



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 October 2018
EMA/CHMP/633386/2018 Corr¹
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP) Minutes of the meeting on 23-26 July 2018

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

Health and safety information

In accordance with the Agency's health and safety policy, delegates are to be briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

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

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

Note on access to documents

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

¹ Correction in section 3.1.6



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1. Introduction

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

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified as included in the list of participants and restrictions. See (current) July 2018 CHMP minutes for the list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session held 23-26 July 2018.

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

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

1.2. Adoption of agenda

CHMP agenda for 23-26 July 2018

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 25-28 June 2018.

The CHMP adopted the CHMP minutes for 25-28 June 2018. The Minutes of the July 2018 CHMP ORGAM meeting held on 16 July 2018, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. paclitaxel - Orphan - EMEA/H/C/004154

Oasmia Pharmaceutical AB; treatment of ovarian cancer

Scope: Oral explanation

Action: Oral explanation to be held on 24 July 2018 at time 16:00

List of Outstanding Issues adopted on 26.04.2018, 14.09.2017, 18.05.2017. List of Questions adopted on 23.06.2016.

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

See 3.2

2.1.2. Onpattro - patisiran - Orphan - EMEA/H/C/004699

Accelerated assessment

Alnylam Netherlands B.V.; treatment of hereditary transthyretin-mediated amyloidosis

Scope: Oral explanation

Action: Oral explanation to be held on 23 July 2018 at time 16:00

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

List of Outstanding Issues adopted on 26.06.2018. List of Questions adopted on 24.04.2018.

An oral explanation was held on 23 July 2018 at time 16:00.

See 3.1

2.1.3. Imfinzi - durvalumab - EMEA/H/C/004771

AstraZeneca AB; treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC)

Scope: Oral explanation

Action: Oral explanation to be held on 24 July 2018 at time 18:00

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 25.01.2018.

An oral explanation was held on 24 July 2018 at time 18:30.

See 3.1

2.2. Re-examination procedure oral explanations

2.2.1. Dexxience - betrixaban - EMEA/H/C/004309

Portola Pharma UK Limited; treatment of prophylaxis of venous thromboembolism (VTE)

Scope: Oral explanation

Action: Oral explanation to be held on 24 July 2018 at time 09:00

Opinion adopted on 22.03.2018.

An oral explanation was held on 24 July 2018 at time 09:00.

See 3.5

[2.2.2. Eladynos - abaloparatide - EMEA/H/C/004157](#)

Radius International Ltd; treatment of osteoporosis

Scope: Oral explanation, Report from Ad-hoc Expert Group meeting

Action: Oral explanation to be held on 24 July 2018 at time 11:00

Opinion adopted on 22.03.2018.

An oral explanation was held on 24 July 2018 at time 11:00.

See 3.5

2.3. Post-authorisation procedure oral explanations

[2.3.1. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0011](#)

Amgen Europe B.V.

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

Scope: Oral explanation

Action: Oral explanation to be held on 24 July 2018 at time 14:00

Request for Supplementary Information adopted on 26.04.2018, 14.12.2017, 22.06.2017.

An oral explanation was held on 24 July 2018 at time 14:00.

See 5.1

[2.3.2. Xarelto - rivaroxaban - EMEA/H/C/000944/II/0058](#)

Bayer AG

Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue

Scope: Oral explanation

Action: Possible oral explanation to be held on 25 July 2018 at time 11:00

Request for Supplementary Information adopted on 31.05.2018, 22.02.2018.

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

See 5.1

2.3.3. [WS1278](#)
[OPDIVO - nivolumab - EMEA/H/C/003985/WS1278/0042](#)
[Yervoy - ipilimumab - EMEA/H/C/002213/WS1278/0053](#)

Bristol-Myers Squibb Pharma EEIG

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

Scope: Oral explanation

Action: Oral explanation to be held on 25 July 2018 at time 9:00

Request for Supplementary Information adopted on 31.05.2018, 22.02.2018.

An oral explanation was held on 25 July 2018 at time 9:30.

See 5.1

2.3.4. [Keytruda - pembrolizumab - EMEA/H/C/003820/II/0042](#)

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: Oral explanation

Action: Oral explanation to be held on 25 July 2018 at time 16:00

Request for Supplementary Information adopted on 28.06.2018, 26.04.2018.

An oral explanation was held on 25 July 2018 at time 16:00.

See 5.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. [Braftovi - encorafenib - EMEA/H/C/004580](#)

Pierre Fabre Medicament; in combination with binimetinib is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

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

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

Furthermore, the CHMP considered that encorafenib 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.

The CHMP noted the letter of recommendation dated 27 July 2018.

3.1.2. Deferiprone Lipomed - deferiprone - EMEA/H/C/004710

Lipomed GmbH; treatment of iron overload in thalassemia major

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 09.11.2017.

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

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

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

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

The summary of opinion was circulated for information.

3.1.3. Gefitinib Mylan - gefitinib - EMEA/H/C/004826

MYLAN S.A.S.; treatment of non-small cell lung cancer

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

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

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

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

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

The summary of opinion was circulated for information.

3.1.4. Hulio - adalimumab - EMEA/H/C/004429

Mylan S.A.S; treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 26.04.2018. List of Questions adopted on 14.09.2017.

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

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

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

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

The summary of opinion was circulated for information.

3.1.5. Ilumetri - tildrakizumab - EMEA/H/C/004514

Almirall S.A; treatment of adults with moderate-to-severe plaque psoriasis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 20.07.2017.

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

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

timetable.

Furthermore, the CHMP considered that tildrakizumab 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.

3.1.6. [Imfinzi - durvalumab - EMEA/H/C/004771](#)

AstraZeneca AB; treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 25.01.2018.

An oral explanation was held on 24 July 2018 at time 18:30. During the oral explanation the applicant presented improved PFS & OS in the ITT. Applicant proposed a revised target indication statement. The Committee discussed the applicant's proposal, but found that benefit-risk cannot be considered positive (in adults whose tumours express PD-L1 < 1%).

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 durvalumab 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.

3.1.7. [KIGABEQ - vigabatrin - PUMA - EMEA/H/C/004534](#)

ORPHELIA Pharma SAS; Treatment in monotherapy of infantile spasms (West's syndrome) and resistant partial epilepsy in infants and children

Scope: Opinion

Action: For adoption

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

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

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

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

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

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

The summary of opinion was circulated for information.

3.1.8. [Lenalidomide Accord - lenalidomide - EMEA/H/C/004857](#)

Accord Healthcare Limited; treatment of multiple myeloma

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

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

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

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

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

The summary of opinion was circulated for information.

3.1.9. [Mektovi - binimetinib - EMEA/H/C/004579](#)

Pierre Fabre Medicament; in combination with encorafenib is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

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

addressed.

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

Furthermore, the CHMP considered that binimetinib 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.

The CHMP noted the letter of recommendation dated 27 July 2018.

3.1.10. [Slentyto - melatonin - PUMA - EMEA/H/C/004425](#)

RAD Neurim Pharmaceuticals EEC Ltd.; treatment of insomnia in children with Autism Spectrum Disorders and neurogenetic diseases

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.09.2017.

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

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

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

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

The summary of opinion was circulated for information.

3.1.11. [Onpattro - patisiran - Orphan - EMEA/H/C/004699](#)

Accelerated assessment

Alnylam Netherlands B.V.; treatment of hereditary transthyretin-mediated amyloidosis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 26.06.2018. List of Questions adopted on 24.04.2018.

An oral explanation was held on 23 July 2018 at time 16:00. The oral explanation focused on the wording of the indication and the supporting clinical data.

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 patisiran 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.

The CHMP noted the letter of recommendation dated 21 July 2018.

The CHMP adopted the similarity assessment report for Onpattro.

3.1.12. Pelgraz - pegfilgrastim - EMEA/H/C/003961

Accord Healthcare Limited; treatment of neutropenia

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.09.2017.

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

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by 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 noted the letter of recommendation dated 26 July 2018.

3.1.13. Symkevi - tezacaftor / ivacaftor - Orphan - EMEA/H/C/004682

Vertex Pharmaceuticals (Europe) Ltd.; treatment of cystic fibrosis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 28.06.2018, 31.05.2018, 22.03.2018. List of Questions adopted on 14.12.2017.

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

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

Furthermore, the CHMP considered that tezacaftor 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.

The CHMP adopted the similarity assessment report for Symkevi.

The CHMP noted the letter of recommendation dated 30 July 2018.

3.1.14. Udenyca - pegfilgrastim - EMEA/H/C/004413

ERA Consulting GmbH; treatment of neutropenia

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 28.06.2018, 14.12.2017. List of Questions adopted on 23.03.2017.

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

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

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

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

The summary of opinion was circulated for information.

3.1.15. Verzenios - abemaciclib - EMEA/H/C/004302

Eli Lilly Nederland B.V.; treatment of hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer

Scope: Opinion

Action: For adoption

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

Oral explanation held on 25 June 2018. List of Outstanding Issues adopted on 31.05.2018, 26.04.2018. List of Questions adopted on 14.12.2017.

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

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

Furthermore, the CHMP considered that abemaciclib 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. The CHMP noted the letter of recommendation dated 4 July 2018.

3.1.16. Xerava - eravacycline - EMEA/H/C/004237

Tetraphase Pharmaceuticals Ireland Limited; treatment of complicated intra-abdominal infections (cIAI) in adults

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

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

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

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

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

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

The summary of opinion was circulated for information.

The CHMP noted the letter of recommendation dated 23 July 2018.

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

3.2.1. paclitaxel - Orphan - EMEA/H/C/004154

Oasmia Pharmaceutical AB; treatment of ovarian cancer

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 26.04.2018, 14.09.2017, 18.05.2017. List of Questions adopted on 23.06.2016.

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

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

The Committee adopted a 4th list of outstanding issues with a specific timetable.

3.2.2. ropeginterferon alfa-2b - Orphan - EMEA/H/C/004128

AOP Orphan Pharmaceuticals AG; treatment of polycythemia vera

Scope: List of outstanding issues, request for a clock stop extension

Action: For adoption

List of Questions adopted on 22.06.2017.

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. Furthermore, CHMP agreed to the extension of clock-stop.

The CHMP agreed to consult the SAG Oncology and adopted a list of questions to the experts.

3.2.3. buprenorphine - EMEA/H/C/004651

treatment of opioid dependence within a framework of medical, social and psychological treatment

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.01.2018.

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.

3.2.4. doxorubicin hydrochloride - EMEA/H/C/004110

treatment of breast and ovarian cancer

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 14.09.2017.

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 by the applicant of an extension to the clock stop to respond to the LoOI with a specific timetable.

The CHMP adopted the updated similarity assessment report.

3.2.5. galcanezumab - EMEA/H/C/004648

prophylaxis of migraine

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.03.2018.

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.

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

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

Scope: List of outstanding issues, request from applicant dated 10 July 2018 for extension to the clock stop to respond to the List of outstanding issues

Action: For adoption

List of Questions adopted on 09.11.2017.

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 by the applicant of an extension to the clock stop to respond to the LoOI with a specific timetable.

3.2.7. voretigene neparvovec - Orphan - ATMP - EMEA/H/C/004451

Spark Therapeutics Ireland Ltd; treatment of patients with vision loss due to Leber congenital amaurosis or retinitis pigmentosa inherited retinal dystrophy

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 25.05.2018. List of Questions adopted on 08.12.2017.

The draft list of experts for the ad hoc expert group meeting on 5 July 2018 was adopted via written procedure on 5th July 2018.

The Committee was reminded of the status of this application and its remaining outstanding issues. The CHMP was updated on discussions at the CAT during their July 2018 meeting.

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

3.2.8. paclitaxel - EMEA/H/C/004441

treatment of metastatic breast cancer

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

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

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

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

3.2.9. mogamulizumab - Orphan - EMEA/H/C/004232

Kyowa Kirin Limited; treatment of cutaneous T-cell lymphoma

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.02.2018.

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.

3.2.10. influenza vaccine surface antigen inactivated prepared in cell cultures - Article 28 - EMEA/H/C/004814

prophylaxis of influenza in adults and children from 4 years of age

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.03.2018.

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

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

The CHMP agreed to consult the VWP.

3.2.11. pegfilgrastim - EMEA/H/C/004802

treatment of neutropenia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.02.2018.

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.

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

3.3.1. atazanavir - EMEA/H/C/004859

treatment of HIV-1 infection

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. turoctocog alfa pegol - Orphan - EMEA/H/C/004883

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

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. [cemiplimab - EMEA/H/C/004844](#)

as monotherapy, indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma

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. [ciprofloxacin - EMEA/H/C/004394](#)

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

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. [miglustat - EMEA/H/C/004904](#)

treatment of adult patients with mild to moderate type 1 Gaucher disease and only in the treatment of patients for whom enzyme replacement therapy is unsuitable

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. [pegvaliase - Orphan - EMEA/H/C/004744](#)

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

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. [sotagliflozin - EMEA/H/C/004889](#)

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

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. [zanamivir - EMEA/H/C/004102](#)

treatment of influenza A or B virus infection

Scope: Request by the applicant dated 13 July 2018 for an extension of clock-stop to respond to the List of Questions adopted in April 2018

Action: For adoption

List of Questions adopted on 26.04.2018.

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 2018.

3.4.2. [fremanezumab - EMEA/H/C/004833](#)

prevention of episodic and chronic migraine

Scope: Request by the applicant dated 13 July 2018 for extension of clock-stop to respond to the List of Questions adopted in May 2018

Action: For adoption

List of Questions adopted on 31.05.2018.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond the List of Questions adopted in May 2018.

3.4.3. [canakinumab - EMEA/H/C/004754](#)

prevention of major cardiovascular events

Scope: Request by the applicant for extension of clock-stop to respond to the List of Questions adopted in May 2018

Action: For adoption

List of Questions adopted on 31.05.2018.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond the List of Questions adopted in May 2018.

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

3.5.1. [Eladynos - abaloparatide - EMEA/H/C/004157](#)

Radius International Ltd; treatment of osteoporosis

Scope: Opinion

Action: For adoption

Opinion adopted on 22.03.2018.

The CHMP noted the report from the Ad-hoc Expert Group meeting, held on 10 July 2018. The experts considered the effect on vertebral fractures highly relevant. Based on the totality of data (including relevant effects on major osteoporotic fractures and BMD; the similarity of the mode of action to teriparatide), and from a clinical perspective, the view of the majority of experts was that an effect of abaloparatide on reduction of non-vertebral fractures is expected. The methodology expert did not favour this approach.

The observed increase in heart rate could possibly infer a safety risk to certain groups of patients, such as patients who have pre-existing heart disease. This is considered sufficiently addressed in the current SmPC (including contra-indications and recommendation of one-hour observation after the first administration). Valuable additional information could be provided by a PASS. The risk may be somewhat larger than with teriparatide.

There was support for a Drug Utilisation Study (DUS) in particular since this could provide useful information on the EU and US populations and could inform the design of the PASS study. It is expected that the EU and US patient population is different based on differences in availability of healthcare and reimbursement. A further difference in the risk of CV events is expected from the fact that the abaloparatide US label contains no CV contraindications. Therefore the experts call for a PASS sized to have adequate participation from both a US

and a European population. There was no final conclusion on the choice of the comparator. The CHMP discussed the outstanding issues and agreed that an oral explanation is needed. See 2.2

An oral explanation was held on 24 July 2018 at time 11:00. The presentation by the applicant reflected on the efficacy data in support of the sought indication, the safety profile of the product and the proposed post-authorisation measures.

The CHMP considered that the main study did not satisfactorily show that Eladynos is effective at preventing non-vertebral fractures in women who have been through the menopause.

The data from two of the study sites were not reliable and had to be excluded as the study had not been conducted in compliance with 'good clinical practice' at those sites.

From a safety point of view, the CHMP was concerned about the medicine's effects on the heart, such as increases in heart rate and palpitations.

Because most post-menopausal women are at an increased risk of heart problems, the CHMP could not identify a group of patients in whom the benefits would outweigh the risks. Therefore, at that point in time, the Committee was of the opinion that the benefits of Eladynos did not outweigh its risks and recommended that the medicine be refused marketing authorisation.

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

The refusal question and answers document was circulated for information.

3.5.2. Dexxience - betrixaban - EMEA/H/C/004309

Portola Pharma UK Limited; treatment of prophylaxis of venous thromboembolism (VTE)

Scope: Re-examination of Opinion

Report from SAG CVS held on 13 July 2018

Opinion adopted on 22.03.2018.

See 2.2

The CHMP noted the report from SAG CVS meeting held on 13 July 2018. The SAG considered that there are important limitations in the APEX study which do not allow drawing robust conclusions on the clinical relevance of the reported results in the study. The SAG noted that due to the way that subjects were recruited in the study, with an emphasis of baseline D-dimers levels, it is not possible to identify the patients that could potentially benefit from extended thromboprophylaxis in clinical practice.

The SAG expressed their concerns about the higher rate of "clinically relevant non major bleedings" that could be more of a concern in clinical practice as compared to the controlled conditions of a clinical study. PK properties, food effect and PK interactions were considered of concern.

An oral explanation was held on 24 July 2018 at time 09:00. During the oral explanation, the Applicant presented the Phase 3 APEX study design and patient allocation. The applicant

confirmed that totality of evidence in all randomized patients provides the most reliable approach to drawing conclusions from the trial. More specifically the applicant explained the efficacy and safety in the 80mg stratum as the target population.

The CHMP noted the letter from the European Thrombosis and Cardiovascular Specialists regarding the APEX trial.

The CHMP considered that the main study did not satisfactorily show Dextience's effectiveness when used for preventing blood clots in patients admitted to hospital for recent medical illness. Also, patients treated with Dextience had more episodes of bleeding than those treated with the comparator medicine. This was considered an important concern given that the medicine was expected to be used in patients with serious underlying conditions for whom any episode of bleeding could have serious consequences, and Dextience's long persistence in the body could complicate management of bleeding.

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

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

The refusal question and answers document was circulated for information.

3.5.3. Nerlynx - neratinib - EMEA/H/C/004030

Puma Biotechnology Limited; extended adjuvant treatment of adult patients with early-stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab based therapy

Scope: Re-examination of Opinion, final opinion documents

Action: For information

Oral explanation held on 26 June 2018. Opinion adopted on 22.02.2018.

The final opinion documents were adopted via written procedure on 12.07.2018

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. Raligize - axalimogene filolisbac - ATMP - EMEA/H/C/004473

FGK Representative Service GmbH; treatment of cervical cancer

Scope: Withdrawal of initial marketing authorisation application

Action: For information

The CHMP noted the letter from the applicant informing EMA about the withdrawal of the marketing authorisation application.

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

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

4.1.1. Inhixa - enoxaparin sodium - EMEA/H/C/004264/X/0018

Techdow Europe AB

Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst

Scope: "Extension application to add two new strengths of 12,000 IU (120 mg)/0.8 mL and 15,000 IU (150 mg)/1 mL for enoxaparin sodium solution for injection in pre-filled syringe, for subcutaneous, extracorporeal and intravenous administration."

Action: For adoption

List of Outstanding Issues adopted on 28.06.2018, 31.05.2018. List of Questions adopted on 14.12.2017.

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. Inhixa - enoxaparin sodium - EMEA/H/C/004264/X/0026

Techdow Europe AB

Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst

Scope: "Extension application to add two new strengths of 30,000 IU (300 mg)/3 mL and 50,000 IU (500 mg)/5 mL for enoxaparin sodium solution for injection in vial, for subcutaneous, extracorporeal and intravenous administration."

Action: For adoption

List of Outstanding Issues adopted on 28.06.2018. List of Questions adopted on 22.03.2018.

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

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

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

4.1.3. Renvela - sevelamer carbonate - EMEA/H/C/000993/X/0039

Genzyme Europe BV

Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Laurence de Fays

Scope: "Extension application to add a new strength of 0.8 g powder for oral suspension."

Action: For adoption

List of Questions adopted on 22.02.2018.

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 CHMP noted the letter of recommendations dated 24 July 2018.

4.1.4. Sevelamer carbonate Zentiva - sevelamer carbonate - EMEA/H/C/003971/X/0011

Genzyme Europe BV

Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Laurence de Fays

Scope: "Extension application to add a new strength of 0.8 g powder for oral suspension."

Action: For adoption

List of Questions adopted on 22.02.2018.

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 CHMP noted the letter of recommendations dated 24 July 2018.

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. Gilenya - fingolimod - EMEA/H/C/002202/X/0044/G

Novartis Europharm Limited

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension application to introduce a new strength of hard capsules (0.25 mg) to the currently approved presentations of Gilenya, grouped with a type II variation (extension of indication) to add a new indication for the treatment of paediatric patients of 10 years of

age and above with relapsing multiple sclerosis (RMS). As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3, 6 and 8 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. In addition, Annex II is updated to be brought in line with the latest QRD template version 10.”

Action: For adoption

List of Questions adopted on 22.03.2018.

The Committee discussed the issues identified in this application.

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

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

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

sanofi-aventis groupe

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

Scope: “Extension application to add a new strength of 200 mg solution for injection in pre-filled syringe with safety system (PFS-S) and pre-filled pen (PFP), grouped with a type II variation (C.I.6.a) to add the following indications:

- Add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older, who are inadequately controlled with medium-to-high dose inhaled corticosteroids (ICS) plus another medicinal product for maintenance treatment, including those with or without an eosinophilic phenotype;
- Maintenance therapy to improve lung function;
- Maintenance therapy to reduce oral steroid use and improve lung function in steroid-dependent asthma patients;

Based on the pivotal studies DRI12544, QUEST and VENTURE.

As a consequence, SmPC sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated accordingly.

The RMP (version 2.0) is updated accordingly.

In addition, the MAH proposed to merge the SmPCs for the 200 mg and 300 mg strengths.”

Action: For adoption

The Committee discussed the issues identified in this application. The members noted a discrepancy in bioequivalence of the PFP in comparison with the PFS-S in the PK study. In addition the members considered that the sought indication was not sufficiently supported by the available data. The Committee agreed to request further clarification from the MAH.

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

4.3.2. Orenzia - abatacept - EMEA/H/C/000701/X/0117/G

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension application to add 2 new strengths of 50 mg and 87.5 mg for solution for injection in a pre-filled syringe with needle guard, for subcutaneous (SC) administration, grouped with a type II variation (C.I.6.a) to include paediatric use of polyarticular Juvenile Idiopathic Arthritis (2 years and above) for solution for injection (50 mg, 87.5 mg and 125 mg).

The above-described changes are grouped

The RMP (version 25.0) is updated in accordance.

In addition, the applicant took the opportunity to implement minor editorial changes in the product information."

Action: For adoption

The Committee discussed the issues identified in this application. The main discussion related to the wording of the indication. The CHMP agreed to seek further justification on the monotherapy use and the request for an earlier line of treatment.

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

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

Pfizer Limited

Rapporteur: Robert James Hemmings, PRAC Rapporteur: Sabine Straus

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 of indication includes a change in pharmacokinetics.

An updated RMP (version 4.0) has been provided."

Action: For adoption

The Committee discussed the issues identified in this application, relating to the comparability of the new formulation. The members noted the absence of comparative data in the European populations. The presented data in a Japanese population suggested an inferiority of the new formulation without safety advantages, although the once daily administration was noted. It was agreed to consult the MAH for further clarification.

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

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

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. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0011

Amgen Europe B.V.

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

Scope: "Extension of Indication to include the treatment of adults with minimal residual disease (MRD) positive B-cell precursor acute lymphoblastic leukaemia (ALL) for BLINCYTO; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, and to update the safety information. The Labelling is updated in accordance.

RMP version 4.0 is included in this submission."

Action: For adoption

Request for Supplementary Information adopted on 26.04.2018, 14.12.2017, 22.06.2017.

See 2.3

An oral explanation was held on 24 July 2018 at 14:00. The MAH presented data on Minimal Residual Disease (MRD) in relation to leukaemia and overall survival. Furthermore they presented clinical efficacy and safety data.

