version 10<br>• Deletion of the additional risk minimisation activities about IFIS from Annex II of the Product Information, in accordance with the outcome of the PSUSA procedure and RMP version 11.5<br>In addition, in order to have the same approved RMP for the mentioned medicinal products; it is submitted for Urorec and Silodyx the RMP version 11.5 that has been approved for Silodosin Recordati (EMEA/H/C/004964).” | Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| **WS1619**<br>**Cymbalta-EMEA/H/C/000572/WS1619/0080**<br>**Duloxetine Lilly-EMEA/H/C/004000/WS1619/0017**<br>**Xeristar-EMEA/H/C/000573/WS1619/0083**<br>**Yentreve-EMEA/H/C/000545/WS1619/0065**<br>Eli Lilly Nederland B.V., Lead Rapporteur: Maria Concepcion Prieto Yerro<br>Opinion adopted on 06.06.2019. | Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1622/G**<br>**Thymanax-EMEA/H/C/000916/WS1622/0042/G**<br>**Valdoxan-EMEA/H/C/000915/WS1622/0044/G**<br>Les Laboratoires Servier, Lead Rapporteur: Bjorg Bolstad<br>Opinion adopted on 14.06.2019. | Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1628**<br>**Aflunov-EMEA/H/C/002094/WS1628/0051**<br>**Foclivia-EMEA/H/C/001208/WS1628/0046**<br>Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri<br>Request for Supplementary Information adopted on 20.06.2019. | Request for supplementary information adopted with a specific timetable. |
| **WS1633/G**<br>**Blitzima-EMEA/H/C/004723/WS1633/0026/G**<br>**Ritemvia-EMEA/H/C/004725/WS1633/0026/G**<br>**Truxima-EMEA/H/C/004112/WS1633/0029/G**<br>Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz, “Update of section 5.1 of the SmPC to reflect the final results of the PRIMA study (MO18264), a study in Patients with Advanced Follicular Lymphoma Evaluating the Benefit of Maintenance Therapy with Rituximab after Induction of Response with Chemotherapy plus Rituximab in Comparison with No Maintenance Therapy.<br>The annexes are also updated to comply with the CHMP guideline on excipients regarding the sodium content.<br>Extension of indication to include the | Positive Opinion adopted by consensus on 27.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| maintenance of remission of polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package leaflet is updated accordingly. In addition, the MAH took the opportunity to implement a terminology change in Annex II.<br>Extension of indication to include the treatment of patients with moderate to severe pemphigus vulgaris (PV); as a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8 and 5.1 of the SmPC are updated. Data from a phase III, randomized, controlled, multicenter, open-label study (Study ML22196) evaluating rituximab treatment plus short-term, low dose prednisone treatment compared to long-term, standard dose prednisone treatment as first-line treatment in patients with moderate to severe pemphigus had been provided. The Package leaflet is updated accordingly. Minor corrections are also proposed for the sake of accuracy and clarity. ."<br>Opinion adopted on 27.06.2019. | |

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

| | |
|---|---|
| **Vyndaqel - tafamidis - EMEA/H/C/002294/II/0051, Orphan**<br>Pfizer Europe MA EEIG, Rapporteur: Joseph Emmerich, "C.I.4 (Type II) To update sections 4.2, 4.5, 4.6, 4.9, 5.1, 5.2 and 5.3 of the Vyndaqel (Tafamidis Meglumine) 20mg soft capsules SmPC to update the pharmacokinetic and safety information following final results from new population pharmacokinetic (PK) analyses and study B3461028 "A Multicenter, International, Phase 3, Double-Blind, Placebo-Controlled, and Randomized Study to Evaluate the Efficacy, Safety, and Tolerability of Daily Oral Dosing of Tafamidis Meglumine (PF-06291826) 20 mg or 80 mg in Comparison to Placebo in Subjects Diagnosed With Transthyretin Cardiomyopathy (TTR-CM)".<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to make administrative changes throughout the SmPC, Package Leaflet and Labelling and to update section 4.4 of the SmPC to align with the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' with regard to fructose and sorbitol; the Package Leaflet has been | The MAH withdrew the procedure on 18.06.2019. |

updated accordingly."
Withdrawal request submitted on 18.06.2019.