The members discussed the presented data and whether it was sufficient to support the extension of indication request.

The CHMP adopted a negative opinion by majority (23 negative out of 28 votes), recommending the refusal of the marketing authorisation application. The CHMP adopted the assessment report.

The Norwegian Member was in agreement with the CHMP recommendation.

The divergent position (Koenraad Norga, Agnes Gyurasics, Concepcion Prieto Yerro, Bart van der Schueren, Sol Ruiz) was appended to the opinion.

The refusal question and answers document was circulated for information.

5.1.2. [Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0018](#)

Amgen Europe B.V.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová

Scope: "Extension of Indication to include the children 1 month and older to the authorised population for the treatment of adults with Philadelphia chromosome-negative relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL) for BLINCYTO; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated in order to include the new population, updated the posology and update the safety information. The Package Leaflet is updated in accordance. RMP version 6.0 has been submitted"

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018, 22.03.2018, 12.10.2017.

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.

The CHMP adopted the similarity assessment report for Blincyto.

5.1.3. [Coagadex - human coagulation factor X - Orphan - EMEA/H/C/003855/II/0007](#)

Bio Products Laboratory Limited

Rapporteur: Andrea Laslop, PRAC Rapporteur: Julie Williams

Scope: "Update of sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include safety and efficacy data in children aged less than 12 years of age based on final results from the study Ten02, a phase III open-label multicentre study to confirm the safety, pharmacokinetics and efficacy of BPL's high purity factor X in the prophylaxis of bleeding in factor X deficient children under the age of 12 years, provided in accordance with the agreed paediatric investigational plan. The Package Leaflet is updated accordingly. The RMP version 7.0 has also been submitted."

Action: For adoption

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

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

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

5.1.4. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/II/0011

Janssen-Cilag International NV

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of Indication to include the combination with bortezomib, melphalan and prednisone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant for Darzalex; 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. The RMP version 3.1 (in version 2 of the RMP template) has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the Lithuanian and Slovenian local representatives in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 22.03.2018.

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

The Committee adopted a positive opinion 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.

The CHMP adopted the similarity assessment report for Darzalex.

5.1.5. Hemlibra - emicizumab - EMEA/H/C/004406/II/0002

Roche Registration GmbH

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of Indication to include routine prophylaxis of bleeding episodes in patients with hemophilia A without factor VIII inhibitors, for Hemlibra. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated with efficacy and safety information of the pivotal trials:

- Study BH30071 (HAVEN 3) - an ongoing, multicenter, open-label, randomized Phase III clinical study evaluating the efficacy, safety and PK of emicizumab prophylaxis at doses of 1.5 mg/kg/week (QW) and 3 mg/kg/every 2 weeks (Q2W) versus no prophylaxis in adults and adolescent patients (age of 12 or above) with haemophilia A without inhibitors against factor VIII (FVIII).

- Study BO39182 (HAVEN 4) - an ongoing multicenter, open-label, non-randomized Phase III study evaluating the efficacy, safety and PK of emicizumab given as the dose of 6

mg/kg/every 4 weeks (Q4W) in adults and adolescent patients (age of 12 or above) with hemophilia A with or without FVIII inhibitors.

- Study BH29992 (HAVEN 2) - a multicenter, open-label, non-randomized Phase III study evaluating the efficacy, safety and PK of emicizumab at the QW dose in pediatric patients (<12 years old or 12-17 years old and <40kg) with hemophilia A with FVIII inhibitors. The Package Leaflet and the Risk Management Plan (v.2.0) is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor corrections and clarity to sections 4.4, 4.5 and 4.6 of the SmPC."

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.

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

The CHMP agreed to consult an ad hoc expert group and adopted list of questions to this group.

5.1.6. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0063/G

Vertex Pharmaceuticals (Europe) Ltd

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

Scope: "1) C.I.6.a (type II) - Extension of Indication to include the combination regimen with tezacaftor 100 mg/ivacaftor 150 mg tablets for the treatment of patients with cystic fibrosis (CF) aged 12 years and older who are homozygous for the F508del mutation or who are heterozygous for the F508del mutation and have one of the following mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272 26A→G, and 3849+10kbC→T;

2) B.IIe.5.a.2 (type IB) - to add a blister card pack presentation containing 28-tablets for the 150 mg film-coated tablets (EU/1/12/782/005);

As a consequence, section 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 5.1, 5.2, 5.3, 6.4, 6.5, 6.6, 7 and 8 of the SmPC are updated. Annex A, Annex II, the Package Leaflet and Labelling are updated in accordance. An updated RMP (version 7.10) is included."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018, 31.05.2018, 22.03.2018, 14.12.2017.

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.

The CHMP adopted the similarity assessment report

5.1.7. [Keytruda - pembrolizumab - EMEA/H/C/003820/II/0042](#)

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include treatment as monotherapy of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) on or after platinum-containing chemotherapy based on the results from KEYNOTE-040 (KN040) with supportive data from two additional single arm studies (KEYNOTE-012/ KEYNOTE-055). KN040 is a randomized, multi-center, pivotal phase III study investigating KEYTRUDA as a monotherapy versus standard treatment (methotrexate, docetaxel or cetuximab) in 495 patients with recurrent or metastatic HNSCC who have previously progressed on prior platinum. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to include in SmPC section 5.2 the description of pembrolizumab PK results on time-dependent change in clearance using a time-dependent pharmacokinetic (TDPK) model structure rather than the static PK model structure.

An updated RMP version 15.1 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018, 26.04.2018.

See 2.3

An oral explanation was held on 25 July 2018 at time 16:00. During the oral explanation the applicant considered that based on the totality of the efficacy and safety data, the PD-L1 CPS ≥ 1 population of KEYNOTE-040 should be considered for approval. According to the applicant, pembrolizumab showed a clinically meaningful overall survival benefit in patients with CPS ≥ 1 compared with standard treatment.

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/0043](#)

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include 1st line treatment of non-squamous non-small cell lung cancer (NSCLC) in combination with pemetrexed and platinum chemotherapy based on the efficacy and safety data from pivotal study KEYNOTE-189, supported by data from KEYNOTE-021 cohorts C and G.

KEYNOTE-189 is a phase 3, randomized, placebo-controlled study undertaken to evaluate the efficacy and safety of pembrolizumab + pemetrexed + carboplatin or cisplatin (pembro combo) versus saline placebo + pemetrexed + carboplatin or cisplatin (control) in previously untreated subjects with advanced/metastatic nonsquamous NSCLC with no EGFR or ALK genomic tumor aberrations.

As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated and the Package Leaflet is updated in accordance.

An updated RMP version 16.2 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018.

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

The Committee adopted a positive opinion 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.

5.1.9. [Keytruda - pembrolizumab - EMEA/H/C/003820/II/0047](#)

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include (as monotherapy) adjuvant treatment of melanoma in adults with lymph node involvement who have undergone complete resection, based on study KEYNOTE-054; a randomized, double-blind, phase 3 study conducted in collaboration with the European Organisation for Research and Treatment of Cancer (EORTC), undertaken to evaluate adjuvant therapy with pembrolizumab compared to placebo in patients with resected high-risk melanoma (Stage IIIA [> 1 mm lymph node metastasis], IIIB and IIIC). As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly. An updated RMP version 17.1 was provided as part of the application."

Action: For adoption

The Committee discussed the issues identified in this application.

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

5.1.10. NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0104

Novo Nordisk A/S

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Nithyanandan Nagercoil

Scope: "Extension of Indication to extend patient population of NovoSeven for use in patients with Glanzmann's thrombasthenia without antibodies to platelets, or where platelets are not readily available, based on a prospective observational registry and literature references. As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in section 4.8 of the SmPC and in Package Leaflet."

Action: For adoption

The Committee discussed the issues identified in this application.

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

5.1.11. Nucala - mepolizumab - EMEA/H/C/003860/II/0013/G

GlaxoSmithKline Trading Services Limited

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Type II-C.I.6-Extension of Indication to include children and adolescents aged 6 to 17 years for Nucala; as a consequence, Sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC and Sections 1, 2, 3, 4 and Information for Healthcare Professionals in the Package Leaflet are updated accordingly.

In addition to the proposed SmPC/PL updates specific to the paediatric indication, as Nucala is a biological medicine, GSK is including wording in the NUCALA SmPC (Section 4.4) and PL (Information for Health Care Professionals) that the name and batch number of the administered product should be clearly recorded in the patient file.

Action: For adoption

Request for Supplementary Information adopted on 22.03.2018.

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

The Committee adopted a positive opinion 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.

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

Novartis Europharm Limited

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

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

Action: For adoption

The Committee discussed the issues identified in this application. There were following questions outstanding: justification is needed that, benefit/risk ratio of eltrombopag+IST is positive in the claimed indication in the absence of a phase III trial in which eltrombopag+IST is compared to IST alone. In addition, the number of children aged 2 to 11 years included in the main study (n=7) was very limited but complete response was not seen in any of them. The use in children 2 to 11 years needs to be further justified; otherwise the therapeutic indication should be modified. Furthermore, the applicant should justify how the dose has been selected for adults and children for the proposed indication.

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

5.1.13. Xarelto - rivaroxaban - EMEA/H/C/000944/II/0058

Bayer AG

Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue

Scope: "Extension of Indication to include prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD) at high risk of ischaemic events for Xarelto 2.5 mg co-administered with acetylsalicylic acid; as a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance.

In addition, section 4.8 of the SmPC is updated for all other dose strengths (10/15/20 mg) of Xarelto with relevant exposure information based on the provided clinical data.

Furthermore, the PI for all dose strengths is brought in line with the latest ORD template version 10. The RMP has been updated to version 11.4."

Report from the SAG CVS

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018, 22.02.2018.

See 2.3

The CHMP noted the report from the SAG CVS meeting held on 13th July. The SAG was asked to discuss the risk of cardiovascular events (CVE) in patients with PAD without coexisting diagnosed CAD and current standard of care with respect to prevention of CVE as well as the strength and relevance of the results in the COMPASS study with respect to reduction of MACE as well as the risk of bleedings in the group of patients with PAD only. The experts considered that there is a continuum between CAD and PAD (with many patients having both), as both conditions are linked with atherosclerosis which has

developed in different territories. Therefore, there is no biological rationale to distinguish between the two. The experts also noted that there is a transition in the Standard of Care for patients with PAD, with treatment aiming at reducing the risk of cardiovascular events in such patients. With regards to the results of the COMPASS study, the experts noted that the results in the pre-specified PAD only sub-group did not reach statistical significance for the reduction of CVE. This was however considered to be due to the smaller sample size of this group and chance fluctuation of treatment effect. The results in this sub-group of patients are consistent with those for the overall study population and the experts considered these as sufficient of demonstrating efficacy in the applied indication.

The SAG was also asked to discuss the B/R in elderly patients and concluded that they did not find any reason that precluded the use of rivaroxaban in in CAD/PAD patients ≥ 75 years. It was considered that labelling with warnings about this risk would be appropriate to effectively manage this risk.

The CHMP agreed that oral explanation is not needed this time.

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

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

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

The summary of opinion was circulated for information.

5.1.14. [Xtandi - enzalutamide - EMEA/H/C/002639/II/0039/G](#)

Astellas Pharma Europe B.V.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Eva A. Segovia

Scope: "C.I.4: Update of sections 4.4, 4.7, 4.8 and 5.2 of the SmPC in order to amend the warning on possible association with seizure, to amend the effects on driving or operating machines, to amend the identified adverse reactions and to amend the 'Race' subsection regarding pharmacokinetic properties based on the results from the completed studies PROSPER, a Phase 3 Randomized Controlled Study, designed to investigate the Safety and Efficacy of Enzalutamide in Patients with Non-Metastatic Castration-Resistant Prostate Cancer; and Asian PREVAIL, a Multinational Phase 3, Randomized, Double-blind, Placebo-controlled Efficacy and Safety Study of Oral Enzalutamide in Chemotherapy-naive Subjects with Progressive Metastatic Prostate Cancer Who Have Failed Androgen Deprivation Therapy; and the updated integrated clinical safety database.

The Package Leaflet is updated in accordance.

C.I.6.a: Extension of Indication to include patients with non-metastatic castration-resistant prostate cancer (CRPC) for Xtandi;

as a consequence, sections 4.1 and 5.1 of the SmPC are updated, based on the supportive clinical study results of MDV3100-14 (PROSPER), a Phase 3 Randomized Controlled Study, designed to investigate the Safety and Efficacy of Enzalutamide in Patients with Non-Metastatic Castration-Resistant Prostate Cancer; MDV3100-09 (STRIVE), a Multicenter Phase 2 Study to investigate the Safety and Efficacy of Enzalutamide Versus Bicalutamide in Men With Non-Metastatic or Metastatic Castration-Resistant Prostate Cancer; and based on

supportive non-clinical data from 7 new reports.

The Package Leaflet is updated in accordance.

An update RMP version 12.1 was submitted in order to include the changes related to the extension of indication.”

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018.

The Committee discussed the issues identified in this application, mainly relating to the clinical relevance of the primary endpoint and the proposed wording of the indication.

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

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

5.1.15. [WS1274](#)
[Mekinist - trametinib - EMEA/H/C/002643/WS1274/0023](#)
[Tafinlar - dabrafenib - EMEA/H/C/002604/WS1274/0031](#)

Novartis Europharm Limited

Lead Rapporteur: Paula Boudewina van Hennik, Lead Co-Rapporteur: Filip Josephson, PRAC
Rapporteur: Ulla Wändel Liminga

Scope: “Extension of indication to include the combination adjuvant treatment with trametinib and dabrafenib of adult patients with stage III melanoma with a BRAF V600 mutation, following complete resection. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the Mekinist and Tafinlar SmPCs are updated. The Package Leaflet and the Risk Management plan (version 14.1 for Mekinist and version 9.1 for Tafinlar, according to GVP module V revision 2) are updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to correct some typos throughout the Mekinist and Tafinlar product information, to include a cross reference to the Mekinist SmPC in section 4.6 of the Tafinlar SmPC regarding fertility, to update the list of local representatives for Bulgaria, Hungary, Estonia, Latvia and Lithuania in the Package Leaflet of both products.”

SAG report

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018, 22.02.2018.

The CHMP noted the SAG report from 18th June 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.

5.1.16. [WS1278](#)
[OPDIVO - nivolumab - EMEA/H/C/003985/WS1278/0042](#)
[Yervoy - ipilimumab - EMEA/H/C/002213/WS1278/0053](#)

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of indication to include the combination treatment with nivolumab and ipilimumab of adult patients with intermediate/poor-risk advanced renal cell carcinoma. As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the Opdivo and Yervoy SmPCs are updated. The Package Leaflet and the Risk Management Plan (version 19.0 for Yervoy and version 13.0 for Opdivo) are updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to correct some typos throughout the Yervoy and Opdivo product information."

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018, 22.02.2018.

See 2.3

An oral explanation was held on 25 July 2018 at time 9:30. The presentation by the MAH focused on the clinical benefit of the combination relative to nivolumab monotherapy as well as a proposed study design for further investigation of the benefit of the combination.

After the oral explanation the CHMP discussed whether the contribution of ipilimumab to the efficacy of the combination therapy in the proposed dosage has been sufficiently demonstrated and some concern was expressed.

The Committee adopted a negative opinion by majority (24 negative out of 26 votes) the refusal of the variation to the terms of the marketing authorisations. The CHMP adopted the CHMP Assessment Report.

The Norwegian CHMP member was in agreement with the CHMP recommendations.

The divergent position (Kristina Dunder, Jan Mueller-Berghaus) was appended to the opinion.

The refusal question and answers document was circulated for information.

Post meeting note: The applicant requested a re-examination with SAG involvement.

The final opinion documents were adopted by the written procedure on 3 August 2018.

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

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of Indication to include first-line treatment of adult patients with metastatic Non-Small Cell Lung Carcinoma (NSCLC) for OPDIVO and Yervoy; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to

add information from the pivotal study CA209227 (an open-label, randomised phase 3 trial of nivolumab, or nivolumab plus ipilimumab, or nivolumab plus platinum doublet chemotherapy versus platinum doublet chemotherapy in subjects with chemotherapy-naïve stage IV or recurrent NSCLC). The Package Leaflet and RMP (version 14.0 for Opdivo and version 21.0 for Yervoy) are updated in accordance. In addition, the MAH has taken the opportunity to introduce minor editorial and formatting revisions in the PI.”

Action: For adoption

The Committee discussed the issues identified in this application, which concerned some clinical efficacy aspects, in particular some methodological issues in relation to the pivotal study and the combination therapy.

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

5.1.18. [WS1406 Abseamed-EMA/H/C/000727/WS1406/0070](#), [Binocrit-EMA/H/C/000725/WS1406/0070](#), [Epoetin alfa Hexal-EMA/H/C/000726/WS1406/0069](#)

Sandoz GmbH,

Lead Rapporteur: Alexandre Moreau, Lead PRAC Rapporteur: Ghania Chamouni

Scope: “Extension of indication to include the treatment of symptomatic anaemia (haemoglobin concentration of ≤ 10 g/dl) in adults with low- or intermediate-1-risk primary myelodysplastic syndromes (MDS) who have low serum erythropoietin (< 200 mU/ml) for Binocrit, Epoetin alfa Hexal and Abseamed; as a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated with safety and efficacy information. The Package Leaflet and the risk management plan (finally agreed version 17.1) are updated in accordance. In addition, the worksharing applicant (WSA) took the opportunity to align information with the reference medicinal product and with the EC guideline on Excipients, to improve the quality and readability of the translations in the product information and to update the Annex A in line with EMA guideline.”

Action: For adoption

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

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

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

The summary of opinion was circulated for information.

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

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

8.1.1. emapalumab - Orphan - H0004386

Novimmune B.V., Treatment of Primary Haemophagocytic Lymphohistiocytosis (HLH)

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

Action: For adoption

The CHMP did not agree to the request for accelerated assessment and adopted the briefing

note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.1.2. larotrectinib sulphate - H0004919

for the treatment of adult and paediatric patients with locally advanced or metastatic solid tumours (excluding primary Central Nervous System tumours) with a Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusion after prior standard therapy or as initial therapy when there is no adequate treatment option

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

Action: For adoption

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

8.1.3. onasemnogene abeparvovec - Orphan - ATMP - H0004750

AveXis EU Ltd; Treatment of paediatric patients diagnosed with SMA Type 1 indicated for the one-time-only treatment of pediatric patients with spinal muscular atrophy (SMA) Type 1

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

Action: For adoption

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

8.1.4. Autologous haematopoietic stem cells transduced with lentiviral vector encoding the human beta-A-T87Q-globin gene - Orphan - ATMP - H0003691

bluebird bio GmbH; Treatment of adolescents and adults with transfusion-dependent β -thalassaemia (TDT) who do not have a $\beta 0$ mutation at both alleles of the β -globin (HBB) gene (i.e., patients with a non- $\beta 0/\beta 0$ genotype)

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

Action: For adoption

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

8.1.5. ibalizumab - H0004961

is indicated, in combination with other antiretroviral medicinal products, for the treatment of adults infected with HIV-1 resistant to at least 1 agent in 3 different classes
Scope: Briefing note and the Rapporteurs' recommendation on the request for accelerated

assessment.

Action: For adoption

The CHMP agreed by written procedure on 31 July 2018 to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

Action: For information

The CHMP noted the list of applications received.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 5 recommendations for eligibility to PRIME: 2 were accepted to PRIME and 3 were denied.

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

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Victrelis – boceprevir – EMEA/H/C/2332

Merck Sharp & Dohme Ltd; treatment of chronic hepatitis C (HCV)

Rapporteur: Joseph Emmerich, Co-Rapporteur: Johann Lodewijk Hillege

Scope: Withdrawal of the marketing authorisation

Action: For information

The CHMP noted the withdrawal of the marketing authorisation.

9.1.2. Intanza 15 microgram/strain - influenza vaccine (split virion, inactivated) - EMEA/H/C/000957

Sanofi Pasteur Europe

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Kristina Dunder

Scope: Withdrawal of the marketing authorisation

Action: For information

The CHMP noted the withdrawal of the marketing authorisation.

9.1.3. Sovaldi - sofosbuvir - EMEA/H/C/002798/R/0050

Gilead Sciences International Limited

Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Julie Williams

Scope: Renewal

Action: For adoption

The CHMP adopted an opinion by consensus concluding that the risk-benefit balance of the above mentioned medicinal product remains favourable and therefore recommended the renewal of the marketing authorisation.

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

The CHMP noted the letter of recommendation dated 25 July 2018.

9.1.4. Velcade - bortezomib - EMEA/H/C/000539/II/0088

Janssen-Cilag International NV

Rapporteur: Daniela Melchiorri

Scope: "Update of sections 4.2 and 5.1 of the SmPC in order to add a new dosing schedule for Velcade (bortezomib) in combination with melphalan and prednisone (VMP) for the treatment of patients with newly diagnosed multiple myeloma, who are not eligible for high-dose chemotherapy with hematopoietic stem cell transplant.

The proposed new dosing schedule is supported by analyses comparing the current approved VcMP schedule (from 26866138MMY3002 [VISTA] study) with pooled modified less intensive ("once-weekly") VcMP schedules (from 54767414MMY3007 [ALCYONE], GIMENA MM-03-05 [GIMENA]). Additional supportive efficacy and safety data come from GEM2005MAS65 [PETHEMA].

The PL (section 3) is amended accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the PL."

Action: For adoption

Request for Supplementary Information adopted on 22.03.2018.

The Committee discussed the issues identified in this application and it was noted that the

MAH should further discuss the possibility to provide clinical data from direct comparisons to support the proposed changes in the section 4.2 of the SmPC.

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

9.1.5. Cinryze - c1-esterase inhibitor, human - EMEA/H/C/001207

Shire Services BVBA

Scope: supply shortage, DHPC and communication plan

Action: For adoption

The CHMP adopted the DHPC and communication plan.

10. Referral procedures

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

10.1.1. Xofigo - EMEA/H/A-20/1459

Bayer AG

Rapporteurs for the Article 20 referral: PRAC Rapporteur: Patrick Batty; PRAC Co-rapporteur: Martin Huber

CHMP Rapporteur: Harald Enzmann; CHMP Co-Rapporteur: Daniela Melcchiorri;

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

Action: For adoption

The CHMP was informed about discussions at the PRAC and the SAG-oncology meeting.

The CHMP, having considered the PRAC recommendation, adopted an opinion by majority (23 out of 31 votes) recommending that the marketing authorisations for Xofigo (radium Ra223 dichloride) should be varied.

The divergent position (Alexandre Moreau, Concepcion Prieto Yerro, Daniela Melchiorri, Greg Markey, Jayne Crowe, Johann Lodewijk Hillege, Robert James Hemmings, Sol Ruiz, Svein Rune Andersen) was appended to the opinion.

The Icelandic Member was in agreement with the CHMP opinion and the Norwegian Member was against.

The CHMP agreed the wording of a DHPC and communication plan.

The CHMP noted the EMA public health communication.

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

10.2.1. Gentamicin – EMEA/H/A-5(3)/1468

MAHs: various

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Jorge Camarero Jiménez

Scope: CHMP list of outstanding issues

Action: For adoption

Review of histamine levels in Gentamicin-containing solutions for injection/infusion

The CHMP discussed the outstanding issues and identified the need for further data on levels of histamine known to have been associated with hypotension and hypersensitivity reactions in more sensitive individuals and the paediatric population. Furthermore the need for the MAHs to closely monitor and notify the authorities of any new reports of hypersensitivity and hypotension was highlighted.

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

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. Paclitaxel Hetero - EMEA/H/A-29(4)/1466

Hetero Europe S.L.

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

Scope: CHMP list of outstanding issues

Action: For adoption

Decentralised Procedure number: PT/H/1256/001/DC, notification by the Portuguese Agency dated 29 March 2018 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC.

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

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

Syner-Medica Ltd

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Sol Ruiz

Scope: Start of procedure, appointment of Rapporteurs, list of questions

Action: For adoption

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

The CHMP appointed Nithyanandan Nagercoil as Rapporteur (interest level 3) and Sol Ruiz as Co-Rapporteur (interest level 1).

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

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

10.5.1. Septanest and associated names – Articaïne (hydrochloride)/ Adrenaline (tartrate) - EMEA/H/A-30/1461

Septodont group of companies and associated companies

Rapporteur: Romaldas Maciulaitis, Co-rapporteur: Fatima Ventura

Scope: List of questions, timetable

Action: For adoption

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

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

Submission of responses: 24 October 2018

Re-start of the procedure: 29 October 2018

Rapporteur/co-rapporteur joint assessment report(s) circulated to CHMP: 31 October 2018

Comments: 7 November 2018

Updated Rapporteur/co-rapporteur joint assessment report(s) circulated to CHMP: 9 November 2018

CHMP list of outstanding issues/ CHMP opinion: November 2018 CHMP

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

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

MAHs: various

Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

Scope: Request for an extension to the clock stop to respond to the list of outstanding issues adopted in June CHMP

Action: For adoption

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

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

Start: 26 July 2018

Submission of responses: 06 September 2018

Clock restart: 20 September 2018

CHMP Rapporteur AR: 03 October 2018

SAG-CVS meeting: October 2018

Comments: 08 October 2018

Updated Co-Rapporteur AR: 11 October 2018

Opinion or LoOI: October 2018 CHMP

10.6.2. Valsartan-containing medicinal products - EMEA/H/A-31/1471

MAHs: various

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Martina Weise ,

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

Action: For adoption

Referral notification from European Commission regarding an API manufacturer (Zhejiang Huahai Pharmaceutical, China), who has detected the presence of a previously undetected impurity, N-nitrosodimethylamine (NDMA, also known as dimethylnitrosamine) in the valsartan API manufactured at its site in Chuannan. Zhejiang Huahai is one of the API manufacturers that are supplying valsartan for medicinal products authorised in the EU.

The CHMP appointed Daniela Melchiorri as Rapporteur (interest level 2) and Martina Weise as Co-rapporteur (interest level 2).

The CHMP adopted a list of questions to the MAHs and API manufacturers with a specific timetable.

Submission of responses: 30 July 2018

Re-start of the procedure: 23 August 2018

Rapporteur/Co-rapporteur assessment report(s) circulated to CHMP: 10 September 2018

Comments: 13 September 2018

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 14 September 2018

LoOI /CHMP opinion: September 2018 CHMP

Post-meeting note: the CHMP adopted the theoretical calculation of the risk numbers document for valsartan via written procedure on 2nd August 2018.

10.6.3. Gadolinium-containing contrast agents (GdCA): Gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP) - EMEA/H/A-31/1097

Applicant: various

Lead Rapporteur: Patrick Batty

Scope: Annual cumulative reviews on NSF cases submission as a post-authorisation measure resulting from the 2010 Article 20 and Article 31 referral procedures for gadolinium-containing contrast agents

Timetable

Action: For adoption

The CHMP adopted the procedural timetable for assessment of the Annual cumulative reviews.

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

July 2018 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

The CHMP noted the July 2018 ENS.

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. Concepts of significant benefit (follow-up to CHMP Work Plan 2017)

Action: For discussion

Postponed

14.1.2. EMA Implementation plan of the new medical device and in vitro diagnostic regulation

Action: For discussion

Follow-up from June ORGAM

The CHMP noted the information. Sponsors from CHMP were appointed for the various workstreams. Further discussions are expected at the September ORGAM meeting.

14.1.3. Rules of Procedure for standing working parties

Action: For discussion

The CHMP noted the update.

14.1.4. Telematics strategy 2020-2025: Concept Paper

Action: For discussion

The CHMP noted the updated. The Committee was asked to provide comments on the Concept Paper with particular focus on the tables describing how Network business activities

will need to change and improve with support of Telematics (pages 6-13). The CHMP should nominate one or two CHMP members to consolidate comments on the concept paper.

The consolidated comments should be sent to the Telematics Secretariat by **15 October 2018**.

A follow up discussion is expected to take place at the September ORGAM.

14.1.5. Timetable for August 2018 written procedure

Action: For adoption

The CHMP adopted the timetable for the August 2018 written procedure.

14.1.6. Joint CHMP-PDCO Strategic Review and Learning meeting under EU Austrian Presidency

CHMP coordinator: Andrea Laslop

Draft Agenda for 26-28 September 2018 in Vienna, Austria

Action: For information

The CHMP noted the proposal for agenda topics. Comments on the draft agenda should be sent

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 9-12 July 2018

Action: For information

The CHMP noted the summary of recommendations and advice.

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for July 2018

Action: For adoption

The CHMP adopted the document.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 18-20 July 2018

Action: For information

The CHMP noted the draft minutes.

Revised draft Guideline on quality, non-clinical and clinical aspects of medicinal products

containing genetically modified cells (EMA/CAT/GTWP/671639/2018 Rev. 1)

CAT Rapporteur: Marcos Timon

Action: For adoption for 12 months public consultation

The CHMP adopted the revised draft guideline for 12 months public consultation.

14.2.3. [Committee for Herbal Medicinal Products \(HMPC\)](#)

Report from the HMPC meeting held on 23-24 July 2018

Action: For information

The CHMP noted the report.

14.2.4. [Paediatric Committee \(PDCO\)](#)

PIPs reaching D30 at July 2018 PDCO

Action: For information

The CHMP noted the document.

Report from the PDCO meeting held on 24-27 July 2018

Action: For information

The CHMP noted the report.

Joint CHMP/PDCO session

Agenda for joint session

Action: For discussion

Joint session was held.

14.2.5. [Committee for Orphan Medicinal Products \(COMP\)](#)

Report from the COMP meeting held on 17-19 July 2018

Action: For information

The CHMP noted the report.

14.2.6. [Coordination Group for Mutual Recognition and Decentralised Procedures – Human \(CMDh\)](#)

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 23-25 July 2018

Action: For information

The CHMP noted the report.

Influenza vaccines effectiveness response to vaccines Europe

Action: For adoption

The CMDh and EMA received a request for clarification by Vaccines Europe with regards to regulatory aspects related to the submission of yearly vaccine effectiveness data generated with seasonal influenza vaccines centrally and nationally authorised. The CMDh discussed the points raised by EU vaccine manufacturers during their July plenary meeting.

The CHMP adopted the response document.

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

14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 9-12 July 2018. Table of conclusions

Action: For information

The CHMP noted the report.

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

Nomination of a replacement SAWP member and his/her alternate following resignation of Jan Sjoberg

Action: For adoption

The CHMP nominated Filip Josephson as member and Kristian Wennmalm as alternate.

14.3.2. Name Review Group (NRG)

No items

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP July 2018 meeting to CHMP for adoption:

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

Action: For adoption

The CHMP adopted the BWP reports.

Response to CMDh question on requirements for Module 3 for the transfer of test methods to already approved QC testing site for a biological medicinal product (EMA/CHMP/BWP/492172/2018)

CHMP: Sol Ruiz

Action: For adoption

The CHMP adopted the response.

14.3.4. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus

Election of vice-chair to RIWP

Action: For adoption

The CHMP elected Romaldas Mačiulaitis as Vice-chair to RIWP.

Response from RIWP and PKWP to CMDh questions on Classification as Narrow Therapeutic Index (NTI) drug and advice on requirements for bioequivalence studies – colchicine

Action: For adoption

Postponed

14.3.5. Blood Products Working Party (BPWP)

Chair: Jacqueline Kerr

Guideline on core SmPC for human albumin solution (EMA/CHMP/BPWP/494462/2011/Rev.1)

Action: For adoption

The CHMP adopted the guideline.

Guideline on the clinical investigation of recombinant and human plasma-derived factor VIII products (EMA/CHMP/BPWP/144533/2009 rev. 2)

Action: For adoption

The CHMP adopted the guideline.

Guideline on core SmPC for human plasma derived and recombinant coagulation factor VIII products rev. 3 (EMA/CHMP/BPWP/1619/1999 rev. 3)

Action: For adoption

The CHMP adopted the guideline.

14.3.6. SmPC Advisory Group

Proposal for the development of an eLearning product information review curriculum: call for volunteers

Action: For discussion

Follow-up from June CHMP Plenary and July ORGAM meeting

The CHMP noted the call for volunteers. The volunteers were welcomed.

14.3.7. Guideline Consistency Group (GCG)

Election of Chair to the Guideline Consistency Group (GCG)

Action: For adoption

The CHMP elected Aranzazu Sancho-Lopez as Chair to the Guideline Consistency Group.

14.3.8. Biosimilar Medicinal Product Working Party (BMWP)

Chair: Elena Wolff-Holz/Niklas Ekman

Guideline on similar biological medicinal products containing recombinant granulocyte-colony stimulating factor (rG-CSF) (EMA/483392/2018 Rev 1)

Action: For adoption for 6 months public consultation

The CHMP adopted the guideline for 6 months public consultation.

It is a revision of the guideline. The non-clinical section provides guidance on in vitro pharmacodynamic studies and, if needed, in vivo toxicological assessment. The clinical section provides guidance on pharmacokinetic and pharmacodynamic studies and, if needed, a clinical immunogenicity study, as well as the risk management plan. Whereas the previous version of this guideline requested a comparative clinical trial in most cases, the revised guideline focusses on demonstration of biosimilarity based on a strong and convincing physicochemical and functional data package and comparable pharmacokinetic and pharmacodynamic profiles. In addition, the non-clinical section has been amended to follow a risk-based approach. Specific considerations on pegylated rG-CSF have been included, where relevant.

14.3.9. Oncology Working Party

Chair: Pierre Demolis/Paolo Foggi

Guideline on the use of minimal residual disease as a clinical endpoint in multiple myeloma studies (EMA/CHMP/183565/2018)

Action: For adoption for 3 month public consultation

Guidance is provided on the basis and regulatory requirements for the use of minimal residual disease (MRD) as an intermediate endpoint to predict clinical benefit in trials in MM and it is not applicable to other clinical settings.

Novel immune therapies present unique challenges with the techniques used to detect MRD and there are insufficient data available. At present, this guidance is not applicable for the use of MRD assessment in clinical trials with novel immune-therapies.

The CHMP adopted the guideline for 3 month public consultation.

14.3.10. Pharmacokinetics Working Party (PKWP)

PKWP response to CMDh request on referral procedure vaginal ring

Action: For adoption

The CHMP adopted the PKWP response.

14.3.11. Quality Working Party (QWP)

Letter to EDQM to seek input from the European Pharmacopoeia Inhalation Working Party (EMA/CHMP/CVMP/QWP/126810/2018)

Action: For adoption

The CHMP adopted the letter to EDQM.

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

14.5.1. SADC and ECOWAS joint assessment meetings

Action: For information

The CHMP noted the update.

14.5.2. International Council on Harmonisation (ICH)

ICH M9 Guideline: Biopharmaceutics Classification System-based Biowavers – Step1

Action: Draft guideline for adoption and release for 6 month public consultation

The CHMP adopted the guideline for 6 months public consultation.

Report on ICH June 2018 meeting in Kobe, Japan

Action: For information

The CHMP noted the report.

CESHARP: Call for expression of interest of one expert

Action: For information

The CHMP noted the call.

Continuous Manufacturing (ICH Q13): nomination of experts

Action: For adoption

The CHMP nominated Nick Lee (HPRA) and Dolores Hernan (EMA) as experts.

Analytical Procedure Development and Revision of Q2 (R1) Analytical Validation: nomination of experts

Action: For adoption

The CHMP nominated Tone Agasoster (NOMA) and Rob Bream (EMA) as experts.

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. Relocation information to delegates

Action: For information

EMA and the Dutch Government have signed a Seat Agreement, which ensures that EMA can function properly and independently in the Netherlands. It also provides assurance that EMA staff members and their families who need to relocate early to the Netherlands can do so under the protection of the Seat Agreement immediately. EMA's new permanent headquarters, a tailor-made building in the Zuidas business district of Amsterdam, are planned for completion in November 2019.

The building has been commissioned by the Dutch government and will be built by the Central

Government Real Estate Agency (CGREA) together with a consortium of construction companies. The laying of the foundation stone was marked with a ceremony on 28 May 2018.

The Dutch government has offered temporary premises to EMA, the Spark building in the Sloterdijk area of Amsterdam, from 1 January 2019 until its permanent building is completed.

This will allow EMA to move all staff to Amsterdam before the end of March 2019 and ensure EMA's business continuity in Amsterdam until its new permanent building is ready.

On 7 June 2018 a new 'Relocate EMA' website was launched by the Dutch government. It provides information on what has been done so far, and what actions will be taken in the coming months to ensure a smooth relocation of EMA to the Netherlands.

A Twitter account (@relocatema) was published in June. It provides relevant information on the relocation, the progress of the construction of the EMA building, photos from the temporary premises, news, photos, milestones.

The CHMP noted the information.

15.2. Preparedness of the system and capacity increase

Action: For information

There are temporary cuts in EMA activities required, because it has also become clear that the Agency will lose more staff than initially anticipated. Staff, who will not relocate to Amsterdam have already started to leave the Agency and this trend is expected to accelerate. Overall, EMA expects a staff loss of about 30%, with a high degree of uncertainty regarding mid-term staff retention.

EMA has put in place supporting measures to facilitate the relocation of staff to Amsterdam and additional support is provided by the Dutch government. Other mitigating actions, such as a comprehensive staff recruitment programme, are already underway. However, in the short- to mid-term EMA will have to reprioritise its resources to fully maintain its core activities related to the evaluation and supervision of medicines to the level of quality and within the timelines expected.

Following the implementation of phase 1 and 2 of the business continuity plan, in phase 3 EMA will start to temporarily scale back or suspend additional activities through to 2019. This contributes to protecting EMA's essential public health activities and allows for training of EMA staff who will be re-assigned to new duties ahead of the peak relocation time which will start in early 2019.

The implementation date for phase 3 of EMA's business continuity plan is 1 October 2018 at the latest. Detailed plans for the implementation of these measures are currently being developed and will be communicated to stakeholders concerned and the public as soon as they are available.

Activities initially impacted by phase 3 of the business continuity plan include working parties. Non-product-related working parties will be temporarily reduced as a consequence of the scaling back of guideline development or revision.

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 23 – 26 July 2018 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Bart Van der Schueren	Member	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Katarina Vučić	Member	Croatia	No interests declared	
Loizos Panayi	Alternate	Cyprus	No interests declared	
Tomas Boran	Alternate	Czech Republic	No interests declared	
Mark Ainsworth	Alternate	Denmark	No participation in final deliberations and voting on:	3.3.2. turoctocog alfa pegol - Orphan - EMEA/H/C/004883 5.1.10. NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0104
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Joseph Emmerich	Alternate	France	No interests declared	
Harald Enzmann	Member (Vice-Chair)	Germany	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Maria Orfanou	Alternate	Greece	No interests declared	
Agnes Gyurasics	Member	Hungary	No interests declared	
Hrefna Gudmundsdottir	Alternate	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Peter Kiely	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No restrictions applicable to this meeting	
Juris Pokrotnieks	Member	Latvia	No restrictions applicable to this meeting	
Romaldas Mačiulaitis	Member	Lithuania	No participation in final deliberations and voting on:	5.1.5. Hemlibra - emicizumab - EMEA/H/C/004406/II/0002
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Svein Rune Andersen	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No participation in discussion, final deliberations and voting on:	10.1.1. XOFIGO - EMEA/H/A-20/1459
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Simona Badoi	Member	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Jorge Camarero Jiménez	Alternate	Spain	No participation in final deliberations and voting on:	5.1.5. Hemlibra - emicizumab - EMEA/H/C/004406/II/0002
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	
Robert James Hemmings	Co-opted member	United Kingdom	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Koenraad Norga	Co-opted member	Belgium	No participation in final deliberations and voting on:	5.1.11. Nucala - mepolizumab - EMEA/H/C/003860/II/0013/G 3.4.1. zanamivir - EMEA/H/C/004102
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	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Maria Escudero Galindo	Expert - in person*	Spain	No participation in discussions, final deliberations and voting on:	3.1.3. Gefitinib Mylan - gefitinib - EMEA/H/C/004826 3.1.4. Hulio - adalimumab - EMEA/H/C/004429
Kristina Bech Jensen	Expert - in person*	Denmark	No interests declared	
Pia Annunen	Expert - in person*	Finland	No participation in discussions, final deliberations and voting on:	2.3.3. and 5.1.16. WS1278 OPDIVO - nivolumab - EMEA/H/C/003985/WS1278/0042 Yervoy - ipilimumab - EMEA/H/C/002213/WS1278/0053 4.3.2. Orencia - abatacept - EMEA/H/C/000701/X/0117/G 5.1.17. WS1372 OPDIVO - nivolumab - EMEA/H/C/003985/WS1372/0053 Yervoy - ipilimumab - EMEA/H/C/002213/WS1372/0057
Valerie Lescrainier	Expert - in person*	Belgium	No interests declared	
Pierfrancesco Lanzilotti	Expert - in person*	United Kingdom	No interests declared	
Jozefus Hagemeyer	Expert - in person*	Netherlands	No interests declared	
Patrick Batty	Expert - in person*	United Kingdom	No interests declared	
Abidali Fazal	Expert - in person*	United Kingdom	No interests declared	
Jasbinder Sumal	Expert - in person*	United Kingdom	No interests declared	
Johannes Petrus Theodorus Span	Expert - in person*	Netherlands	No interests declared	
Emmely de Vries	Expert - in person*	Netherlands	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Nuria García-Escribano	Expert - via telephone*	Spain	No restrictions applicable to this meeting	
Didier Meulendijks	Expert - via telephone*	Netherlands	No interests declared	
Jorn Mulder	Expert - via telephone*	Netherlands	No restrictions applicable to this meeting	
Hinke Johanna Van der Woude	Expert - via telephone*	Netherlands	No interests declared	
Philippe Lechat	Expert - via telephone*	European Union	No interests declared	
Yang Yu	Expert - via telephone*	Netherlands	No interests declared	
Peter Van Meer	Expert - via telephone*	Netherlands	No interests declared	
Eva A. Segovia	Expert - via telephone*	Spain	No interests declared	
Marcos Timón	Expert - via telephone*	Spain	No interests declared	
Henrike Potthast	Expert - via telephone*	Germany	No interests declared	
Steven Teerenstra	Expert - via telephone*	Netherlands	No interests declared	
Mary O'Grady	Expert - via telephone*	Ireland	No interests declared	
Linda Trauffler	Expert - via telephone*	Austria	No interests declared	
Anneliese Hilger	Expert - via telephone*	Germany	No interests declared	
Jacqueline Kerr	Expert - via telephone*	Germany	No interests declared	
Aaron Emmanuel Sosa Mejia	Expert - via Adobe*	Denmark	No interests declared	
Wilhelm Schlumbohm	Expert - via Adobe*	Germany	No interests declared	
Stephanie Buchholz	Expert - via Adobe*	Germany	No interests declared	
Tim Leest	Expert - via Adobe*	Belgium	No interests declared	
Stephan Lehr	Expert - via Adobe*	Austria	No interests declared	

Representative from the European Commission attended the meeting

Meeting run with the help of EMA staff

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

17. Explanatory notes

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

Oral explanations (section 2)

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

Initial applications (section 3)

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(section 5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

particular medicine or class of medicines on behalf of the EU. Further information on such procedures can be found [here](#).

Pharmacovigilance issues (section 11)

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

Inspections Issues (section 12)

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

Innovation task force (section 13)

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

Scientific advice working party (SAWP) (section 14.3.1)

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

Satellite groups / other committees (section 14.2)

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

Invented name issues (section 14.3)

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

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



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Annex to 23-26 July 2018 CHMP Minutes

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A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for July 2018: **For adoption** Adopted

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

Final Outcome of Rapporteurship allocation for July 2018: **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

Chenodeoxycholic acid Leadiant - chenodeoxycholic acid - EMEA/H/C/004061/S/0006, Orphan Leadiant GmbH, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Adam Przybylkowski	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
Elaprase - idursulfase - EMEA/H/C/000700/S/0075 Shire Human Genetic Therapies AB, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
Firdapse - amifampridine - EMEA/H/C/001032/S/0053, Orphan BioMarin International Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams Request for Supplementary Information adopted	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Marketing Authorisation remains under

on 28.06.2018.	exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
Qarziba - dinutuximab beta - EMEA/H/C/003918/S/0006, Orphan EUSA Pharma (UK) Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Brigitte Keller-Stanislawski	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Fortacin - lidocaine / prilocaine - EMEA/H/C/002693/R/0023 Recordati Ireland Ltd, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Dolores Montero Corominas Request for Supplementary Information adopted on 31.05.2018.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that an additional five-year renewal was required. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/R/0053 Biogen Idec Ltd, Rapporteur: Martina Weise, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Martin Huber	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that an additional five-year renewal was required. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Brintellix - vortioxetine - EMEA/H/C/002717/R/0019 H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Laurence de Fays Request for Supplementary Information adopted on 26.07.2018.	Request for supplementary information adopted with a specific timetable.
Diacomit - stiripentol -	Positive Opinion adopted by consensus together

<p>EMEA/H/C/000664/R/0021 BIOCDEX, Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Julie Williams</p>	<p>with the CHMP assessment report and translation timetable.</p> <p>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p>Grastofil - filgrastim - EMEA/H/C/002150/R/0020 Apotex Europe BV, Rapporteur: Robert James Hemmings, Co-Rapporteur: Sol Ruiz, PRAC Rapporteur: Patrick Batty</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</p> <p>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p>Izba - travoprost - EMEA/H/C/002738/R/0011 Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Almath Spooner Request for Supplementary Information adopted on 26.07.2018.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p>Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/R/0039 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Doris Stenver Request for Supplementary Information adopted on 31.05.2018.</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</p> <p>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p>Levetiracetam Hospira - levetiracetam - EMEA/H/C/002783/R/0018 Hospira UK Limited, Generic, Generic of Keppra, Rapporteur: Juris Pokrotnieks, PRAC Rapporteur: Laurence de Fays Request for Supplementary Information adopted on 26.07.2018.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p>Neuraceq - florbetaben (18F) - EMEA/H/C/002553/R/0025 Life Radiopharma Berlin GmbH, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Patrick Batty</p>	<p>Request for supplementary information adopted with a specific timetable</p>

Request for Supplementary Information adopted
on 26.07.2018.

**Sovaldi - sofosbuvir -
EMA/H/C/002798/R/0050**

Gilead Sciences Ireland UC, Rapporteur: Filip
Josephson, Co-Rapporteur: Alar Irs, PRAC
Rapporteur: Julie Williams

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

Based on the review of the available
information, the CHMP was of the opinion that
the renewal of the marketing authorisation can
be granted with unlimited validity.

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

**Tivicay - dolutegravir -
EMA/H/C/002753/R/0040**

ViiV Healthcare B.V., Rapporteur: Filip
Josephson, Co-Rapporteur: Joseph Emmerich,
PRAC Rapporteur: Julie Williams

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

Based on the review of the available
information, the CHMP was of the opinion that
the renewal of the marketing authorisation can
be granted with unlimited validity.

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

**Xigduo - dapagliflozin / metformin -
EMA/H/C/002672/R/0044**

AstraZeneca AB, Rapporteur: Kristina Dunder,
Co-Rapporteur: Agnes Gyurasics, PRAC
Rapporteur: Julie Williams

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

Based on the review of the available
information, the CHMP was of the opinion that
the renewal of the marketing authorisation can
be granted with unlimited validity.

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

B.2.3. Renewals of Conditional Marketing Authorisations

**Adcetris - brentuximab vedotin -
EMA/H/C/002455/R/0058, Orphan**

Takeda Pharma A/S, Rapporteur: Paula
Boudewina van Hennik, PRAC Rapporteur:
Sabine Straus

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

The CHMP was of the opinion that the renewal
for this conditional Marketing Authorisation can
be granted.