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

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

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

**apixaban - EMEA/H/C/005358**
prevention of venous thromboembolic events (VTE)

**crizanlizumab - EMEA/H/C/004874, Orphan**
Novartis Europharm Limited, Treatment of sickle cell disease

**dasatinib - EMEA/H/C/005317**
treatment of leukaemia

**bupivacaine - EMEA/H/C/004586**
Indicated for prolonged acute pain management and reduction in need for opioids in adults compared to immediate-release bupivacaine

**insulin aspart - EMEA/H/C/005033**
treatment of diabetes mellitus

**obiltoxaximab - EMEA/H/C/005169, Orphan**
SFL Regulatory Services GmbH, treatment of inhalational anthrax due to Bacillus anthracis

**doxorubicin - EMEA/H/C/005320**
treatment of breast cancer, ovarian cancer, progressive multiple myeloma and AIDS-related Kaposi's sarcoma

**idebenone - EMEA/H/C/005123, Orphan**
Santhera Pharmaceuticals (Deutschland) GmbH, treatment of respiratory dysfunction in patients with Duchenne muscular dystrophy (DMD) not using glucocorticoids

**lefamulin - EMEA/H/C/005048**
treatment of community-acquired pneumonia (CAP)

**trastuzumab - EMEA/H/C/005209**
treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)

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

**Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/X/0081/G**

Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins“Extension application to introduce a new strength (45/200 mg film-coated tablets) and a new pharmaceutical form (oral granules) associated with new strengths (33.75/150 and 45/200 mg). The new presentations are indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in patients aged 3 to <12 years. The extension application is grouped with a type II variation (C.I.6.a) to include paediatric use in patients aged 3 to < 12 years who weigh greater than or equal to 35 kg to the existing presentations of 90/400 mg film-coated tablets.
The RMP (version 8.3) is updated in accordance. In addition, the MAH took the opportunity to implement minor linguistic corrections throughout the Product Information.”

**Sovaldi - sofosbuvir - EMEA/H/C/002798/X/0059/G**

Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, “Extension application to introduce a new strength (200 mg film-coated tablets) and a new pharmaceutical form (oral granules) associated with new strengths (150 and 200 mg). The new presentations are indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in patients aged 3 to <12 years. The extension application is grouped with a type II variation (C.I.6.a) to include paediatric use in patients aged 3 to < 12 years who weigh greater than or equal to 35 kg to the existing presentations of 400 mg film-coated tablets.
The RMP (version 8.3) is updated in accordance. In addition, the MAH took the opportunity to implement minor linguistic corrections throughout the Product Information.”

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

**gilteritinib - EMEA/H/C/004752, Orphan**

Astellas Pharma Europe B.V., treatment of

patients who have relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutation
List of Questions adopted on 27.05.2019.

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

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

**Clopidogrel ratiopharm - clopidogrel - EMEA/H/C/004006/R/0014**
Teva B.V., Generic, Duplicate, Generic of Plavix, Duplicate of Clopidogrel Teva, Rapporteur: Rajko Kenda, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

**IKERVIS - ciclosporin - EMEA/H/C/002066/R/0017**
Santen Oy, Rapporteur: Peter Kiely, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Jan Neuhauser

**Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/R/0033**
Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Martin Huber

**Orbactiv - oritavancin - EMEA/H/C/003785/R/0027**
Menarini International Operations Luxembourg S.A., Rapporteur: Janet Koenig, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Adam Przybylkowski

**Sivextro - tedizolid phosphate - EMEA/H/C/002846/R/0031**
Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Maria del Pilar Rayon

### 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

**Alunbrig - brigatinib / brigatinib - EMEA/H/C/004248/II/0003**
Takeda Pharma A/S, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Extension of indication to

| | |
|---|---|
| include first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously untreated with an ALK inhibitor for Alunbrig.<br>The addition of a new indication is supported by data from study 301 (AP26113-13-301; ALTA 1L), a phase 3, randomized, open label, comparative, multicenter, international phase 3 study.<br>As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package leaflet and labelling are updated in accordance. The RMP version 5.1 has also been submitted. Minor editorial corrections are also proposed."<br>Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004) | |
| **ECALTA - anidulafungin - EMEA/H/C/000788/II/0040**<br>Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, "Extension of the approved indication "treatment of invasive candidiasis (ICC)" to include paediatric patients aged from 1 month to less than 18 years of age; consequently, sections 4.1, 4.2, 4.4, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated in order to add paediatric dosing instructions, warnings and precautions, clinical, and non-clinical information. The Package Leaflet is updated accordingly consequent to the revisions to the SmPC. In addition, the Marketing Authorisation Holder (MAH) has taken the opportunity to update the information in the SmPC and Package Leaflet in line with the current excipient's guideline for fructose.<br>The RMP Version number 13.0 dated 08 March 2019 which includes GVP module V rev 2 changes has also been submitted." | |
| **Erleada - apalutamide - EMEA/H/C/004452/II/0001**<br>Janssen-Cilag International N.V., Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Natalja Karpova, PRAC Rapporteur: Ghania Chamouni, "Extension of indication to include the treatment of metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT) for Erleada based on the results of study 56021927PCR3002 (TITAN | |

| | |
|---|---|
| study), a randomised, double-blind, placebo-controlled phase 3 study comparing apalutamide plus ADT versus ADT in patients with mHSPC. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add a warning on ischaemic cardiovascular events and to reflect new safety and efficacy information. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to make editorial update to the SmPC and Labelling. The RMP version 2.0 has also been submitted." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004) | |