The Marketing Authorisation remains
conditional.

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

Lartruvo - olaratumab -**EMA/H/C/004216/R/0010, Orphan**

Eli Lilly Nederland B.V., Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus

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

The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.

The Marketing Authorisation remains conditional.

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

NINLARO - ixazomib -**EMA/H/C/003844/R/0012, Orphan**

Takeda Pharma A/S, Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga

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

The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.

The Marketing Authorisation remains conditional.

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

Venclyxto - venetoclax -**EMA/H/C/004106/R/0013, Orphan**

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty

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

The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.

The Marketing Authorisation remains conditional.

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

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 9-12 July 2018 PRAC:

Signal of autoimmune hepatitis

Adopted

Abacavir, dolutegravir, lamivudine, zidovudine, atazanavir, cobicistat, darunavir, emtricitabine, tenofovir alafenamide, didanosine, rilpivirine, efavirenz, tenofovir disoproxil, elvitegravir, rilpivirine, enfuvirtide, etravirine, fosamprenavir, indinavir, zidovudine, lopinavir, maraviroc, nevirapine, raltegravir, saquinavir, stavudine, tipranavir - ZIAGEN, TRIUMEO, KIVEXA, TRIZIVIR, REYATAZ, EVOTAZ, PREZISTA, REZOLSTA, SYMTUZA, TIVICAY, JULUCA, STOCRIN, SUSTIVA, ATRIPLA, GENVOYA, STRIBILD, EMTRIVA, ODEFSEY, EVIPLERA, DESCOVY, TRUVADA, FUZEON, INTELENCE, TELZIR, CRIXIVAN, EPIVIR, COMBIVIR, KALETRA, CELSENTRI, VIRAMUNE, ISENTRESS; EDURANT, NORVIR, INVIRASE, ZERIT, VIREAD, APTIVUS

PRAC recommendation on a variation: **For adoption**

Signal of lupus-like syndrome and related terms

Adopted.

Human normal immunoglobulin - FLEBOGAMMA DIF, HIZENTRA, HYQVIA, KIOVIG, PRIVIGEN

PRAC recommendation on a variation: **For adoption**

Signal of interaction possibly leading to decreased levothyroxine efficacy and hypothyroidism

Noted.

Ritonavir; lopinavir; levothyroxine – NORVIR; KALETRA; VIEKIRAX

Follow-up from February PRAC meeting - justification from MAH for not following the PRAC recommendation: **For information**

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its July 2018 meeting:

EMA/H/C/PSUSA/00002948/201712

(ticagrelor)

CAPS:

Brilique (EMA/H/C/001241) (ticagrelor), AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "01 January 2017 - 31 December 2017"

The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following changes:

Update of section 4.4 of the SmPC to revise a warning on discontinuation of ticagrelor prior to surgery. The Package leaflet is updated accordingly.

EMA/H/C/PSUSA/00003085/201712

(ustekinumab)

CAPS:

Stelara (EMA/H/C/000958) (ustekinumab), Janssen-Cilag International NV, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "01 January 2017 - 31 December 2017"

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):

To remove the additional risk minimisation measures consisting of educational materials for HCP and patients from the conditions or restrictions with regards to the safe and effective use of the medicinal product (Annex II of the product information).

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

EMA/H/C/PSUSA/00010028/201712

(concentrate of proteolytic enzymes enriched in bromelain)

CAPS:

NexoBrid (EMA/H/C/002246) (concentrate of proteolytic enzymes enriched in bromelain), MediWound Germany GmbH, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, "18 December 2016 to 17 December 2017"

The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following changes:

Update of the instructions for the preparation of the wound area in section 4.2 of the SmPC and relevant section of the PL.

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

EMA/H/C/PSUSA/00010128/201712

The CHMP, having considered in accordance with

(ponatinib)

CAPS:

Iclusig (EMA/H/C/002695) (ponatinib), Incyte Biosciences Distribution B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "14 December 2016 – 13 December 2017"

Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):

Update of section 4.4 and 4.8 of the SmPC to add posterior reversible encephalopathy syndrome (PRES) with frequency 'uncommon'. The Package leaflet is updated accordingly.

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

EMA/H/C/PSUSA/00010341/201712

(secukinumab)

CAPS:

Cosentyx (EMA/H/C/003729) (secukinumab), Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Eva A. Segovia, "26 DEC 2016 - 25 DEC 2017"

The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):

"Update of section 4.4 of the SmPC to revise existing warnings on inflammatory bowel disease (Crohn's disease and ulcerative colitis) and infections. The Package leaflet is updated accordingly."

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

EMA/H/C/PSUSA/00010379/201801

(nivolumab)

CAPS:

OPDIVO (EMA/H/C/003985) (nivolumab), Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "04 July 2017 to 03 January 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:

Update of section 4.8 of the SmPC to add 'pericardial disorders' with frequency 'Uncommon' for nivolumab monotherapy and frequency and 'not known' for nivolumab in combination with ipilimumab. The Package leaflet is updated accordingly.

EMA/H/C/PSUSA/00010391/201712

The CHMP, having considered in accordance with

<p>(lutetium (177Lu) chloride) CAPS: EndolucinBeta (EMA/H/C/003999) (lutetium (177Lu) chloride), ITG Isotope Technologies Garching GmbH, Rapporteur: Peter Kiely LuMark (EMA/H/C/002749) (lutetium, isotope of mass 177), I.D.B. Holland B.V., Rapporteur: Nithyanandan Nagercoil NAPS: NAPs - EU , PRAC Rapporteur: Almath Spooner, "20.06.2017 - 19.12.2017"</p>	<p>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:</p> <p>Update of section 4.8 of the SmPC to add carcinoid crisis with frequency unknown and nausea and vomiting with frequency very common. The Package Leaflet is updated accordingly.</p> <p>In addition, the MAH for EndolucinBeta took the opportunity to introduce minor editorial corrections throughout the PI.</p>
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B.4. EPARs / WPARs

<p>Cablivi - caplacizumab - EMEA/H/C/004426, Orphan Ablynx NV, indicated for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP)., New active substance (Article 8(3) of Directive No 2001/83/EC)</p>	<p>For information only. Comments can be sent to the EPL in case necessary.</p>
<p>Duzallo - allopurinol / lesinurad - EMEA/H/C/004412 Grunenthal GmbH, gout, Fixed combination application (Article 10b of Directive No 2001/83/EC)</p>	<p>For information only. Comments can be sent to the EPL in case necessary.</p>
<p>Kymriah - tisagenlecleucel - EMEA/H/C/004090, Orphan, ATMP Novartis Europharm Limited, treatment of B cell acute lymphoblastic leukaemia (ALL) and diffuse large B cell lymphoma (DLBCL), New active substance (Article 8(3) of Directive No 2001/83/EC)</p>	<p>For information only. Comments can be sent to the EPL in case necessary.</p>
<p>Mepsevii - vestronidase alfa - EMEA/H/C/004438, Orphan Ultragenyx Germany GmbH, Mepsevii is indicated for the treatment of Mucopolysaccharidosis VII (MPS VII; Sly syndrome) for patients of all ages, New active substance (Article 8(3) of Directive No 2001/83/EC)</p>	<p>For information only. Comments can be sent to the EPL in case necessary.</p>
<p>Nerlynx - neratinib - EMEA/H/C/004030 Puma Biotechnology Limited, extended adjuvant treatment of adult patients with early-stage</p>	<p>For information only. Comments can be sent to the EPL in case necessary.</p>

HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab based therapy, New active substance (Article 8(3) of Directive No 2001/83/EC)

Raligize - axalimogene filolisbac - EMEA/H/C/004473, ATMP
FGK Representative Service GmbH, treatment of cervical cancer, New active substance (Article 8(3) of Directive No 2001/83/EC)
WPAR

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

Ulipristal Acetate Gedeon Richter - ulipristal acetate - EMEA/H/C/005017
Gedeon Richter Plc., treatment of uterine fibroids, Informed Consent of Esmya, Informed consent application (Article 10c of Directive No 2001/83/EC)

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

VEYVONDI - vonicog alfa - EMEA/H/C/004454
Baxalta Innovations GmbH, Treatment of von Willebrand Disease (VWD), New active substance (Article 8(3) of Directive No 2001/83/EC)

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

Vyxeos - daunorubicin / cytarabine - EMEA/H/C/004282, Orphan
Jazz Pharmaceuticals Ireland Limited, treatment of adults with high-risk acute myeloid leukaemia (AML), Known active substance (Article 8(3) of Directive No 2001/83/EC)

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

YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480, Orphan, ATMP
Kite Pharma EU B.V., treatment of diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL) and transformed follicular lymphoma (TFL), New active substance (Article 8(3) of Directive No 2001/83/EC)

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

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0056/G, Orphan
Takeda Pharma A/S, Rapporteur: Paula

Request for supplementary information adopted with a specific timetable.

Boudewina van Hennik
Request for Supplementary Information adopted
on 05.07.2018.

**ATryn - antithrombin alfa -
EMA/H/C/000587/II/0033/G**

Laboratoire Francais du Fractionnement et des
Biotechnologies, Rapporteur: Alexandre Moreau
Opinion adopted on 19.07.2018.
Request for Supplementary Information adopted
on 03.05.2018, 15.02.2018.

Positive Opinion adopted by consensus on
19.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Benepali - etanercept -
EMA/H/C/004007/II/0035**

Samsung Bioepis UK Limited, Rapporteur:
Andrea Laslop
Opinion adopted on 12.07.2018.
Request for Supplementary Information adopted
on 17.05.2018.

Positive Opinion adopted by consensus on
12.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**BiResp Spiromax - budesonide / formoterol
- EMA/H/C/003890/II/0024/G**

Teva Pharma B.V., Duplicate, Duplicate of
DuoResp Spiromax, Rapporteur: Nithyanandan
Nagercoil
Opinion adopted on 26.07.2018.
Request for Supplementary Information adopted
on 21.06.2018.

Positive Opinion adopted by consensus on
26.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Cimzia - certolizumab pegol -
EMA/H/C/001037/II/0068/G**

UCB Pharma S.A., Rapporteur: Kristina Dunder
Opinion adopted on 19.07.2018.
Request for Supplementary Information adopted
on 15.03.2018.

Positive Opinion adopted by consensus on
19.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Circadin - melatonin -
EMA/H/C/000695/II/0053/G**

RAD Neurim Pharmaceuticals EEC Limited,
Rapporteur: Bruno Sepodes
Opinion adopted on 05.07.2018.

Positive Opinion adopted by consensus on
05.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Cuprior - trientine -
EMA/H/C/004005/II/0001/G**

GMP-Orphan SA, Rapporteur: Jayne Crowe
Request for Supplementary Information adopted
on 26.07.2018.

Request for supplementary information adopted
with a specific timetable.

**Cyramza - ramucirumab -
EMA/H/C/002829/II/0024/G**

Eli Lilly Nederland B.V., Rapporteur: Paula
Boudewina van Hennik
Request for Supplementary Information adopted

Request for supplementary information adopted
with a specific timetable.

on 26.07.2018.

**Cyramza - ramucirumab -
EMA/H/C/002829/II/0025**

Eli Lilly Nederland B.V., Rapporteur: Paula
Boudewina van Hennik
Request for Supplementary Information adopted
on 19.07.2018.

Request for supplementary information adopted
with a specific timetable.

**DuoResp Spiromax - budesonide /
formoterol -
EMA/H/C/002348/II/0024/G**

Teva Pharma B.V., Rapporteur: Nithyanandan
Nagercoil
Opinion adopted on 26.07.2018.
Request for Supplementary Information adopted
on 21.06.2018.

Positive Opinion adopted by consensus on
26.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Dupixent - dupilumab -
EMA/H/C/004390/II/0006/G**

sanofi-aventis groupe, Rapporteur: Jan Mueller-
Berghaus
Request for Supplementary Information adopted
on 19.07.2018.

Request for supplementary information adopted
with a specific timetable.

**Entyvio - vedolizumab -
EMA/H/C/002782/II/0029**

Takeda Pharma A/S, Rapporteur: Greg Markey
Request for Supplementary Information adopted
on 17.05.2018.

Request for supplementary information adopted
with a specific timetable.

**Episalvan - birch bark extract -
EMA/H/C/003938/II/0010**

Amryt AG, Rapporteur: Kristina Dunder
Opinion adopted on 05.07.2018.

Positive Opinion adopted by consensus on
05.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Eptifibatide Accord - eptifibatide -
EMA/H/C/004104/II/0004**

Accord Healthcare Limited, Generic, Generic of
Integrilin, Rapporteur: Jayne Crowe
Opinion adopted on 12.07.2018.
Request for Supplementary Information adopted
on 07.06.2018.

Positive Opinion adopted by consensus on
12.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Evicel - human fibrinogen / human
thrombin - EMA/H/C/000898/II/0059**

Omrix Biopharmaceuticals N. V., Rapporteur:
Jan Mueller-Berghaus
Opinion adopted on 26.07.2018.

Positive Opinion adopted by consensus on
26.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**EXJADE - deferasirox -
EMA/H/C/000670/II/0061**

Novartis Europharm Limited, Rapporteur:
Alexandre Moreau

Request for supplementary information adopted
with a specific timetable.

Request for Supplementary Information adopted on 26.07.2018.

Eylea - aflibercept -
EMA/H/C/002392/II/0046
Bayer AG, Rapporteur: Alexandre Moreau
Opinion adopted on 26.07.2018.
Request for Supplementary Information adopted on 31.05.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Fuzeon - enfuvirtide -
EMA/H/C/000514/II/0051/G
Roche Registration GmbH, Rapporteur: Kristina Dunder
Request for Supplementary Information adopted on 26.07.2018.

Request for supplementary information adopted with a specific timetable.

Gardasil - human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) - EMA/H/C/000703/II/0077
MSD Vaccins, Rapporteur: Kristina Dunder
Opinion adopted on 26.07.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Gardasil - human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) - EMA/H/C/000703/II/0078
MSD Vaccins, Rapporteur: Kristina Dunder
Opinion adopted on 26.07.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMA/H/C/003852/II/0025
MSD Vaccins, Rapporteur: Kristina Dunder
Opinion adopted on 26.07.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Gazyvaro - obinutuzumab - EMA/H/C/002799/II/0028, Orphan
Roche Registration GmbH, Rapporteur: Sinan B. Sarac
Opinion adopted on 19.07.2018.

Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Gliolan - aminolevulinic acid - EMA/H/C/000744/II/0016/G
medac Gesellschaft für klinische Spezialpräparate mbH, Rapporteur: Bruno Sepodes
Opinion adopted on 19.07.2018.
Request for Supplementary Information adopted on 17.05.2018.

Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Herzuma - trastuzumab - EMA/H/C/002575/II/0005
Celltrion Healthcare Hungary Kft., Rapporteur:

Request for supplementary information adopted with a specific timetable.

Jan Mueller-Berghaus
Request for Supplementary Information adopted
on 26.07.2018.

**Imatinib Teva - imatinib -
EMA/H/C/002585/II/0033**
Teva B.V., Generic, Generic of Glivec,
Rapporteur: Jorge Camarero Jiménez
Opinion adopted on 05.07.2018.
Request for Supplementary Information adopted
on 03.05.2018.

Positive Opinion adopted by consensus on
05.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Keytruda - pembrolizumab -
EMA/H/C/003820/II/0046**
Merck Sharp & Dohme B.V., Rapporteur:
Daniela Melchiorri
Opinion adopted on 26.07.2018.
Request for Supplementary Information adopted
on 21.06.2018.

Positive Opinion adopted by consensus on
26.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Keytruda - pembrolizumab -
EMA/H/C/003820/II/0051/G**
Merck Sharp & Dohme B.V., Rapporteur:
Daniela Melchiorri
Request for Supplementary Information adopted
on 19.07.2018.

Request for supplementary information adopted
with a specific timetable.

**Kineret - anakinra -
EMA/H/C/000363/II/0060**
Swedish Orphan Biovitrum AB (publ),
Rapporteur: Mark Ainsworth
Request for Supplementary Information adopted
on 26.07.2018.

Request for supplementary information adopted
with a specific timetable.

**Lemtrada - alemtuzumab -
EMA/H/C/003718/II/0021/G**
Genzyme Therapeutics Ltd, Duplicate, Duplicate
of Lemtrada (WD), Rapporteur: Mark Ainsworth
Opinion adopted on 19.07.2018.
Request for Supplementary Information adopted
on 07.06.2018.

Positive Opinion adopted by consensus on
19.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Litak - cladribine -
EMA/H/C/000504/II/0015**
Lipomed GmbH, Rapporteur: Robert James
Hemmings
Opinion adopted on 05.07.2018.

Positive Opinion adopted by consensus on
05.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Lynparza - olaparib -
EMA/H/C/003726/II/0022**
AstraZeneca AB, Rapporteur: Alexandre Moreau
Opinion adopted on 26.07.2018.

Positive Opinion adopted by consensus on
26.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

<p>Naglazyme - galsulfase - EMEA/H/C/000640/II/0070 BioMarin International Limited, Rapporteur: Greg Markey Opinion adopted on 26.07.2018. Request for Supplementary Information adopted on 12.04.2018.</p>	<p>Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0026/G Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 19.07.2018.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p>Olanzapine Apotex - olanzapine - EMEA/H/C/001178/II/0034 Apotex Europe BV, Generic, Generic of Zyprexa, Rapporteur: John Joseph Borg Opinion adopted on 05.07.2018.</p>	<p>Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Repatha - evolocumab - EMEA/H/C/003766/II/0026/G Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 19.07.2018.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p>Respreeza - alpha-1-proteinase inhibitor (human) - EMEA/H/C/002739/II/0023/G CSL Behring GmbH, Rapporteur: Kristina Dunder Opinion adopted on 26.07.2018. Request for Supplementary Information adopted on 28.06.2018.</p>	<p>Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Rotarix - human rotavirus, live attenuated - EMEA/H/C/000639/II/0106/G GlaxoSmithKline Biologicals S.A., Rapporteur: Bart Van der Schueren Opinion adopted on 26.07.2018.</p>	<p>Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Simponi - golimumab - EMEA/H/C/000992/II/0082/G Janssen Biologics B.V., Rapporteur: Kristina Dunder Opinion adopted on 05.07.2018. Request for Supplementary Information adopted on 31.05.2018.</p>	<p>Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Strensiq - asfotase alfa - EMEA/H/C/003794/II/0030/G, Orphan Alexion Europe SAS, Rapporteur: Greg Markey</p>	<p>Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP</p>

Opinion adopted on 12.07.2018.	recommendation.
<p>Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0126</p> <p>GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder</p> <p>Opinion adopted on 19.07.2018.</p>	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<p>Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0127/G</p> <p>GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder</p> <p>Request for Supplementary Information adopted on 19.07.2018.</p>	Request for supplementary information adopted with a specific timetable.
<p>Trulicity - dulaglutide - EMEA/H/C/002825/II/0030</p> <p>Eli Lilly Nederland B.V., Rapporteur: Greg Markey</p> <p>Opinion adopted on 19.07.2018.</p>	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<p>Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0008</p> <p>Pfizer Limited, Rapporteur: Johann Lodewijk Hillege</p> <p>Opinion adopted on 05.07.2018.</p>	Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<p>Vaniqa - eflornithine - EMEA/H/C/000325/II/0051</p> <p>Almirall S.A, Rapporteur: Peter Kiely</p> <p>Opinion adopted on 19.07.2018.</p> <p>Request for Supplementary Information adopted on 26.04.2018, 22.03.2018, 26.10.2017.</p>	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<p>Xiapex - collagenase clostridium histolyticum - EMEA/H/C/002048/II/0099</p> <p>Swedish Orphan Biovitrum AB (publ), Rapporteur: Martina Weise</p> <p>Opinion adopted on 26.07.2018.</p>	Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
<p>Yervoy - ipilimumab - EMEA/H/C/002213/II/0058/G</p> <p>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik</p> <p>Request for Supplementary Information adopted on 12.07.2018.</p>	Request for supplementary information adopted with a specific timetable.
<p>Zerbaxa - ceftolozane / tazobactam - EMEA/H/C/003772/II/0015/G</p> <p>Merck Sharp & Dohme B.V., Rapporteur: Robert James Hemmings</p>	Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 05.07.2018.
Request for Supplementary Information adopted
on 26.04.2018.

WS1339/G
Fertavid-
EMA/H/C/001042/WS1339/0038/G
Puregon-
EMA/H/C/000086/WS1339/0096/G

Merck Sharp & Dohme B.V., Lead Rapporteur:
Nithyanandan Nagercoil
Opinion adopted on 12.07.2018.
Request for Supplementary Information adopted
on 15.03.2018.

Positive Opinion adopted by consensus on
12.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

WS1393/G
Hexacima-
EMA/H/C/002702/WS1393/0080/G
Hexaxim-
EMA/H/W/002495/WS1393/0085/G

Hexyon-
EMA/H/C/002796/WS1393/0084/G
Sanofi Pasteur Europe, Duplicate, Duplicate of
Hexacima, Lead Rapporteur: Jan Mueller-
Berghaus
Request for Supplementary Information adopted
on 19.07.2018.

Request for supplementary information adopted
with a specific timetable.

WS1404
Nuwiq-EMA/H/C/002813/WS1404/0022
Vihuma-
EMA/H/C/004459/WS1404/0004

Octapharma AB, Lead Rapporteur: Jan Mueller-
Berghaus
Request for Supplementary Information adopted
on 05.07.2018.

Request for supplementary information adopted
with a specific timetable.

WS1415
Blitzima-
EMA/H/C/004723/WS1415/0015
Ritemvia-
EMA/H/C/004725/WS1415/0015

Rituzena-
EMA/H/C/004724/WS1415/0016
Truxima-
EMA/H/C/004112/WS1415/0016

Celltrion Healthcare Hungary Kft., Lead
Rapporteur: Sol Ruiz
Request for Supplementary Information adopted
on 26.07.2018.

Request for supplementary information adopted
with a specific timetable.

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

Abraxane - paclitaxel -

EMA/H/C/000778/II/0089

Celgene Europe Limited, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.6 and 5.3 of the SmPC based on information available for the paclitaxel active substance in available literature and product information. No additional non-clinical data was submitted." Opinion adopted on 19.07.2018.

Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

BESPONSA - inotuzumab ozogamicin - EMA/H/C/004119/II/0006, Orphan

Pfizer Europe MA EEIG, Rapporteur: Robert James Hemmings, "Update of sections 4.8, 5.1 and 5.2 of the SmPC based on the supplemental Clinical Study Report for the pivotal phase 3 Study B1931022 (Study 1022) that was prepared following last patient last visit. The Package Leaflet is updated accordingly. The MAH took the opportunity to make minor editorial changes for added clarity in sections 4.2, 4.4, 4.8, 5.1, 5.3 and 6.6 of the SmPC and Package Leaflet." Opinion adopted on 26.07.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Cayston - aztreonam -

EMA/H/C/000996/II/0073, Orphan

Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study GX US 205-0128, listed as a category 3 study in the RMP. This is a prospective, observational, 5 year registry study carried out to monitor the susceptibility to aztreonam of Pseudomonas aeruginosa isolates from patients with Cystic Fibrosis in the US. The population eligible for the registry included paediatric subjects, and the final study population included approximately 26% of subjects of less than 18 years of age.

Request for supplementary information adopted with a specific timetable.

No changes to the SmPC are proposed based on the results from this non-interventional, registry study."

Request for Supplementary Information adopted on 19.07.2018.

Dacogen - decitabine -

EMA/H/C/002221/II/0035, Orphan

Janssen-Cilag International N.V., Rapporteur: Alexandre Moreau, "Update of section 4.4, and

Request for supplementary information adopted with a specific timetable.

4.8 of the SmPC in order to add the adverse events "Hepatic Function abnormal" and "Hyperbilirubinaemia" with the frequency common and to include clinical recommendations in patients developing signs or symptoms of hepatic impairment based on a cumulative review of post-marketing data; the Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the local representative in Portugal in the Package Leaflet. Furthermore, the term "(for pH adjustment)" has been removed from the Annex IIIA in accordance with the revision 2 of the European Commission guideline on Excipients in the labelling and package leaflet of medicinal products for human use."

Request for Supplementary Information adopted on 26.07.2018.

DaTSCAN - ioflupane (123i) - EMEA/H/C/000266/II/0055

GE Healthcare Ltd, Rapporteur: Robert James Hemmings, "Update of section 4.8 of the SmPC in order to add, as side effects, erythema, pruritus, rash, urticaria, hyperhidrosis, dyspnea, vomiting, blood pressure decreased and 'feeling hot' with a not known frequency and 'burning sensation' with an uncommon frequency. The Package leaflet has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 11 of the SmPC in line with ICRP Publication 128, Radiation Dose to Patients from "Radiopharmaceuticals: a Compendium of Current Information Related to Frequently Used Substances, 2015". The Marketing authorisation holder (MAH) took also the opportunity to bring the PI in line with the latest QRD template version 10.0."

Opinion adopted on 19.07.2018.

Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Dukoral - cholera vaccine (inactivated, oral) - EMEA/H/C/000476/II/0058

Valneva Sweden AB, Rapporteur: Kristina Dunder, "Update of the 'instructions for use' in the Package Leaflet in order to increase clarity and reduce the risk of medication errors. Minor corresponding editorial changes have been implemented in section 4.2 of the SmPC. In

Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10, to update Annex II with regards to PSUR requirements, to correct the description of the container of the vaccine suspension and to introduce minor linguistic and layout improvements to the Annexes.”
Opinion adopted on 19.07.2018.

Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0024/G

MSD Vaccins, Rapporteur: Kristina Dunder, “Update of section 5.1 of the SmPC in order to update the information following results from long-term follow-up (LTFU) studies. Specifically:

- a long-term effectiveness sub-section is added, based on the first interim reports from the 9vHPV studies V503-021-01 and V503-002-20 (two category 3 studies included in the pharmacovigilance plan of the 9vHPV vaccine - MEA-004 and MEA 005, respectively).

- update of the immunogenicity sub-section based on the data from the two 9vHPV studies listed above as well as final results from studies V503-001-04 and V503-010-01.

- update of the qHPV clinical data based on the efficacy/effectiveness results and/or immunogenicity results of the qHPV studies V501-015-21 (4th interim report), V501-019-21 (final study report), V501-020-21 (final study report) and the extension of study V501-167.”
Opinion adopted on 26.07.2018.

Request for Supplementary Information adopted on 31.05.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Humira - adalimumab - EMEA/H/C/000481/II/0179

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC in order to add Lichenoid skin reactions with a rare frequency following a signal detection request (EPITT ref. No. 19128) for cumulative review (SDA106). The Package Leaflet is updated accordingly. The MAH took also the opportunity to include some minor QRD and editorial changes in the Package leaflet.”

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 26.07.2018.
Request for Supplementary Information adopted
on 31.05.2018.

**HyQvia - human normal immunoglobulin -
EMA/H/C/002491/II/0040/G**

Baxalta Innovations GmbH, Rapporteur: Jan
Mueller-Berghaus, "Update of section 4.8 of the
SmPC to include aseptic meningitis as adverse
reaction. The PL is updated accordingly.
Update of section 4.2 of the SmPC to include
the option of hand-push administration of the
rHuPH20 component (in addition to
administration with a pump). This change is a
correction in order to harmonise with the PL."

Opinion adopted on 26.07.2018.
Request for Supplementary Information adopted
on 25.05.2018.

Positive Opinion adopted by consensus on
26.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**IBRANCE - palbociclib -
EMA/H/C/003853/II/0011**

Pfizer Limited, Rapporteur: Filip Josephson,
"Update of section 5.1 of the SmPC to update
the clinical efficacy data from pivotal Phase 3
Study A5481008 (PALOMA-2), a study of
IBRANCE in combination with
letrozoleto, to include the results from recent
analyses of the study with a data cutoff date of
31 May 2017. In addition, the MAH took the
opportunity to update section 4.2 to include that
when coadministered
with an aromatase inhibitor, the later should be
administered according to the dose schedule
reported in the Summary of Product
Characteristics."

Request for Supplementary Information adopted
on 26.07.2018, 17.05.2018.

Request for supplementary information adopted
with a specific timetable.

**Inflectra - infliximab -
EMA/H/C/002778/II/0061**

Hospira UK Limited, Duplicate, Duplicate of
Remsima, Rapporteur: Greg Markey, "To submit
the final report from study CT-P13 3.4, listed as
a category 3 study in the RMP. A Randomized,
Double-Blind, Parallel-Group, Phase 3 Study to
Demonstrate Noninferiority in
Efficacy and to Assess Safety of CT-P13
Compared to Remicade in Patients with Active
Crohn's Disease."

Opinion adopted on 19.07.2018.
Request for Supplementary Information adopted
on 17.05.2018.

Positive Opinion adopted by consensus on
19.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Isentress - raltegravir -
EMA/H/C/000860/II/0073**

Merck Sharp & Dohme B.V., Rapporteur: Greg Markey, "Update of sections 4.6 and 5.3 of the SmPC, upon request by PRAC following the assessment of the latest PSUR (PSUSA/00010373/201703), to include revised safety information about pregnancy and risk of malformative or foetal toxicity (LEG). The Package Leaflet has been updated accordingly." Request for Supplementary Information adopted on 26.07.2018, 12.04.2018.

Request for supplementary information adopted with a specific timetable.

**Lemtrada - alemtuzumab -
EMA/H/C/003718/II/0023**

Genzyme Therapeutics Ltd, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth, "Update of section 4.8 of the SmPC in order to update the table of frequencies of adverse reactions in accordance with the SmPC guideline following request from PRAC in procedure EMA/H/C/PSUSA/00010055/201703. This procedure also included an update in section 4.4 to add warning on acute acalculous cholecystitis following a cumulative review of the cases. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 12.07.2018.

Request for supplementary information adopted with a specific timetable.

**Lucentis - ranibizumab -
EMA/H/C/000715/II/0069**

Novartis Europharm Limited, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to include information on the diabetic retinopathy score (DRSS) in diabetic macular edema patients (DME) based on pooled data from studies RFB002D2301 (RESTORE), RFB002D2303 (REVEAL) and RFB002D2305 (REFINE)." Opinion adopted on 26.07.2018. Request for Supplementary Information adopted on 28.06.2018, 22.02.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Orgalutran - ganirelix -
EMA/H/C/000274/II/0041**

Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, "Update of section 4.3 of the SmPC to expand the existing contraindication regarding hypersensitivity to include also wording regarding dry natural rubber/latex and sections 4.4 and 6.5 of the SmPC to clarify that this product is in contact with dry natural

Request for supplementary information adopted with a specific timetable.

rubber/latex. The labelling and Package Leaflet have been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representative in Belgium in the Package Leaflet."

Request for Supplementary Information adopted on 26.07.2018.

**Ozempic - semaglutide -
EMA/H/C/004174/II/0001**

Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC in order to reflect final results from the SUSTAIN 7 trial (NN9535-4216), a 40-week open-label trial comparing the safety and efficacy of 0.5 mg of Ozempic to 0.75 mg of dulaglutide and 1 mg of Ozempic to 1.5 mg of dulaglutide in patients on metformin with type-2 diabetes."

Request for Supplementary Information adopted on 26.07.2018, 25.05.2018.

Request for supplementary information adopted with a specific timetable.

**Pandemic influenza vaccine H5N1
AstraZeneca - pandemic influenza vaccine
(H5N1) (live attenuated, nasal) -
EMA/H/C/003963/II/0015**

AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.6 of the SmPC with regard to pregnancy information based on cumulative review of pregnancy data from clinical trials, published literature and MAH pharmacovigilance database.

The MAH took the opportunity to include editorial changes in section 4.8 and 5.1 of the SmPC."

Opinion adopted on 26.07.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Perjeta - pertuzumab -
EMA/H/C/002547/II/0039**

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC and relevant section of the PL to include tumour lysis syndrome (TLS) as a rare adverse reaction."

Opinion adopted on 05.07.2018.

Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Praluent - alirocumab -
EMA/H/C/003882/II/0040**

sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the final clinical study report of study R727-CL-1018 (study title: A Phase 2 Pilot Study with a Randomized Double-Blind Treatment Phase to Evaluate the Pharmacodynamics and Safety of Alirocumab in

Request for supplementary information adopted with a specific timetable.

Patients with Autosomal Dominant Hypercholesterolemia and Gain-of-Function Mutations in 1 or Both Alleles of the PCSK9 Gene or Loss-of-Function Mutations in 1 or More Alleles of the Apolipoprotein B Gene), as per MEA012.”

Request for Supplementary Information adopted on 19.07.2018.

**Remsima - infliximab -
EMA/H/C/002576/II/0052**

Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, “To submit the final report from study CT-P13 3.4, listed as a category 3 study in the RMP. A Randomized, Double-Blind, Parallel-Group, Phase 3 Study to Demonstrate Noninferiority in Efficacy and to Assess Safety of CT-P13 Compared to Remicade in Patients with Active Crohn’s Disease.”

Opinion adopted on 19.07.2018.

Request for Supplementary Information adopted on 17.05.2018.

Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Revestive - teduglutide -
EMA/H/C/002345/II/0043, Orphan**

Shire Pharmaceuticals Ireland Limited, Rapporteur: Mark Ainsworth, “Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC based on the final CSR of study TED-C14-006 (“a 24-Week Double-blind, Safety, Efficacy, and Pharmacodynamic Study Investigating Two Doses of Teduglutide in Pediatric Subjects Aged 1 Year Through 17 Years With Short Bowel Syndrome who are Dependent on Parenteral Support”; a category 3 study in the RMP). The Package Leaflet is updated accordingly.”

Request for Supplementary Information adopted on 26.07.2018, 31.05.2018.

Request for supplementary information adopted with a specific timetable.

**Savene - dexrazoxane -
EMA/H/C/000682/II/0036**

Clinigen Healthcare Ltd, Rapporteur: Alexandre Moreau, “Update of section 4.4, 4.6 and 5.3 of the SmPC in order to add a warning on mutagenic activity of dexrazoxane and to update the contraception recommendations based on toxicological data and literature review, the Package Leaflet is updated accordingly.”

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

In addition the MAH took the opportunity to

make an administrative amendment to the description of the pharmaceutical form for Savene in order to align with the relevant EDQM standard terms.”

Opinion adopted on 26.07.2018.

Request for Supplementary Information adopted on 14.06.2018.

**Somavert - pegvisomant -
EMA/H/C/000409/II/0084**

Pfizer Limited, Rapporteur: Joseph Emmerich, “Update of sections 4.2 and 4.4 of the SmPC to introduce posology recommendations to recommend an assessment of baseline levels of liver tests (LTs) [serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum total bilirubin (TBIL), and alkaline phosphatase (ALP)] prior initiation of treatment with Somavert following analysis of the interim result for study “A6291010 (ACROSTUDY) - A multicenter, post marketing surveillance study of pegvisomant therapy in patients with acromegaly – extension” as requested in procedure EMA/H/C/000409/MEA 061.1. The PL has been updated accordingly.”

Request for Supplementary Information adopted on 12.07.2018.

Request for supplementary information adopted with a specific timetable.

**Spinraza - nusinersen -
EMA/H/C/004312/II/0004, Orphan**

Biogen Idec Ltd, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga, “Update of sections 4.4 and 4.8 of the SmPC to include new safety information related to communicating hydrocephalus. The PIL and the RMP (new version 10.0) are updated accordingly. Section 4.2 of the SmPC is updated to move an existing wording on the route of administration of the product in order to improve readability.”

Opinion adopted on 12.07.2018.

Request for Supplementary Information adopted on 14.06.2018, 12.04.2018, 08.02.2018.

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Stelara - ustekinumab -
EMA/H/C/000958/II/0063**

Janssen-Cilag International NV, Rapporteur: Greg Markey, “Update of section 4.8 of the SmPC in order to revise the immunogenicity rate in patients with psoriasis from “less than 8%” to “up to 12.4 %” following based on new

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

data

generated from a Phase 3b study in psoriasis patients, CNTO1275PSO3009 (PSTELLAR) - A Study of Ustekinumab to Evaluate a "Subject-tailored" Maintenance Dosing Approach in Subjects With Moderate-to-Severe Plaque Psoriasis (PSTELLAR).

In addition, the MAH took the opportunity to update section 4.4 of the SmPC and package leaflet with additional warning of the excipient sodium to align with the recent updates to the Annex of the EC guideline on excipients in labelling."

Opinion adopted on 26.07.2018.

Request for Supplementary Information adopted on 31.05.2018, 22.03.2018.

**Sustiva - efavirenz -
EMA/H/C/000249/II/0145/G**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, "Update of sections 4.3 and 4.5 of the SmPC in order to add contraindication with elbasvir/grazoprevir due to the potential for significant decreases in plasma concentrations of elbasvir and grazoprevir, based on the post-approval and literature data, the Package Leaflet is updated accordingly.

Update of sections 4.4 and 4.5 to include warnings in relation to the co-administration of efavirenz and sofosbuvir/velpatasvir; efavirenz and velpatasvir/sofosbuvir/voxilaprevir and efavirenz and glecaprevir/pibrentasvir; based on the post-approval and literature data, the Package Leaflet is updated accordingly.

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

Request for Supplementary Information adopted on 26.07.2018.

Request for supplementary information adopted with a specific timetable.

**Tivicay - dolutegravir -
EMA/H/C/002753/II/0034**

ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC to add the new ADR 'acute hepatic failure' with a frequency of rare based on post-marketing and clinical trial data. The Package Leaflet has been updated accordingly."

Opinion adopted on 12.07.2018.

Request for Supplementary Information adopted

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 17.05.2018.

Tivicay - dolutegravir -

EMA/H/C/002753/II/0041/G

ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC with Week 24 data (secondary analysis) from the pivotal Phase III studies, 204861 [GEMINI-1] and 205543 [GEMINI-2] in ART-naïve adult subjects. The Package Leaflet has been updated accordingly."

Request for Supplementary Information adopted on 26.07.2018.

Request for supplementary information adopted with a specific timetable.

Triumeq - dolutegravir / abacavir / lamivudine - EMA/H/C/002754/II/0053

ViiV Healthcare UK Limited, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC to add the new ADR 'acute hepatic failure' with a frequency of rare based on post-marketing and clinical trial data, and to implement minor changes for increased clarity. The Package Leaflet has been updated accordingly."

Opinion adopted on 12.07.2018.

Request for Supplementary Information adopted on 17.05.2018.

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Truvada - emtricitabine / tenofovir disoproxil - EMA/H/C/000594/II/0147

Gilead Sciences Ireland UC, Rapporteur: Greg Markey, "Update of sections 4.8 and 5.1 of the Truvada SmPC based on the final results from study Study ATN-113 (CO-US-164-0455): listed as a category 3 study in the RMPI;

this is a Project PeEPare - An open label demonstration project and phase II safety study of pre-exposure prophylaxis use among 15 to 17 year old men who have sex with men (YMSM) in the United States."

Opinion adopted on 26.07.2018.

Request for Supplementary Information adopted on 25.05.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Vargatef - nintedanib -

EMA/H/C/002569/II/0021

Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to add 'pruritus' as a new adverse drug reaction with a frequency 'common' following a routine review of post-marketing data. The Package Leaflet is updated accordingly."

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 26.07.2018.

**VELCADE - bortezomib -
EMA/H/C/000539/II/0088**

Janssen-Cilag International NV, Rapporteur:
Daniela Melchiorri, "Update of sections 4.2 and
5.1 of the SmPC in order to add a new dosing
schedule for VELCADE (bortezomib) in
combination with melphalan and prednisone
(VMP) for the treatment of patients with newly
diagnosed multiple myeloma who are not
eligible for high-dose chemotherapy with
hematopoietic stem cell transplant.

Request for supplementary information adopted
with a specific timetable.

The proposed new dosing schedule is supported
by analyses comparing the current approved
VcMP schedule (from 26866138MMY3002
[VISTA] study) with pooled modified less
intensive ("once-weekly") VcMP schedules (from
54767414MMY3007 [ALCYONE], GIMENA MM-
03-05 [GIMENA]). Additional supportive efficacy
and safety data come from GEM2005MAS65
[PETHEMA].

The PL (section 3) is amended accordingly.

In addition, the Marketing authorisation holder
(MAH) took the opportunity to update the list of
local representatives in the PL."

Request for Supplementary Information adopted
on 26.07.2018, 22.03.2018.

**Viekirax - ombitasvir / paritaprevir /
ritonavir - EMA/H/C/003839/II/0047**

AbbVie Deutschland GmbH & Co. KG,
Rapporteur: Filip Josephson, "Submission of the
final report from study (M14-567) listed as a
category 3 study in the RMP. This is a
randomized, open-label study to evaluate the
safety and efficacy of the co-administration of
ombitasvir/ABT-450/Ritonavir (ombitasvir/ABT-
450/r) with sofosbuvir (SOF) with or without
ribavirin (RBV) in subjects with genotype 2
chronic hepatitis C virus (HCV) infection or
genotype 3 HCV infection with or without
Cirrhosis."

Opinion adopted on 26.07.2018.

Positive Opinion adopted by consensus on
26.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Vimpat - lacosamide -
EMA/H/C/000863/II/0070/G**

UCB Pharma S.A., Rapporteur: Filip Josephson,
"Update of sections 4.8, 5.1, and 5.2 of the

Positive Opinion adopted by consensus on
26.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

SmPC in order to update clinical efficacy and safety data in the paediatric population with the final results from study SP0969: a phase 3, multicentre, double-blind, randomized, placebo-controlled, parallel-group study to evaluate the efficacy and safety of lacosamide as adjunctive therapy in subjects with epilepsy ≥ 4 years to < 17 years of age with uncontrolled partial-onset seizures; Nasopharyngitis, pharyngitis, and pyrexia have been added as new adverse reactions based on the results of the above mentioned study;

Update of section 5.2 of the SmPC in order to update the pharmacokinetic data in the paediatric population based on results from the CL0430 population pharmacokinetic (PK) analyses;

Update of section 4.8 of the SmPC in order to update the incidence of decreased appetite, lethargy, and abnormal behaviour in the paediatric population based on results from the updated safety data for Pool SPX-1 with clinical cut-off date of 01 November 2016.

The Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the PI and revised Annex A as requested."

Opinion adopted on 26.07.2018.

Request for Supplementary Information adopted on 21.06.2018, 22.03.2018.

Visudyne - verteporfin -

EMA/H/C/000305/II/0097

Novartis Europharm Limited, Rapporteur: Alexandre Moreau, "Update of section 4.4. of the SmPC to amend the existing warning on hypersensitivity reactions and of section 4.8 to include "Anaphylactic Reaction" with frequency 'not known'. The Package Leaflet has been updated accordingly."

Opinion adopted on 26.07.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Votubia - everolimus -

EMA/H/C/002311/II/0051, Orphan

Novartis Europharm Limited, Rapporteur: Harald Enzmann, "Update of sections 4.8 (all pharmaceutical pharms) and 5.1 (dispersible tablets only) of the SmPC in order to update the safety and efficacy information based on final results from study CRAD001M2304, listed as a category 3 study in the RMP; this is a three-

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

arm, randomized, double-blind, placebo-controlled study of the efficacy and safety of two trough-ranges of everolimus as adjunctive therapy in patients with tuberous sclerosis complex (TSC) who have refractory partial-onset seizures. The Package Leaflet is updated accordingly.”

Opinion adopted on 12.07.2018.

**Xyrem - sodium oxybate -
EMA/H/C/000593/II/0075**

UCB Pharma S.A., Rapporteur: Bruno Sepodes, “Update of section 4.9 of the SmPC in order to include safety information on hypernatremia based on a cumulative review of post-marketing data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in sections 4.2 and 4.4 of the SmPC and in the Package Leaflet, as well as to align the annexes with the latest QRD template v.10. Moreover, the Package Leaflet was updated to include information on hypoaesthesia.”

Opinion adopted on 26.07.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1346

Aprovel-

EMA/H/C/000141/WS1346/0170

CoAprovel-

EMA/H/C/000222/WS1346/0185

Irbesartan Hydrochlorothiazide Zentiva-

EMA/H/C/000783/WS1346/0099

Irbesartan Zentiva-

EMA/H/C/000785/WS1346/0078

Karvea-EMA/H/C/000142/WS1346/0174

Karvezide-

EMA/H/C/000221/WS1346/0187

Sanofi Clir SNC, Lead Rapporteur: Concepcion Prieto Yerro, “Update of section 4.8 of the SmPC to add ‘anaphylactic reaction including anaphylactic shock’ to the list of adverse drug reactions. The PL is updated accordingly. In addition, the MAH took the opportunity to update the information on local representatives in Bulgaria and Germany and to update the product information in line with the latest QRD template (version 10).”

Opinion adopted on 26.07.2018.

Request for Supplementary Information adopted on 25.05.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1348

Positive Opinion adopted by consensus on

Exviera-EMEA/H/C/003837/WS1348/0035 26.07.2018. The Icelandic and Norwegian CHMP
Viekirax- Members were in agreement with the CHMP
EMEA/H/C/003839/WS1348/0042 recommendation.

AbbVie Deutschland GmbH & Co. KG, Lead
Rapporteur: Filip Josephson, "Update of sections
4.2, 4.3, 4.4 of the SmPC to reflect that Viekirax
is contraindicated in patients with moderate
hepatic impairment (Child-Pugh B) and update
of section 5.2 to reflect that in HCV infected
subjects paritaprevir AUC increased to 2.2- to
2.4 fold for those with compensated cirrhosis
(Child-Pugh A) and 3- to 4-fold for those with
Child-Pugh B cirrhosis based on the results of
the final report from study (M14-227) listed as a
category 3 study in the RMP. This is a Phase 3b
study designed to evaluate the safety and
efficacy of ombitasvir/paritaprevir/ritonavir and
dasabuvir in HCV infected patients with Child-
Pugh B decompensated cirrhosis."
Opinion adopted on 26.07.2018.
Request for Supplementary Information adopted
on 12.04.2018.

WS1351 Positive Opinion adopted by consensus on
Eviplera- 19.07.2018. The Icelandic and Norwegian CHMP
EMEA/H/C/002312/WS1351/0090 Members were in agreement with the CHMP
Stribild-EMEA/H/C/002574/WS1351/0091 recommendation.
Truvada-
EMEA/H/C/000594/WS1351/0146
Viread-EMEA/H/C/000419/WS1351/0185

Gilead Sciences Ireland UC, Lead Rapporteur:
Joseph Emmerich, "Update of section 4.4 of the
SmPC for Viread, Truvada and Stribild and
Section 4.5 of the SmPC for Viread, Truvada,
Eviplera and Stribild in order to add the results
from study Study GS-US-367-1657,
listed as a a category 3 study in the RMP; this is
a Phase 1 Multiple Dose Study to Evaluate the
Pharmacokinetic Drug-Drug Interaction Potential
between Sofosbuvir/Velpatasvir/GS-9857 Fixed-
Dose Combination and HIV Antiretroviral in
Healthy Subjects.

The corresponding section 2 of the Package
Leaflet for Viread, Truvada and Stribild has been
updated.

In addition, the Worksharing applicant (WSA)
took the opportunity to make administrative
updates to Section 4.1 and 4.5 of the Stribild
SmPC and to implement some linguistic

amendments (MLAs) to the translations of the product information annexes.”
Opinion adopted on 19.07.2018.
Request for Supplementary Information adopted on 17.05.2018.