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

| | |
|---|---|
| **Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0069, Orphan** Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik | |
| **AJOVY - fremanezumab - EMEA/H/C/004833/II/0002** TEVA GmbH, Rapporteur: Jan Mueller-Berghaus | |
| **Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0007** Seqirus Netherlands B.V., Rapporteur: Sol Ruiz | |
| **Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0093** AstraZeneca AB, Rapporteur: Bart Van der Schueren | |

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

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

**B.6.11. PRAC assessed procedures**

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

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

**B.6.14. PRAC assessed ATMP procedures**

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

---

**WS1635**
**Ryzodeg-EMEA/H/C/002499/WS1635/0033**
**Tresiba-EMEA/H/C/002498/WS1635/0039**
**Xultophy-EMEA/H/C/002647/WS1635/0031**
Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder

---

**WS1640**
**PegIntron-EMEA/H/C/000280/WS1640/0138**
**ViraferonPeg-EMEA/H/C/000329/WS1640/0131**
Merck Sharp & Dohme B.V., Lead Rapporteur: Filip Josephson

---

**WS1641**
**Corlentor-EMEA/H/C/000598/WS1641/0053**
**Ivabradine Anpharm-EMEA/H/C/004187/WS1641/0013**
**Procoralan-EMEA/H/C/000597/WS1641/0052**
Les Laboratoires Servier, Duplicate, Duplicate of Procoralan, Lead Rapporteur: Johann Lodewijk Hillege

---

**WS1646**
**Fluenz Tetra-EMEA/H/C/002617/WS1646/0091**
**Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/WS1646/0024**
AstraZeneca AB, Lead Rapporteur: Bart Van der Schueren

---

**WS1650**
**Olanzapine Glenmark-EMEA/H/C/001085/WS1650/0031**

---

**Olanzapine Glenmark Europe-EMEA/H/C/001086/WS1650/0028**
**Olazax-EMEA/H/C/001087/WS1650/0024**
**Olazax Disperzi-EMEA/H/C/001088/WS1650/0025**
Glenmark Arzneimittel GmbH, Generic, Generic of Olansek (SRD), Zyprexa, Zyprexa Velotab, Lead Rapporteur: Alexandre Moreau, “To updated section 4.8 of the SmPC to add "stuttering", section 5.2 of the SmPC to include new section with a sub heading 'Hepatic Impairment' and text related to smoking in line with PI text of the reference product. The PL has been updated accordingly. In addition the MAH has taken the opportunity to align the annexes with minor linguistic changes in line with the reference product.”

**WS1652/G**
**Idacio-EMEA/H/C/004475/WS1652/0002/G**
**Kromeya-EMEA/H/C/005158/WS1652/0002/G**
Fresenius Kabi Deutschland GmbH, Lead Rapporteur: Johann Lodewijk Hillege

**WS1657**
**Advate-EMEA/H/C/000520/WS1657/0101**
**ADYNOVI-EMEA/H/C/004195/WS1657/0006**
Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus

**WS1670**
**Adjupanrix-EMEA/H/C/001206/WS1670/0065**
**Ambirix-EMEA/H/C/000426/WS1670/0102**
**Fendrix-EMEA/H/C/000550/WS1670/0069**
**Infanrix hexa-EMEA/H/C/000296/WS1670/0261**
**Prepandrix-EMEA/H/C/000822/WS1670/0081**
**Rotarix-EMEA/H/C/000639/WS1670/0114**
**Synflorix-EMEA/H/C/000973/WS1670/0139**
**Twinrix Adult-EMEA/H/C/000112/WS1670/0137**
**Twinrix Paediatric-EMEA/H/C/000129/WS1670/0138**
GlaxoSmithkline Biologicals SA, Lead

Rapporteur: Bart Van der Schueren

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

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

**B.7.2. Monthly Line listing for Type I variations**

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

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

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

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

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

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

**E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES**

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

**E.1. PMF Certification Dossiers:**

**E.1.1. Annual Update**

**E.1.2. Variations:**

**E.1.3. Initial PMF Certification:**

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

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

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

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

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

**G. ANNEX G**

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

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

### G.2. PRIME

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

#### G.2.1. List of procedures concluding at 24-27 June 2019 CHMP plenary:

| *Endocrinology-Gynaecology-Fertility-Metabolism* | |
|---|---|
| ATMP; Treatment of glycogen storage disease type Ia | The CHMP denied eligibility to PRIME and adopted the critical summary report. |

#### G.2.2. List of procedures starting in June 2019 for July 2019 CHMP adoption of outcomes

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