WS1380
Ebymect-
EMA/H/C/004162/WS1380/0033
Edistride-
EMA/H/C/004161/WS1380/0027
Forxiga-
EMA/H/C/002322/WS1380/0046
Xigduo-EMA/H/C/002672/WS1380/0045
AstraZeneca AB, Lead Rapporteur: Kristina Dunder, “Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to reflect the final study results from study D1690C00024 (DERIVE); A Multicentre, Double-Blind, Placebo-Controlled, Parallel Group, Randomized, Phase III Study to Evaluate the Glycaemic Efficacy and Renal Safety of Dapagliflozin in Patients with Type 2 Diabetes Mellitus and Moderate Renal Impairment (CKD 3A) Who Have Inadequate Glycaemic Control.
In addition, the Worksharing applicant took the opportunity to implement minor editorial changes in Edistride, Ebymect and Xigduo SmPCs, as well as Ebymect Labelling. The Package Leaflets for Xigduo and Ebymect are updated accordingly.”
Request for Supplementary Information adopted on 26.07.2018.

Request for supplementary information adopted with a specific timetable.

WS1392
ProQuad-
EMA/H/C/000622/WS1392/0125
MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus, “Update of section 4.8 of the SmPC in order to add the adverse reaction (ADR) meningitis with a frequency “not known” and to add a clarifying foot note for immunocompromised or immunocompetent individuals applicable to the ADR meningitis, herpes zoster and encephalitis. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the product information and to update the list of local representatives in the package leaflet.”
Request for Supplementary Information adopted

Request for supplementary information adopted with a specific timetable.

on 05.07.2018.

WS1400

Exviera-EMEA/H/C/003837/WS1400/0039
Viekirax-
EMEA/H/C/003839/WS1400/0046

AbbVie Deutschland GmbH & Co. KG, Lead
Rapporteur: Filip Josephson, "Submission of the
final report from study M14-224: An Open-Label
Study to Evaluate the Safety, Efficacy and
Pharmacokinetics of Ombitasvir/ABT-
450/Ritonavir (Ombitasvir/ABT-450/r) and
Dasabuvir Co-administered With or Without
Sofosbuvir (SOF) and Ribavirin (RBV) in Direct-
Acting Antiviral Agent (DAA) Treatment-
Experienced Adults With Genotype 1 Chronic
Hepatitis C Virus (HCV) Infection, listed as a
category 3 study in the RMP."
Opinion adopted on 19.07.2018.

Positive Opinion adopted by consensus on
19.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

WS1401

Genvoya-
EMEA/H/C/004042/WS1401/0047
Stribild-EMEA/H/C/002574/WS1401/0094
Tybost-EMEA/H/C/002572/WS1401/0044

Gilead Sciences Ireland UC, Lead Rapporteur:
Robert James Hemmings, "Update of section 4.6
the SmPC for Tybost, Stribild and Genvoya
based on pharmacokinetics data in pregnancy
from IMPAACT study P1026s (ClinicalTrials.gov
ID NCT00042289); this is an ongoing,
nonrandomized, open-label, parallel-group,
multi-centre phase 4 prospective
study of antiretroviral (ARV) pharmacokinetics
(PK) and safety in HIV-1 infected pregnant
women that includes an arm for EVG/COBI.

Request for supplementary information adopted
with a specific timetable.

The Package Leaflet is updated accordingly.

In addition, the Worksharing applicant (WSA)
took the opportunity to bring the PI in line with
the latest QRD template version 10."

Request for Supplementary Information adopted
on 12.07.2018.

B.5.3. CHMP-PRAC assessed procedures

Dacogen - decitabine -
EMEA/H/C/002221/II/0033, Orphan
Janssen-Cilag International N.V., Rapporteur:

Request for supplementary information adopted
with a specific timetable.

Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of section sections 4.2, 4.8, 5.1 and 5.2 of the SmPC to reflect the results from paediatric study DACOGENAML2004 titled 'Phase 1-2 Safety and Efficacy Study of DACOGEN in sequential administration with Cytarabine in children with relapsed or refractory acute myeloid leukemia', provided as per the requirement of article 46. The RMP version 3.1 (in line with the revision 2 of the RMP template) has also been submitted.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.4 of the SmPC to align the safety warning related to sodium excipient with the Annex to the revised European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. The Package Leaflet is updated in accordance. Moreover, the contact details of the local representative in Slovenia have been updated in the Package Leaflet."

Request for Supplementary Information adopted on 26.07.2018, 31.05.2018.

Erivedge - vismodegib -

EMA/H/C/002602/II/0039/G

Roche Registration GmbH, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "C.I.4 Update of SmPC section 4.4 in order to update the special warnings and precautions for use on the effects of post-natal development and 4.8. in order to include a new adverse event (precocious puberty) observed in children in post marketing.

C.I.11.z To submit the final study report for observational study ML28296 (post approval commitment MEA 18) and reflect the newly available information in the RMP version 13.0. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some editorial changes in the product information." Opinion adopted on 12.07.2018.

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Herzuma - trastuzumab -

EMA/H/C/002575/II/0006

Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted

on 26.07.2018.

**Invokana - canagliflozin -
EMA/H/C/002649/II/0034**

Janssen-Cilag International NV, Rapporteur:
Martina Weise, PRAC Rapporteur: Martin Huber,
"Modification of the indication in section 4.1 as
well as update of sections 4.4, 4.8 and 5.1 of
the SmPC in order to update the safety and
efficacy information on cardiovascular events
following final results from CANVAS Program
(DIA3008 and DIA4003); the Package Leaflet is
updated accordingly.

Study DIA3008 is phase 3 Randomized,
Multicenter, Double-Blind, Parallel, Placebo-
Controlled Study of the Effects of JNJ-28431754
on Cardiovascular Outcomes in Adult Subjects
With Type 2 Diabetes Mellitus

Study DIA4004 is phase 4 Randomized,
Multicenter, Double-Blind, Parallel, Placebo-
Controlled Study of the Effects of Canagliflozin
on Renal Endpoints in Adult Subjects With Type
2 Diabetes Mellitus

The RMP version 7.3 in Rev.2 of the GVP
module V has also been submitted."

Opinion adopted on 26.07.2018.

Request for Supplementary Information adopted
on 31.05.2018, 25.01.2018.

Positive Opinion adopted by consensus on
26.07.2018. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Ocrevus - ocrelizumab -
EMA/H/C/004043/II/0002**

Roche Registration GmbH, Rapporteur: Mark
Ainsworth, PRAC Rapporteur: Julie Williams,
"Update of sections 4.4 and 4.5 of the SmPC in
order to include information on vaccination
based on interim results from study BN29739
listed as a category 3 study in the RMP; this is a
phase IIIb, multicentre, randomised, parallel-
group, open-label study to evaluate the effects
of ocrelizumab on immune response in patients
with relapsing forms of multiple sclerosis. The
Package Leaflet is updated accordingly. The RMP
version 2.0 has also been submitted."

Request for Supplementary Information adopted

Request for supplementary information adopted
with a specific timetable.

on 12.07.2018, 17.05.2018.

Olumiant - baricitinib -

EMA/H/C/004085/II/0006

Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Patrick Batty, "Update of section 4.8 of the SmPC in order to include pneumonia as adverse drug reaction with frequency 'common' following the PRAC recommendation on a relevant signal (EPITT no 18950). The Package Leaflet is updated accordingly. The RMP version 8 has also been agreed as part of this application." Opinion adopted on 26.07.2018.
Request for Supplementary Information adopted on 28.06.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Remicade - infliximab -

EMA/H/C/000240/II/0209

Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the current warning on colon cancer and dysplasia of Section 4.4 of the SmPC based on final report of the OPUS Registry (Prospective, Observational, Non-Interventional, Post-marketing Safety Surveillance Program in Subjects with UC; P04808) as per MEA 121. In addition, the MAH is taking the opportunity to add a warning on screening tests for tuberculosis to align it with current medical practice, add a reminder on the patient alert card in package leaflet and include some editorial changes in line with the QRD template." Opinion adopted on 12.07.2018.
Request for Supplementary Information adopted on 17.05.2018, 11.01.2018.

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Remicade - infliximab -

EMA/H/C/000240/II/0214

Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the RMP (v 17.0) and Annex II-D of the Product Information to remove the Educational material for health care professionals. In addition, the MAH is taking the opportunity to update the package leaflet with some missing warnings and ADRs already reflected in the SmPC, as requested by CHMP, and to introduce some minor QRD related changes." Request for Supplementary Information adopted

Request for supplementary information adopted with a specific timetable.

on 26.07.2018.

Stayveer - bosentan -

EMA/H/C/002644/II/0023

Marklas Nederlands BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, "Update of Annex II.D and the RMP following the submission of the final (13th) study report for the DUO Registry (a Category 3 non-interventional post-approval safety study and additional risk minimisation measure in the bosentan European Risk Management Plan)." Request for Supplementary Information adopted on 14.06.2018.

TAGRISO - osimertinib -

EMA/H/C/004124/II/0024

AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Sabine Straus, "Update of sections 4.2 and 5.2 of the SmPC based on the results from Study D5160C00008, undertaken to determine the pharmacokinetics, safety and tolerability of AZD9291 following a single oral dose to patients with advanced solid tumours and normal hepatic function or mild or moderate hepatic impairment. An updated RMP version 11 was agreed during the procedure." Opinion adopted on 19.07.2018. Request for Supplementary Information adopted on 14.06.2018, 17.05.2018.

Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Tarceva - erlotinib -

EMA/H/C/000618/II/0058

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Update of sections 4.2, and 5.1 of the SmPC based on phase III clinical study MO22162 (CURRENTS) comparing a higher dose of Tarceva (300 mg) over the recommended daily dose (150 mg) in current smokers with locally advanced or metastatic non-small cell lung cancer (NSCLC) in the second-line setting after failure of chemotherapy. The Package Leaflet is updated accordingly. The RMP version 7.0 has been submitted, as part of this application. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in sections 4.4, 4.5, 4.6, 4.7, 4.8 and 5.2 of the SmPC." Request for Supplementary Information adopted on 26.07.2018.

Request for supplementary information adopted with a specific timetable.

Tasigna - nilotinib -

Positive Opinion adopted by consensus on

EMA/H/C/000798/II/0095, Orphan

Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Update of section 4.6 of the SmPC to include the recommendation that women should not breast-feed during Tasigna treatment and for 2 weeks after the last dose. The Package Leaflet has been updated accordingly. Further, the MAH took the opportunity to implement minor editorial changes, corrections and/or additions in the SmPC and Package Leaflet based on data already submitted and assessed previously, including the alignment of section 4 of the Package Leaflet with section 4.8 of the SmPC, the completeness of the list of excipients in SmPC section 6.1 and minor changes to SmPC sections 4.4 and 4.5. Furthermore, the MAH took the opportunity to update the contact details in the list of local representatives in the Package Leaflet."

Opinion adopted on 19.07.2018.

Request for Supplementary Information adopted on 14.06.2018.

19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Tracleer - bosentan -**EMA/H/C/000401/II/0086**

Actelion Registration Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, "Update of Annex II.D and the RMP following the submission of the final (13th) study report for the DUO Registry (a Category 3 non-interventional post-approval safety study and additional risk minimisation measure in the bosentan European Risk Management Plan)."

Request for Supplementary Information adopted on 14.06.2018.

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Tremfya - guselkumab -**EMA/H/C/004271/II/0002/G**

Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski "Update of sections 1, 2, 3, 5.1, 6.4, 6.5, 6.6, of the SmPC with details of a new presentation, based on the results from study CNTO1959PSO3006; this study is an open-label, randomized, study to assess the design features of an investigational prefilled syringe-facilitated injection device (PFS-FID) and the ability of subjects with rheumatoid arthritis or psoriasis to self-administer Placebo with the PFS-FID.

The Package Leaflet and Labelling are updated

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

accordingly. The RMP version 2.0 has also been submitted.

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

Opinion adopted on 12.07.2018.

**Truberzi - eluxadoline -
EMA/H/C/004098/II/0005/G**

Allergan Pharmaceuticals International Ltd,
Rapporteur: Harald Enzmann, PRAC Rapporteur:
Adam Przybylkowski, "C.I.13: Submission of the
final report from study ELX-PH-08 listed as a
category 3 study. This is an in vitro evaluation
study aimed to investigate the effects on
treating primary cultures of cryopreserved
human hepatocytes with eluxadoline on the
expression of cytochrome P450 (CYP) enzymes

Request for supplementary information adopted
with a specific timetable.

C.I.13: Submission of the final report from
study 3030-102-002 listed as a category 3
study. This is a randomised, open label study
aimed to evaluate the effect of eluxadoline as a
potential time dependent inhibitor of CYP3A4
with the substrate midazolam.

C.I.11.a: To update the RMP for Truberzi to
version v2.0 to update the important identified
risk from "SO spasm" to "SO spasm (Sphincter
of Oddi dysfunction, SOD)" and to include
pancreatitis as an important identified risks.
This change has been agreed by the
CHMP/PRAC in the outcome of
EMA/H/C/PSUSA/00010528/201703."
Request for Supplementary Information adopted
on 12.07.2018, 17.05.2018, 08.03.2018.

**Varuby - rolapitant -
EMA/H/C/004196/II/0007/G**

Tesaro UK Limited, Rapporteur: Alexandre
Moreau, PRAC Rapporteur: Adam Przybylkowski,
"- Update of SmPC section 4.5 regarding
interaction with OCT1 substrates following the
submission of the non-clinical study: in vitro
evaluation of the substrate and inhibitor
potential of rolapitant for efflux and update of
transporters (17TESAP2R1).
- Update of SmPC section 4.5 regarding
interaction with UGT substrates following the
submission of the 2 non-clinical studies:
evaluation of potential UGT inhibition by
rolapitant in cryopreserved human hepatocytes

Request for supplementary information adopted
with a specific timetable.

(170594) and evaluation of potential rolapitant metabolism by recombinantly expressed human UGT enzymes (TSRP/REP/07CRD75486/2017)
- Update of SmPC section 4.5 following the submission of the open-label, single-d0se study to assess the effects of rolapitant (oral) on the pharmacokinetics of caffeine (CYP1A2) in healthy subjects (1000-01-001)
The RMP version 1.2 has also been submitted.”
Request for Supplementary Information adopted on 12.07.2018.

Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0034

Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, “Modification of the indication in section 4.1 as well as update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information on cardiovascular events following final results from CANVAS Program (DIA3008 and DIA4003); the Package Leaflet is updated accordingly.

Study DIA3008 is phase 3 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of JNJ-28431754 on Cardiovascular Outcomes in Adult Subjects With Type 2 Diabetes Mellitus.

Study DIA4004 is phase 4 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of Canagliflozin on Renal Endpoints in Adult Subjects With Type 2 Diabetes Mellitus.

The RMP version 7.3 in Rev.2 of the GVP module V has also been submitted.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.”
Opinion adopted on 26.07.2018.
Request for Supplementary Information adopted on 31.05.2018, 25.01.2018.

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**WS1335
Rixathon-
EMEA/H/C/003903/WS1335/0010
Riximyo-
EMEA/H/C/004729/WS1335/0010**

Sandoz GmbH, Lead Rapporteur: Jan Mueller-

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Berghaus, Lead PRAC Rapporteur: Doris Stenver, "Submission of final study reports for studies GP13-302 (a randomized, double-blind, parallel-group safety study with the aim to specifically address a potential safety risk of a switch from treatment with originator rituximab (Mabthera/Rituxan) to treatment with GP2013) and GP13-201 (a 52-week multicenter, randomized, double-blind, parallel-arm, comparative study in patients with active Rheumatoid Arthritis (RA) refractory or intolerant to standard DMARDs and one or up to three anti-TNFs therapies). The RMP (version 3.1) has been updated accordingly."
Opinion adopted on 12.07.2018.
Request for Supplementary Information adopted on 12.04.2018.

WS1396
Kisplyx-EMEA/H/C/004224/WS1396/0011
Lenvima-

EMEA/H/C/003727/WS1396/0015

Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren, Lead PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.5 of the SmPC to include that there is no significant drug-drug interaction risk with midazolam, based on the results of study E7080-A001-109 (A Phase 1 Study to determine DDI of lenvatinib and midazolam, a cytochrome P450 3A4 (CYP3A4) substrate, in subjects with advanced solid tumors). The RMP is updated (version 10.4)"

Request for Supplementary Information adopted on 12.07.2018.

Request for supplementary information adopted with a specific timetable.

WS1406
Abseamed-
EMEA/H/C/000727/WS1406/0070

Binocrit-
EMEA/H/C/000725/WS1406/0070

Epoetin alfa Hexal-
EMEA/H/C/000726/WS1406/0069

Sandoz GmbH, Lead Rapporteur: Alexandre Moreau, Lead PRAC Rapporteur: Ghania Chamouni, "Extension of indication to include the treatment of symptomatic anaemia (haemoglobin concentration of ≤ 10 g/dl) in adults with low- or intermediate-1-risk primary myelodysplastic syndromes (MDS) who have low serum erythropoietin (< 200 mU/ml) for Binocrit, Epoetin alfa Hexal and Abseamed; as a

Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated with safety and efficacy information. The Package Leaflet and the risk management plan (version 17.0) are updated in accordance. In addition, the worksharing applicant (WSA) took the opportunity to align information with the reference medicinal product and with the EC guideline on Excipients, to improve the quality and readability of the translations in the product information and to update the Annex A in line with EMA guideline." Opinion adopted on 26.07.2018.

B.5.4. PRAC assessed procedures

PRAC Led

Bosulif - bosutinib -

EMA/H/C/002373/II/0030

Pfizer Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "Submission of an updated RMP version 4.3 in line with changes requested by the CHMP following variation II/25/G in fulfilment of PAM (REC 014). In addition, the MAH took the opportunity to extend due date of SOB (Specific Obligation). Annex II has been updated accordingly." Request for Supplementary Information adopted on 26.07.2018.

Request for supplementary information adopted with a specific timetable.

PRAC Led

Inflectra - infliximab -

EMA/H/C/002778/II/0060

Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "To update the RMP for Inflectra to version 8.0 to introduce the new RMP template, update some milestones of the Pharmacovigilance plan and delete some safety concerns from the educational material to Health Care Professionals." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 17.05.2018.

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led

Lucentis - ranibizumab -

EMA/H/C/000715/II/0070/G

Novartis Europharm Limited, Rapporteur:

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "1. Type II- C.I.13: Submission of the final report from study LUMINOUS study (CRFB002A2406), an observational, multicenter study to assess the long term safety and effectiveness of ranibizumab in routine clinical practice, in fulfilment of the post-authorisation measures MEA 036, MEA 048 and MEA 054. Consequentially, the RMP has been updated to reflect these changes.

2. Type II-C.I.11: Submission of an updated RMP version 17.0 (RMP template Rev. 2) according to GVP Module V to include changes not consequential to LUMINOUS study. In addition, the MAH is proposing the removal of the use of educational materials and targeted follow-up checklists listed in Annex II-D of the Product Information."

Opinion adopted on 12.07.2018.
Request for Supplementary Information adopted on 14.06.2018, 12.04.2018.

recommendation.

PRAC Led
**MabThera - rituximab -
EMA/H/C/000165/II/0144**

Request for supplementary information adopted with a specific timetable.

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Update the RMP to remove the additional risk minimization measure of Educational Outreaches for the important identified risk of Infusion Related Reactions and Acute Infusion Related Reactions (IRR). Therefore, the RMP has been updated accordingly to version 16.0."

Request for Supplementary Information adopted on 12.07.2018, 12.04.2018.

PRAC Led
**Neulasta - pegfilgrastim -
EMA/H/C/000420/II/0099**

Request for supplementary information adopted with a specific timetable.

Amgen Europe B.V., Rapporteur: Robert James Hemmings, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Robert James Hemmings, "Submission of an updated RMP version 5.1 in order to add study 20160176, a retrospective cohort study of female breast cancer patients aged 66 years and over selected from the US SEER-Medicare database to estimate the risk of acute myeloid leukemia/myelodysplastic syndrome for breast cancer patients, as a new Pharmacovigilance activity (category 3). In

addition the MAH submitted the draft protocol for study 20160176.”
Request for Supplementary Information adopted on 12.07.2018.

PRAC Led
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0078
Pfizer Limited, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, “To update the RMP (version 8.1). The update includes changes approved in procedure II-49 and II-73. The RMP is also being revised to align with current EU RMP template, as per GVP Module V Rev. 2 including proposals for the removal of some Important Potential Risks: Guillain-Barré syndrome, Purpura, Vasculitis, Acute disseminated encephalomyelitis, Brachial neuritis, Anaphylaxis, Administration via the intravascular, intradermal or subcutaneous route, and Administration to patients with thrombocytopenia or any coagulation disorder with a risk of haemorrhage. The MAH also proposes removal of the missing information: Use in patients with chronic diseases and Use during lactation”
Opinion adopted on 12.07.2018.

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led
Remsima - infliximab - EMEA/H/C/002576/II/0051
Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, “To update the RMP for Remsima to version 8.0 to introduce the new RMP template, update some milestones of the Pharmacovigilance plan and delete some safety concerns form the educational material to HCP.”
Opinion adopted on 12.07.2018.
Request for Supplementary Information adopted on 17.05.2018.

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led
TAGRISO - osimertinib - EMEA/H/C/004124/II/0023
AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Sabine Straus, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP version 9 in order to remove the category 3 PASS Study

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

D5160C00022 (ASTRIS) from the Pharmacovigilance plan.”
Opinion adopted on 12.07.2018.
Request for Supplementary Information adopted on 14.06.2018, 17.05.2018.

PRAC Led
Tamiflu - oseltamivir - EMEA/H/C/000402/II/0133
Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, PRAC-CHMP liaison: Outi Mäki-Ikola, “Update of the RMP (v.16) to discontinue the guided questionnaires (GQ) for neurological and psychiatric adverse events (NPAE), hepatobiliary disorders and hypothermia.”
Opinion adopted on 12.07.2018.

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led
Tasigna - nilotinib - EMEA/H/C/000798/II/0092, Orphan
Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, “Submission of an updated RMP version 21.1 in order to delete the important identified risk 'Myelosuppression', to implement changes in the definition of the identified risks 'Hepatotoxicity' and 'Fluid retention', and to reflect the discontinuation of the educational material as additional risk minimisation measure. Annex II has been updated accordingly.”
Opinion adopted on 12.07.2018.
Request for Supplementary Information adopted on 12.04.2018.

Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led
Volibris - ambrisentan - EMEA/H/C/000839/II/0055
Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Concepcion Prieto Yerro, “C.I.11: Submission of an updated RMP (version 7.6) in order to remove the provision of the educational materials for healthcare professionals given the availability of the SmPC and the experience of using ambrisentan as requested by the PRAC in the PSUR procedure PSUSA/00000129/201706. The Annex II of the product information is updated accordingly. In addition, the MAH also took the opportunity to update the Annex II as requested by the Portuguese Agency following

Request for supplementary information adopted with a specific timetable.

the approval of the last update to the educational materials (risks of decreases in haemoglobin or haematocrit, renal impairment, peripheral oedema and fluid retention, and hypersensitivity reaction) and to correct typographical errors in the Annex II of the product information.”

Request for Supplementary Information adopted on 12.07.2018.

PRAC Led

Zavesca - miglustat -

EMA/H/C/000435/II/0062/G, Orphan

Actelion Registration Limited, Rapporteur:

Kristina Dunder, PRAC Rapporteur: Ulla Wändel

Liminga, PRAC-CHMP liaison: Kristina Dunder,

“C.I.13: Submission of the final report of the

9th NPC registry report including an RMP update

within the context of variation

EMA/H/C/000435/II/0056

C.I.11: Submission of an updated RMP version

14 in order to remove the important identified

risks: reduced platelet counts and weight loss

based on the current ongoing PSUR procedure

for miglustat

(EMA/H/C/PSUSA/00002062/201710)”

Opinion adopted on 12.07.2018.

Positive Opinion adopted by consensus on

12.07.2018. The Icelandic and Norwegian CHMP

Members were in agreement with the CHMP

recommendation.

PRAC Led

WS1370

Zoledronic acid Mylan-

EMA/H/C/002482/WS1370/0015

Mylan S.A.S, Generic, Generic of Zometa, Lead

PRAC Rapporteur: Doris Stenver, PRAC-CHMP

liaison: Sinan B. Sarac, “The RMP has been

updated to the latest template. In addition the

MAH has included “and other anatomical sites”

in addition to “Osteonecrosis of the jaw” as an

important identified risk, to be in line with CHMP

assessment report for zoledronic acid,

procedure number

EMA/H/C/PSUSA/00003149/201608, dated 21

April 2017.”

Request for Supplementary Information adopted

on 10.07.2018.

Request for supplementary information adopted

with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

Zalmoxis - allogeneic T cells genetically modified with a retroviral vector encoding

Positive Opinion adopted by consensus on

26.07.2018. The Icelandic and Norwegian CHMP

for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - EMEA/H/C/002801/II/0009/G, Orphan, ATMP

MolMed S.p.A, Rapporteur: Johannes Hendrikus Ovelgonne, CHMP Coordinator: Paula Boudewina van Hennik
Opinion adopted on 26.07.2018.
Request for Supplementary Information adopted on 20.04.2018.

Members were in agreement with the CHMP recommendation.

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

WS1353/G

Hexacima-

EMEA/H/C/002702/WS1353/0079/G

Hexaxim-

EMEA/H/W/002495/WS1353/0084/G

Hexyon-

EMEA/H/C/002796/WS1353/0083/G

Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

Request for Supplementary Information adopted on 19.07.2018, 17.05.2018.

Request for supplementary information adopted with a specific timetable.

WS1365/G

Ambirix-

EMEA/H/C/000426/WS1365/0091/G

Fendrix-

EMEA/H/C/000550/WS1365/0063/G

Infanrix hexa-

EMEA/H/C/000296/WS1365/0240/G

Twinrix Adult-

EMEA/H/C/000112/WS1365/0125/G

Twinrix Paediatric-

EMEA/H/C/000129/WS1365/0126/G

GlaxoSmithKline Biologicals, Lead Rapporteur: Bart Van der Schueren
Opinion adopted on 05.07.2018.

Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1377/G

Positive Opinion adopted by consensus on

<p>Infanrix hexa- EMA/H/C/000296/WS1377/0241/G GlaxoSmithKline Biologicals SA, Lead Rapporteur: Bart Van der Schueren</p>	<p>19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>WS1385 Izba-EMA/H/C/002738/WS1385/0009 Travatan- EMA/H/C/000390/WS1385/0058 Novartis Europharm Limited, Lead Rapporteur: Concepcion Prieto Yerro, "To provide an updated Environmental Risk Assessment (ERA) dossier for travoprost-containing products Travatan and Izba, pursuant to the post-authorisation recommendation provided by the Agency in the framework of the following procedures: · Travatan extension of indication - Procedure No. EMA/H/C/000390/II/0046 · Izba initial MAA - Procedure No. EMA/H/C/002738/0000 Based on the updated ERA results, the MAH also proposes to update sections 5.3 Preclinical safety data in both Izba and Travatan SmPC as well as section 6.6 Special precautions for disposal in Travatan SmPC." Request for Supplementary Information adopted on 07.06.2018.</p>	<p>Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>WS1387 Infanrix hexa- EMA/H/C/000296/WS1387/0242 GlaxoSmithKline Biologicals SA, Lead Rapporteur: Bart Van der Schueren</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p>WS1405 Fiasp-EMA/H/C/004046/WS1405/0006 NovoMix- EMA/H/C/000308/WS1405/0094 NovoRapid- EMA/H/C/000258/WS1405/0122 Ryzodeg- EMA/H/C/002499/WS1405/0027 Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder Opinion adopted on 19.07.2018.</p>	<p>Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>WS1408 Enbrel-EMA/H/C/000262/WS1408/0221 LIFMIOR- EMA/H/C/004167/WS1408/0016 Pfizer Limited, Lead Rapporteur: Robert James Hemmings</p>	<p>Positive Opinion adopted by consensus on 26.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>

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

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

sodium oxybate - EMEA/H/C/004962

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

dapagliflozin / saxagliptin / metformin

hydrochloride - EMEA/H/C/004910

, - to improve glycaemic control when metformin with or without sulphonylurea (SU) does not provide adequate glycaemic control and where simultaneous addition of dapagliflozin and saxagliptin is considered necessary - to improve glycaemic control when metformin with or without sulphonylurea (SU) and either dapagliflozin or saxagliptin does not provide adequate glycaemic control - when already being treated with dapagliflozin and saxagliptin and metformin.

deferasirox - EMEA/H/C/005014

, treatment of chronic iron overload, Generic, Generic of EXJADE

ravulizumab - EMEA/H/C/004954, Orphan

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

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

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

ELOCTA - efmoroctocog alfa - EMA/H/C/003964/X/0021

Swedish Orphan Biovitrum AB (publ),
Rapporteur: Jan Mueller-Berghaus, "Extension application to introduce new strength of 4000 IU, 5000 IU and 6000 IU primarily enabling prophylactic dosing in adult patients."
List of Questions adopted on 31.05.2018.

apalutamide - EMA/H/C/004452

, treatment of non metastatic castration resistant prostate cancer (NM CRPC)
List of Questions adopted on 28.06.2018.

romosozumab - EMA/H/C/004465

, Treatment of osteoporosis
List of Questions adopted on 26.04.2018.

pegfilgrastim - EMA/H/C/004915

, treatment of neutropenia
List of Questions adopted on 22.03.2018.

macimorelin - EMA/H/C/004660

, Diagnosis of Adult growth hormone deficiency (AGHD)
List of Questions adopted on 22.03.2018.

trastuzumab - EMA/H/C/004916

, treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)
List of Questions adopted on 22.03.2018.

Orkambi - lumacaftor / ivacaftor - EMA/H/C/003954/X/0034/G

Vertex Pharmaceuticals (Europe) Ltd.,
Rapporteur: Nithyanandan Nagercoil, Co-
Rapporteur: Daniela Melchiorri, PRAC
Rapporteur: Almath Spooner, "1. Extension application to introduce a new pharmaceutical form (granules) in 2 strengths (100/125 mg and 150/188 mg) for paediatric use (2 to 5 years). An updated RMP (v 4.0) has been submitted.
2. Type II (C.I.4): Update of sections 4.1, 4.2, 4.5, 4.8 and 5.3 of the SmPC of the tablets formulation to bring it in line with the proposed paediatric 2-5 years old extension application."
List of Questions adopted on 28.06.2018.

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

clofarabine - EMEA/H/C/000613/S/0059

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

**Granupas - para-aminosalicylic acid -
EMEA/H/C/002709/R/0026, Orphan**
Eurocept International B.V., Rapporteur: Greg
Markey, Co-Rapporteur: Alexandre Moreau,
PRAC Rapporteur: Patrick Batty

**Jardiance - empagliflozin -
EMEA/H/C/002677/R/0040**
Boehringer Ingelheim International GmbH,
Rapporteur: Johann Lodewijk Hillege, Co-
Rapporteur: Bart Van der Schueren, PRAC
Rapporteur: Eva A. Segovia

**Mepact - mifamurtide -
EMEA/H/C/000802/R/0047, Orphan**
Takeda France SAS, Rapporteur: Johann
Lodewijk Hillege, Co-Rapporteur: Alexandre
Moreau, PRAC Rapporteur: Sabine Straus

**OCALI VA - obeticholic acid -
EMEA/H/C/004093/R/0009, Orphan**
Intercept Pharma Ltd, Rapporteur: Jorge
Camarero Jiménez, PRAC Rapporteur: Menno
van der Elst

**Pregabalin Pfizer - pregabalin -
EMEA/H/C/003880/R/0025**
Pfizer Limited, Rapporteur: Johann Lodewijk
Hillege, Co-Rapporteur: Bruno Sepodes, PRAC
Rapporteur: Sabine Straus

**Ulnar Breezhaler - indacaterol /
glycopyrronium -
EMEA/H/C/003875/R/0028**
Novartis Europharm Limited, Rapporteur: Mark
Ainsworth, PRAC Rapporteur: Anette Kirstine
Stark

**Vokanamet - canagliflozin / metformin -
EMEA/H/C/002656/R/0039**
Janssen-Cilag International NV, Rapporteur:
Martina Weise, Co-Rapporteur: Svein Rune

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

Imnovid - pomalidomide -

EMA/H/C/002682/II/0031/G, Orphan

Celgene Europe Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Patrick Batty, "Extension of indication to include treatment with Imnovid in combination with bortezomib and dexamethasone of adult patients with multiple myeloma who have received at least one prior treatment regimen including lenalidomide; as a result, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.

As a consequence the MAH submitted a request to add 14-capsule pack sizes for the 1 mg, 2 mg, 3 mg and 4 mg Imnovid strengths to support the proposed posology and pomalidomide dose modification. The SmPC, Labelling and Package leaflet are updated in accordance.

Update of section 5.1 of the SmPC in order to update the information on pomalidomide mechanism of action based on literature data."

Keytruda - pembrolizumab -

EMA/H/C/003820/II/0057

Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus, "Extension of Indication to include 1st line treatment of locally advanced or metastatic non-small cell lung cancer tumours expressing PD-L1 with a $\geq 1\%$ tumour proportion score (TPS), based on data from study KEYNOTE-042; an international, randomized, open-label Phase 3 study investigating KEYTRUDA monotherapy compared to standard of care platinum-based chemotherapy in patients with locally advanced or metastatic PD-L1 positive (TPS $\geq 1\%$) NSCLC, and on supportive data from the final planned analysis of KEYNOTE-024; a Phase 3

randomized open-label study of KEYTRUDA monotherapy compared to platinum-based chemotherapy in metastatic NSCLC with PD-L1 TPS \geq 50%. As a result, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated. An updated RMP version 18.1 was provided as part of the application."

Praluent - alicrocumab -

EMA/H/C/003882/II/0042

sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of Indication to include the prevention of cardiovascular events in patients with established atherosclerotic cardiovascular disease for Praluent based on the final study report of EFC11570; as a consequence, sections, 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and RMP v4, have been updated accordingly."

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

Alprolix - eftrenonacog alfa -

EMA/H/C/004142/II/0020, Orphan

Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop

Bortezomib Accord - bortezomib -

EMA/H/C/003984/II/0014

Accord Healthcare Limited, Generic, Generic of VELCADE, Rapporteur: Milena Stain

Bortezomib Hospira - bortezomib -

EMA/H/C/004207/II/0008

Hospira UK Limited, Generic, Generic of VELCADE, Rapporteur: Milena Stain

Dupixent - dupilumab -

EMA/H/C/004390/II/0009/G

sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

Fabrazyme - agalsidase beta -

EMA/H/C/000370/II/0106

Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege

Kentera - oxybutynin -**EMA/H/C/000532/II/0047**

Nicobrand Limited, Rapporteur: Bart Van der Schueren

Kyntheum - brodalumab -**EMA/H/C/003959/II/0004/G**

LEO Pharma A/S, Rapporteur: Johann Lodewijk Hillege

Lemtrada - alemtuzumab -**EMA/H/C/003718/II/0025/G**

Genzyme Therapeutics Ltd, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth

Lonquex - lipegfilgrastim -**EMA/H/C/002556/II/0041/G**

Sicor Biotech UAB, Rapporteur: Greg Markey

MULTAQ - dronedarone -**EMA/H/C/001043/II/0041**

sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege

Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine -**EMA/H/C/002226/II/0082**

Pfizer Limited, Rapporteur: Greg Markey

NovoSeven - eptacog alfa (activated) -**EMA/H/C/000074/II/0106**

Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik

Ocrevus - ocrelizumab -**EMA/H/C/004043/II/0004**

Roche Registration GmbH, Rapporteur: Mark Ainsworth

Privigen - human normal immunoglobulin -**EMA/H/C/000831/II/0136/G**

CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Reagila - cariprazine -**EMA/H/C/002770/II/0008**

Gedeon Richter Plc., Rapporteur: Kristina Dunder

Revolade - eltrombopag / eltrombopag olamine - EMA/H/C/001110/II/0052/G

Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro

Shingrix - herpes zoster vaccine (recombinant, adjuvanted) -

EMA/H/C/004336/II/0007

GlaxoSmithKline Biologicals SA, Rapporteur:
Bart Van der Schueren

Somavert - pegvisomant -

EMA/H/C/000409/II/0086/G

Pfizer Limited, Rapporteur: Joseph Emmerich

Tamiflu - oseltamivir -

EMA/H/C/000402/II/0135

Roche Registration GmbH, Rapporteur: Outi
Mäki-Ikola

WS1452

Rixathon-

EMA/H/C/003903/WS1452/0013

Riximyo-

EMA/H/C/004729/WS1452/0013

Sandoz GmbH, Lead Rapporteur: Jan Mueller-
Berghaus

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

Alecensa - alectinib -

EMA/H/C/004164/II/0016

Roche Registration GmbH, Rapporteur: Filip
Josephson, "Submission of the final study
analysis on secondary ALK-mutation
positive/negative samples and correlation with
clinical outcome in fulfilment of a CHMP
recommendation for alectinib, adopted during
the initial Marketing Authorization. The
application is based on an additional analysis
generated from two studies (NP28673 and
NP28761)."

Atripla - efavirenz / emtricitabine /

tenofovir disoproxil -

EMA/H/C/000797/II/0130

Bristol-Myers Squibb and Gilead Sciences Ltd.,
Rapporteur: Martina Weise, "Update of sections
4.3 and 4.5 of the SmPC in order to include
drug-drug interaction data between efavirenz
(EFV) and grazoprevir/elbasvir based on a
review of the antiviral product Zepatier.

The Marketing authorisation holder (MAH) has
taken the opportunity to introduce changes to
the sodium wording in Section 4.4 of the SmPC
and to align the text in Section 4.6 (Fertility,
pregnancy and lactation) for Atripla with the

currently approved wording in the Eviplera SmPC.

The Package Leaflet (PIL) has been updated accordingly.

In addition, the MAH has also taken the opportunity to implement some minor linguistic amendments (MLAs) to the translations of the product information annexes for the following languages: DE, FI, FR, IT, NL and NO.”

**Baraclude - entecavir -
EMA/H/C/000623/II/0059**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, “Update of section 5.1 of the SmPC in order to include information regarding the newly detected resistance information showing reduced susceptibility to entecavir for the rtA 181C substitution in combination with LVDr substitutions, rTL 180M + rtM204V. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10. The MAH also took the opportunity to add the sodium concentration for Baraclude 0.05 mg/ml oral solution in section 2 of the SmPC and section 2 of the PL according to the guideline on ‘excipients in the labelling and package leaflet of medicinal products for human use’.”

**Brilique - ticagrelor -
EMA/H/C/001241/II/0041**

AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.2 and 4.4 of the SmPC in order to clarify the posology in patients having an acute coronary syndromes (ACS) event, to update the warning related to bradyarrhythmia based on already assessed studies and post-marketed use (clinical trials PLATO (D5130C05262), PEGASUS (D5132C00001), SOCRATES (D5134C00001) and EUCLID (D5135C00001)) and to introduce “stroke” as a possible even in case of premature discontinuation. Furthermore the MAH took the opportunity to update the PI in relation to sodium content in line with QRD and to update the list of local representatives in the Package Leaflet.”

**Coagadex - human coagulation factor X -
EMA/H/C/003855/II/0009, Orphan**

Bio Products Laboratory Limited, Rapporteur: Andrea Laslop, "Update of section 5.2 of the SmPC in order to include data on long-term use based on final results from the study Ten05, a multicentre, retrospective data collection study on the use of BPL's high purity factor X in the treatment of patients with hereditary factor X deficiency on a compassionate use basis. In addition the Marketing authorisation holder (MAH) took the opportunity to update the number of patients treated with Coagadex in section 4.8 of the SmPC based on studies Ten01, Ten02 and Ten03 as well as to include some editorial changes in section 4.2 of the SmPC. Furthermore, the information on perioperative management in the Package Leaflet has been aligned with information in the SmPC."

**ILARIS - canakinumab -
EMA/H/C/001109/II/0060**

Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus, "Update of section 5.1 of the SmPC based on the final clinical study report (CSR) from Study ACZ885G2306 (β -SPECIFIC 4 Patients: Study of Paediatric efficacy and safety with first-line use of canakinumab: An open-label canakinumab (ACZ885) dose reduction or dose interval prolongation efficacy and safety study in patients with Systemic Juvenile Idiopathic Arthritis (SJIA)). The submission of the final CSR addresses the post-authorisation measure MEA 036.3 (PAES) and the requirements of article 46 of the paediatric regulation."

**Isentress - raltegravir -
EMA/H/C/000860/II/0078/G**

Merck Sharp & Dohme B.V., Rapporteur: Greg Markey, "Submission of the final reports from 3 in vitro studies evaluating the inhibitory effect of raltegravir at higher concentrations on OATP1B3, OCT1, OCT2, MATE1 and MATE2-K transporters and CYP2B6, CYP2D6, UGT2B7 enzyme activities, and a final CSR to assess the drug-drug interaction (DDI) potential of raltegravir at a 1,200 mg once daily clinical dose, according to the request from the CHMP following the assessment of X/59."

**Keytruda - pembrolizumab -
EMA/H/C/003820/II/0054**

Merck Sharp & Dohme B.V., Rapporteur:
Daniela Melchiorri, "Update of section 5.1 of the SmPC based on the final clinical study report (CSR) for KEYNOTE-045 (KN045); a phase III randomized clinical trial of pembrolizumab (MK-3475) versus paclitaxel, docetaxel or vinflunine in subjects with recurrent or progressive metastatic urothelial cancer. The submission addresses the post-authorisation measure 'ANX 020' and Annex IID has been updated accordingly."

**Kyprolis - carfilzomib -
EMA/H/C/003790/II/0030, Orphan**

Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of section 4.4 of the SmPC in order to include a warning of the increased risk of cardiac failure in Asian patients treated with carfilzomib based on postmarketing experience and 3 phase 3, randomized-controlled studies (CLARION-Study 2011-003; ENDEAVOR-Study 20130398 and A.R.R.O.W.-Study 20140355). In addition, the Marketing authorisation holder (MAH) took the opportunity to propose few minor typographical changes to SmPC."

**Latuda - lurasidone -
EMA/H/C/002713/II/0021**

Aziende Chimiche Riunite Angelini Francesco S.p.A., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC to add new paediatric data available in children and adolescent patients (10-17 years of age) with bipolar I disorder, upon request by CHMP following the assessment of the paediatric study D1050326 submitted according to Art. 46 procedure (no. EMA/H/C/002713/P46/008)."

**LUTATHERA - lutetium (177Lu)
oxodotreotide -**

EMA/H/C/004123/II/0005, Orphan

Advanced Accelerator Applications, Rapporteur: Robert James Hemmings, "Update of the SmPC section 5.1 to include information on the quality of life based on analysis of Netter-I Quality of Life data."

**Mircera - methoxy polyethylene glycol-
epoetin beta - EMA/H/C/000739/II/0067**

Roche Registration GmbH, Rapporteur:

Concepcion Prieto Yerro, "Update of sections 4.2., 5.1. and 5.2. of the SmPC in order to update the paediatric information based on results from phase II dose finding study NH 19707 (Dolphin): An Open-Label, Multi-Center, Multiple Dose Study to Determine the Optimum Starting Dose of Intravenous MIRCERA for Maintenance Treatment of Anemia in Pediatric Patients with Chronic Kidney Disease on Hemodialysis; listed as a category 3 study in the RMP. The Package Leaflet is updated accordingly."

Otezla - apremilast -

EMA/H/C/003746/II/0021

Celgene Europe Limited, Rapporteur: Peter Kiely, "Update of sections 4.2 and 5.1 of Otezla SmPC to include data (up to 5 years of treatment) from the following studies (CC-10004-PSA-002, -003, -004, -005 and CC-10004-PSOR-008, - 009)) listed as a category 3 study in the RMP (MEA 002)."

Praluent - alirocumab -

EMA/H/C/003882/II/0041

sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the final clinical study report of study R727-CL-1119 (study title: A Randomized, Double-Blind, Double-Dummy, Active-Controlled Study to Evaluate the Efficacy and Safety of REGN727/SAR236553 in Patients with Primary Hypercholesterolemia Who Are Intolerant to Statins), as per MEA011."

Skilarence - dimethyl fumarate -

EMA/H/C/002157/II/0008/G

Almirall S.A, Rapporteur: Robert James Hemmings, "Submission of the final report from study AML/27. This is an in vitro study aimed to assess the potential of dimethyl fumarate to inhibit human hepatic cytochrome P450 (CYP) enzymes.

Submission of the final report from study AML/28. This is an in vitro study aimed to assess the potential interaction of dimethyl fumarate with p-glycoprotein (P-gp).

Submission of the final report from study Almirall-15-05May2017. This is an in vitro study aimed to assess the interaction of dimethyl fumarate with human BCRP efflux (ABC)

transporters.”

Translarna - ataluren -

EMA/H/C/002720/II/0045, Orphan

PTC Therapeutics International Limited,
Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.4 and 4.5 of the SmPC in order to include information on Drug-Drug Interaction with sensitive probe substrate of organic anion transporting polypeptide 1B3 (OATP1B3) based on study PTC124-GD-042-HV (MEA016). The package leaflet is updated accordingly.”

Translarna - ataluren -

EMA/H/C/002720/II/0046, Orphan

PTC Therapeutics International Limited,
Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update information on patients with moderate to severe renal impairment based on results from study PTC124-GD-032-HV (MEA010). In addition the MAH took the opportunity to amend section 5.2 to propose correction of the biotransformation statement. The Package leaflet is updated accordingly.”

VELCADE - bortezomib -

EMA/H/C/000539/II/0090

Janssen-Cilag International NV, Rapporteur:
Daniela Melchiorri, “Update of section 5.1 of the SmPC to update the information based on final long-term follow-up and overall survival data for LYM-3002, a Randomized, Open-label, Multicenter Phase 3 Study of the Combination of Rituximab, Cyclophosphamide, Doxorubicin, VELCADE, and Prednisone (VcR-CAP) or Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP) in Patients With Newly Diagnosed Mantle Cell Lymphoma who are not Eligible for a Bone Marrow Transplant.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of Local representatives in the Package Leaflet.”

Venclyxto - venetoclax -

EMA/H/C/004106/II/0016, Orphan

AbbVie Deutschland GmbH & Co. KG,
Rapporteur: Filip Josephson, “Submission of the report from study M13-982 listed as a category 3 study in the RMP. This is a Phase 2 Open-Label Study of the Efficacy of ABT199 (GDC-0199) in Subjects with Relapsed/Refractory or

Previously Untreated Chronic Lymphocytic Leukemia Harboring the 17p Deletion.”

**Xadago - safinamide -
EMA/H/C/002396/II/0027**

Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.4 and 4.5 of the SmPC in order to implement information regarding interaction of safinamide and rosuvastatin, following results from study CRO-PK-17-318. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Ireland in the Package Leaflet and to include editorial changes in the English, German and Spanish product information.”

**XALKORI - crizotinib -
EMA/H/C/002489/II/0055**

Pfizer Limited, Rapporteur: Alexandre Moreau, “Update of section 4.2 of the SmPC in order to provide greater clarity in the crizotinib dosing regimen modification recommendations for patients who receive a reduced dose of crizotinib, either because of pre-existing moderate or severe hepatic impairment or severe renal impairment or because of a previous dose reduction while on treatment with crizotinib. The Package Leaflet has been updated accordingly.”

**XALKORI - crizotinib -
EMA/H/C/002489/II/0057**

Pfizer Limited, Rapporteur: Alexandre Moreau, “Submission of a number of analysis pertaining to the mechanisms of tumor resistance to crizotinib due to secondary ROS1 kinase domain mutations in patients with ROS1-positive non-small cell lung cancer (NSCLC).”

**XALKORI - crizotinib -
EMA/H/C/002489/II/0058**

Pfizer Limited, Rapporteur: Alexandre Moreau, “Submission of the final study report for study A8081038, a multinational active safety surveillance study of crizotinib in Europe and the United States.”

**Xultophy - insulin degludec / liraglutide -
EMA/H/C/002647/II/0026**

Novo Nordisk A/S, Rapporteur: Kristina Dunder, “Update of section 5.1 of the SmPC in order to

reflect data for use of Xulthopy in combination with sodium glucose co-transporter 2 inhibitors (SGLT2i) in patients inadequately controlled on SGLT2i ± other oral anti-diabetic drug.

The update is based on data from the clinical trial: NN9068-4229: "A Clinical Trial Comparing Glycaemic Control and Safety of Insulin Degludec/Liraglutide (IDegLira) versus Insulin Glargine (IGlar) as Add-on Therapy to SGLT2i in Subjects with Type 2 Diabetes Mellitus"."

**Zinforo - ceftaroline fosamil -
EMA/H/C/002252/II/0038**

Pfizer Ireland Pharmaceuticals, Rapporteur: Greg Markey, "Update of section 4.2 of the SmPC to amend the recommended duration of ceftaroline fosamil intravenous (IV) infusion for standard dose regimens in adults and paediatrics to a range of 5 to 60 minutes from the currently recommended infusion duration of 1 hour. The PIL is updated accordingly. In addition the MAH has also taken the opportunity to reformat section 4.2 of the SmPC Posology and method of administration and to incorporate minor editorial updates to sections 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC."

Zostavax - shingles (herpes zoster) vaccine (live) - EMA/H/C/000674/II/0117

MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.5 and 5.1 of the SmPC to include that Zostavax can be given concomitantly with pneumococcal vaccine and to reflect the results of an observational post-marketing study comparing the effectiveness of Zostavax when co-administrated with a 23-valent pneumococcal polysaccharide vaccine (Bruxvoort K et al. 2018). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet."

WS1411/G

Aluvia-

EMA/H/W/000764/WS1411/0105/G

Kaletra-

EMA/H/C/000368/WS1411/0171/G

Norvir-

EMA/H/C/000127/WS1411/0150/G

AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Joseph Emmerich, "Update of"

section 4.5 of the SmPC in order to update the safety information on the interaction with ibrutinib based on the company core data sheets. The Package Leaflet is updated accordingly.

Update of section 4.5 of the SmPC in order to update the safety information of ritonavir, lopinavir/ritonavir on the interaction with levothyroxine based on the PRAC signal final assessment report EMA/101535/2018 possibly leading to decreased levothyroxine efficacy and hypothyroidis."

WS1417/G

Invega-

EMA/H/C/000746/WS1417/0060/G

Trevicta-

EMA/H/C/004066/WS1417/0013/G

Xeplion-

EMA/H/C/002105/WS1417/0039/G

Janssen-Cilag International NV, Lead Rapporteur: Kristina Dunder, "Update of sections 4.4 and 4.5 of the SmPC in order to add information regarding concomitant use with psychostimulants (in line with the CMDh recommendations for risperidone) and of section 4.8 of the SmPC to add catatonia as a new side-effect categorised as 'Rare'. The Package Leaflet is updated accordingly."

WS1422

CONTROLOC Control-

EMA/H/C/001097/WS1422/0030

PANTOLOC Control-

EMA/H/C/001100/WS1422/0034

PANTOZOL Control-

EMA/H/C/001013/WS1422/0032

SOMAC Control-

EMA/H/C/001098/WS1422/0031

Takeda GmbH, Lead Rapporteur: Greg Markey, "Update of section 5.3 of the SmPC in order to update the safety information based on the final results of study 14GR325 "A pre- and postnatal developmental toxicity study of pantoprazole sodium (PF-05208751) by oral gavage in rats focused on postnatal evaluation of bone development" as required by the PRAC Recommendation of EMA/H/C/PSUSA/00002285/201708."

WS1429

Descovy-**EMA/H/C/004094/WS1429/0032****Genvoya-****EMA/H/C/004042/WS1429/0048****Odefsey-****EMA/H/C/004156/WS1429/0033**

Gilead Sciences Ireland UC, Lead Rapporteur:
Robert James Hemmings, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with data in patients on chronic haemodialysis from the Study GS-US-292-1825; this is a Phase 3b Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of E/C/F/TAF Fixed Dose Combination (FDC) in HIV-1 Infected Subjects on Chronic Hemodialysis.

The Package Leaflet is updated accordingly.

In addition, the Worksharing applicant (WSA) took the opportunity to introduce changes to the lactose wording for Genvoya and Odefsey and an administrative correction to the Genvoya Patient information leaflet (PIL) in order to add "lurasidone" to the second list of contra-indicated drugs appearing in the PIL.

The WSA has also taken the opportunity to introduce some minor administrative amendments throughout the product information for all three products as well as to implement some minor linguistic amendments (MLAs) to the translations of the respective product information annexes:

- Genvoya: DE, ES, FI, HR, HU, IS, IT, NO, SL and SV languages
- Descovy: DA, DE, ES, FR, HR, NL, NO, PT and SL languages
- Odefsey: CS, DE, LV, MT, NL, PL, SL and SV languages."

WS1433**Clopidogrel Zentiva-****EMA/H/C/000975/WS1433/0061****Clopidogrel/Acetylsalicylic acid Zentiva-****EMA/H/C/001144/WS1433/0051****DuoPlavin-****EMA/H/C/001143/WS1433/0050****Iscover-****EMA/H/C/000175/WS1433/0133****Plavix-EMA/H/C/000174/WS1433/0130**

Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, "In response to PRAC recommendation for the signal of insulin autoimmune syndrome (EPITT ref 19155), update of section 4.8 of the SmPC to the new adverse reaction 'insulin autoimmune syndrome'. The Package Leaflet are updated accordingly."

WS1444

Kispilyx-EMEA/H/C/004224/WS1444/0012

Lenvima-

EMEA/H/C/003727/WS1444/0016

Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren, "Update of Sections 4.4 and 4.8 of the SmPC to add pneumothorax and nephrotic syndrome. The PIL is updated accordingly."

WS1449

Relvar Ellipta-

EMEA/H/C/002673/WS1449/0038

Revinty Ellipta-

EMEA/H/C/002745/WS1449/0035

Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, "Update of section 4.8 of the SmPC in order to add hyperglycaemia as an adverse reaction based on a cumulative review of hyperglycaemia/new onset diabetes associated with fluticasone/vilanterol (FF/VI); the Package Leaflet is updated accordingly.

In addition, the Worksharing applicant (WSA) took the opportunity to update the Package Leaflet with a clarification on the adverse event "blurred vision" already included in the SmPC (WS-1224)."

WS1459

Clopidogrel Zentiva-

EMEA/H/C/000975/WS1459/0062

Clopidogrel/Acetylsalicylic acid Zentiva-

EMEA/H/C/001144/WS1459/0052

DuoPlavin-

EMEA/H/C/001143/WS1459/0051

Iscover-

EMEA/H/C/000175/WS1459/0134

Plavix-EMEA/H/C/000174/WS1459/0131

Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, "Update of section 5.1 of the SmPC in order to reflect the clinical outcome data of 2 randomised investigator-sponsored studies regarding de-escalation of P2Y12 receptor inhibitor to clopidogrel in ACS."

B.6.10. CHMP-PRAC assessed procedures

Aflunov - prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) -

EMEA/H/C/002094/II/0044/G

Seqirus S.r.l, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.4, 4.6, 4.8 and 5.1 of the SmPC following clinical study reports of studies V87_25 and V87_26 listed as post approval commitments; these are Phase 3, stratified, randomized, controlled, observer-blind, multicenter studies; the Package Leaflet and Labelling are updated accordingly.

The updated RMP version 3.0 has also been submitted.

In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some amendments to the PI and make some additional minor editorial corrections."

Brilique - ticagrelor -

EMEA/H/C/001241/II/0042

AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.9 and 5.2 of the SmPC in order to update the safety information in relation to renal impairment based on the final results from study D5130L00067; this is a single dose, randomized, open label, parallel group study conducted to compare the pharmacokinetics (PK), pharmacodynamics (PD), safety and tolerability of ticagrelor in haemodialysis patients to subjects with normal renal function. The RMP version 11 has also been submitted."

CYLTEZO - adalimumab -

EMEA/H/C/004319/II/0004

Boehringer Ingelheim International GmbH, Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study 1297.3 listed as a category 3 study in the RMP. This is an interventional trial to generate long-term safety, efficacy, and immunogenicity data for the administration of the proposed biosimilar Cyltezo in patients with moderate to severe rheumatoid arthritis."

Kisqali - ribociclib -**EMA/H/C/004213/II/0003/G**

Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver, "C.I.4: Update of section 5.2 of the SmPC in order to reflect on results from 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 section 4.2 and 5.2 of the SmPC in order to reflect on 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. The RMP version 2.0 has also been submitted."

NovoMix - insulin aspart -**EMA/H/C/000308/II/0095**

Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2, 4.5 and 5.1 of the SmPC to include data on the use of NovoMix® 30 combination use with GLP-1 receptor agonists. The PIL is updated accordingly. The RMP is also updated (version 3)"

OFEV - nintedanib -**EMA/H/C/003821/II/0021, Orphan**

Boehringer Ingelheim International GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of section 4.8 of the SmPC in order to include 'myocardial infarction' as a new adverse drug reaction with a frequency 'uncommon' in order to fulfil LEG 004.1, following the assessment of PSUSA/00010319/201704. The Package Leaflet is updated accordingly. The RMP version 6.0 (in revision 2 of the template) has also been submitted."

Onivyde - irinotecan hydrochloride trihydrate - EMA/H/C/004125/II/0008, Orphan

Baxalta Innovations GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: David Olsen,

“Update of sections 1, 2, 4.2, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC in order to reflect the expression of strength based on irinotecan anhydrous free-base. The Labelling and Package Leaflet are updated accordingly. In addition the MAH took the opportunity to introduce minor editorial changes. The updated RMP version 2.1 has also been submitted.”

**Plegridy - peginterferon beta-1a -
EMA/H/C/002827/II/0046**

Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams, “Update of sections 4.4 and 4.8 of the SmPC in order to add new warning and safety information about anaphylaxis. The RMP version 3.2 has also been submitted.”

**Ryzodeg - insulin human -
EMA/H/C/002499/II/0028**

Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Update of section 5.1 of the SmPC based on new clinical data from a cardiovascular outcome trial EX1250-4080 (DEVOTE) conducted for insulin degludec. DEVOTE was a randomised, double-blind and event-driven clinical trial with a median duration of 2 years comparing the cardiovascular safety of insulin degludec versus insulin glargine (100 units/mL) in patients with type 2 diabetes mellitus at high risk of cardiovascular events.

Based on the long-term exposure and safety data from DEVOTE which are also relevant for insulin degludec/insulin aspart, the Ryzodeg SmPC is updated with data from the trial in alignment with a recent update of the SmPC for insulin degludec.

Section 6.5 of the SmPC is also being amended for an editorial improvement to more precisely describe the nature of the plunger stopper.

The RMP version 7 has also been submitted, with updates consequent to the data in support of the application.”

**Tamiflu - oseltamivir -
EMA/H/C/000402/II/0136**

Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka,

“Update of sections 4.2, 4.8, 5.1 and 5.2 to guide prescribers on the use of Tamiflu for treatment in immunocompromised (IC) patients based on studyt NV20234, a Phase III, double-blind, randomized, stratified, multicenter study of conventional and double dose oseltamivir for the treatment of influenza in IC patients. The PL and RMP (v15) have been updated accordingly.

In addition, the MAH took the opportunity to correct some minor errors.”

**Toujeo - insulin glargine -
EMA/H/C/000309/II/0105/G**

Sanofi-Aventis Deutschland GmbH, Duplicate,
Duplicate of Lantus, Rapporteur: Johann
Lodewijk Hillege, PRAC Rapporteur: Menno van
der Elst

B.6.11. PRAC assessed procedures

PRAC Led

**Humira - adalimumab -
EMA/H/C/000481/II/0182**

AbbVie Deutschland GmbH & Co. KG,
Rapporteur: Kristina Dunder, PRAC Rapporteur:
Ulla Wändel Liminga, PRAC-CHMP liaison:
Kristina Dunder, “Submission of an updated
RMP version 14.0 in order to include a thorough
review of the currently specified safety concerns
in the Humira RMP, to updated in regards of
previously assessed safety concerns and to
make associated updates in line with GVP
Module V.”

PRAC Led

**Kengrexal - cangrelor -
EMA/H/C/003773/II/0015**

Chiesi Farmaceutici S.p.A., Rapporteur: Johann
Lodewijk Hillege, PRAC Rapporteur: Amelia
Cupelli, PRAC-CHMP liaison: Daniela Melchiorri,
“Submission of an updated RMP version 2.0 in
order to update the requirements for a study
listed as category 3 in the RMP. In addition, the
MAH took the opportunity to revise the RMP in
line with the RMP template version 2.0.”

PRAC Led

MabThera - rituximab -

EMEA/H/C/000165/II/0152

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final study report of the non-interventional drug utilisation study (DUS) BA28478 (MabThera drug utilisation study and patient alert card evaluation in non-oncology patients in Europe: an infusion centre-based approach). Consequently, update of sections 4.2 and 4.4 of the SmPC and Annex II.E to remove the patient alert card as an additional risk minimisation measure for the risks of PML and infections, for the non-oncology indications. The Package leaflet is updated in accordance. The RMP is also updated (version 18). This submission is done in fulfilment of FUM-68.1 and FUM-71."

PRAC Led

Mycamine - micafungin -**EMEA/H/C/000734/II/0038**

Astellas Pharma Europe B.V., Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "Submission of an updated RMP version 20.0 in order to streamline and improve the educational programme and communication to physicians prescribing Mycamine as requested in variation II/0035."

PRAC Led

Neofordex - dexamethasone -**EMEA/H/C/004071/II/0008**

Laboratoires CTRS, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 4.0 in order to propose the removal a category 3 activity 'removal of the score line for subdivision of the 40mg tablet and consequent deletion of the 20mg posology'. In addition, the MAH updated the other category 3 activity 'Development of a 20mg oral dosage form'. The MAH implemented the RMP revision 2 format."

PRAC Led

Pegasys - peginterferon alfa-2a -**EMEA/H/C/000395/II/0101**

Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of an updated RMP version 9.0 in

order to remove the NV25361 study (category 3 study). In addition, the YV25718 (study to establish the efficacy and safety of PEG-IFN monotherapy in children from 3 to less than 18 years of age with CHB) long term follow up milestone is amended from Q3 2020 to Q4 2021. The classification of some risks is also amended as per revision 2 of Module V of GVP including updates in the epidemiology section.”

PRAC Led

Revestive - teduglutide -

EMA/H/C/002345/II/0045, Orphan

Shire Pharmaceuticals Ireland Limited,

Rapporteur: Mark Ainsworth, PRAC Rapporteur:

Anette Kirstine Stark, PRAC-CHMP liaison: Sinan

B. Sarac, “Submission of an updated RMP

version 8 in order to include the safety

information from the final CSR of study TED-

C14-006 (“a 24-Week Double-blind, Safety,

Efficacy, and Pharmacodynamic Study

Investigating Two Doses of Teduglutide in

Pediatric Subjects Aged 1 Year Through 17

Years With Short Bowel Syndrome who are

Dependent on Parenteral Support”; a category 3

study in the RMP) that was submitted within

variation EMA/H/C/002345/II/0043.”

PRAC Led

Simponi - golimumab -

EMA/H/C/000992/II/0084

Janssen Biologics B.V., Rapporteur: Kristina

Dunder, PRAC Rapporteur: Ulla Wändel Liminga,

PRAC-CHMP liaison: Kristina Dunder,

“Submission of an updated RMP version 18.0

in order to remove the Educational program for

prescribing healthcare professionals as an

additional risk minimization measure for

Simponi, based upon the conclusion of the PRAC

PSUR Assessment report

(PSUSA/00001560/201704).”

PRAC Led

Viread - tenofovir disoproxil -

EMA/H/C/000419/II/0188

Gilead Sciences Ireland UC, PRAC Rapporteur:

Adrien Inoubli, PRAC-CHMP liaison: Joseph

Emmerich, “Submission of the final report from

study GS-EU-174-0224 listed as a category 3

study in the RMP. This is a cross-sectional drug

utilisation study in children and adolescents with

Chronic Hepatitis B to assess whether

physicians prescribing Viread to paediatric patients with Chronic Hepatitis B in the EU were following the relevant recommendations in the Viread SmPC and educational brochures.”

PRAC Led

Viread - tenofovir disoproxil -

EMA/H/C/000419/II/0190

Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, “Submission of an updated RMP version 22.1 (in accordance with the revised guidance in the Guideline on good pharmacovigilance practices Module V) to propose removing the additional risk minimization activities for HIV and HBV adults associated with the renal safety concern from the RMP.”

PRAC Led

Votubia - everolimus -

EMA/H/C/002311/II/0055, Orphan

Novartis Europharm Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, “Submission of the final report from the non-interventional study CRAD001MIC03, listed as a category 3 study in the RMP. This is an international disease registry collecting data on manifestations, interventions and outcomes in patients with tuberous sclerosis complex.”

PRAC Led

Xeloda - capecitabine -

EMA/H/C/000316/II/0077

Roche Registration GmbH, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, “To updated Xeloda RMP (version 9.1) in line with the product information changes recently approved within the variation EMA/H/C/000163/II/0074. The following updates are included: Post-authorization exposure updated, Presentation of important identified risk Dihydropyrimidine dehydrogenase deficiency (DPD) updated and updates related to Section 4.4 of EU SmPC for DPD revised as part of procedure EMA/H/C/316/II/0074. In addition MAH took the opportunity to introduce the new EU RMP template.”

PRAC Led

WS1402

Bretaris Genuair-

EMEA/H/C/002706/WS1402/0038

Eklira Genuair-

EMEA/H/C/002211/WS1402/0038

AstraZeneca AB, Lead Rapporteur:

Nithyanandan Nagercoil, Lead PRAC Rapporteur:

Julie Williams, PRAC-CHMP liaison: Robert

James Hemmings, "Submission of an updated RMP version 7.0 in order to proposed changes in categorisation of safety concerns and missing information in the RMP as per the guidance provide for the revision 2 of the RMP and to provide the RMP under the revision 2 template."

PRAC Led

WS1403

Brimica Genuair-

EMEA/H/C/003969/WS1403/0023

Duaklir Genuair-

EMEA/H/C/003745/WS1403/0023

AstraZeneca AB, Lead Rapporteur:

Nithyanandan Nagercoil, Lead PRAC Rapporteur:

Julie Williams, PRAC-CHMP liaison: Robert

James Hemmings, "Submission of an updated RMP version 4.0 in order to proposed changes in categorisation of safety concerns and missing information in the RMP as per the guidance provide for the revision 2 of the RMP and to provide the RMP under the revision 2 template."

B.6.12. CHMP-CAT assessed procedures

talimogene laherparepvec -

EMEA/H/C/002771/II/0024, ATMP

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

WS1407

HyQvia-EMEA/H/C/002491/WS1407/0042

Kiovig-EMEA/H/C/000628/WS1407/0083

Baxalta Innovations GmbH, Lead Rapporteur:

Jan Mueller-Berghaus

WS1409**Kepra-EMEA/H/C/000277/WS1409/0172**

UCB Pharma S.A., Lead Rapporteur: Koenraad Norga,

WS1410**Infanrix hexa-****EMEA/H/C/000296/WS1410/0243**

GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1412**Blitzima-****EMEA/H/C/004723/WS1412/0016****Ritemvia-****EMEA/H/C/004725/WS1412/0016****Rituzena-****EMEA/H/C/004724/WS1412/0017****Truxima-****EMEA/H/C/004112/WS1412/0017**

Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz

WS1416**Kisplyx-EMEA/H/C/004224/WS1416/0014****Lenvima-****EMEA/H/C/003727/WS1416/0018**

Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren

WS1419**Abseamed-****EMEA/H/C/000727/WS1419/0073****Binocrit-****EMEA/H/C/000725/WS1419/0073****Epoetin alfa Hexal-****EMEA/H/C/000726/WS1419/0072**

Sandoz GmbH, Lead Rapporteur: Alexandre Moreau

WS1424**Eviplera-****EMEA/H/C/002312/WS1424/0092****Odefsey-****EMEA/H/C/004156/WS1424/0032**

Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings

WS1425**Nuwiq-EMEA/H/C/002813/WS1425/0023****Vihuma-****EMEA/H/C/004459/WS1425/0005**

Octapharma AB, Lead Rapporteur: Jan Mueller-

Berghaus

WS1437/G

ANORO-

EMEA/H/C/002751/WS1437/0020/G

Elebrato Ellipta-

EMEA/H/C/004781/WS1437/0004/G

Incruse-

EMEA/H/C/002809/WS1437/0019/G

Laventair-

EMEA/H/C/003754/WS1437/0023/G

Rolufta-

EMEA/H/C/004654/WS1437/0006/G

Trelegy Ellipta-

EMEA/H/C/004363/WS1437/0003/G

Glaxo Group Ltd, Lead Rapporteur: Peter Kiely

WS1440/G

Hirobriz Breezhaler-

EMEA/H/C/001211/WS1440/0050/G

Onbrez Breezhaler-

EMEA/H/C/001114/WS1440/0048/G

Oslif Breezhaler-

EMEA/H/C/001210/WS1440/0048/G

Novartis Europharm Limited, Lead Rapporteur:

Mark Ainsworth

WS1443

Actos-EMEA/H/C/000285/WS1443/0080

Competact-

EMEA/H/C/000655/WS1443/0071

Glustin-EMEA/H/C/000286/WS1443/0079

Tandemact-

EMEA/H/C/000680/WS1443/0058

Takeda Pharma A/S, Lead Rapporteur: Peter Kiely, "To bring the annexes in line with QRD version 10 and the EC guideline of excipients on lactose. In addition the MAH took the opportunity to update the local representative in Estonia and Slovakia along with some editorial changes throughout the annexes."

WS1448/G

Ultibro Breezhaler-

EMEA/H/C/002679/WS1448/0027/G

Ulnar Breezhaler-

EMEA/H/C/003875/WS1448/0026/G

Xoterna Breezhaler-

EMEA/H/C/003755/WS1448/0030/G

Novartis Europharm Limited, Lead Rapporteur:

Mark Ainsworth

WS1463

Abseamed-

EMA/H/C/000727/WS1463/0074

Binocrit-

EMA/H/C/000725/WS1463/0074

Epoetin alfa Hexal-

EMA/H/C/000726/WS1463/0073

Sandoz GmbH, Lead Rapporteur: Alexandre

Moreau

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 - EMA 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.

Qualification of Biomarkers:

HTA:

G.2. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 23-26 July 2018 CHMP plenary:

<i>Cardiovascular diseases</i>	
1. ATMP;	The CHMP denied eligibility to PRIME and adopted the critical summary report.

<i>Oncology</i>	
2. (SME); Treatment of patients with relapsed/refractory acute myeloid leukaemia	The CHMP denied eligibility to PRIME and adopted the critical summary report.

<i>Neurology</i>	
3. (SME); Treatment of patients with Early Alzheimer's Disease (AD), defined patients with either Mild Cognitive Impairment due to AD or mild Dementia due to AD	The CHMP denied eligibility to PRIME and adopted the critical summary report.
4. chimeric 2'-O-(2-methoxyethyl) modified oligonucleotide targeted to huntingtin RNA (RO7234292) ; Treatment of Huntington's Disease	The CHMP granted eligibility to PRIME and adopted the critical summary report.
5. Autologous haematopoietic stem cells transduced with lentiviral vector Lenti-D encoding the human ATP-binding cassette, sub-family D (ALD), member 1 (ABCD1) from cDNA Treatment of cerebral adrenoleukodystrophy (CALD)	The CHMP granted eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in July 2018 for August 2018 CHMP adoption of outcomes

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