19 December 2018
EMA/890274/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Minutes of the meeting on 12-15 November 2018

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

Disclaimers

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

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

Note on access to documents

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

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
Send a question via our website www.ema.europa.eu/contact

Table of contents

1. Introduction

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

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced 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) November 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 12-15 November 2018 (to be published post December 2018 CHMP meeting).

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

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

The CHMP welcomed the new German alternate member Janet Koenig replacing Martina Weise, who moved to the member position. The Committee also welcomed the new member Constantinos Markopoulos from Greece replacing Eleftheria Nikolaidi, who moved to the alternate member position.

1.2. Adoption of agenda

CHMP agenda for 12-15 November 2018

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 15-18 October 2018.

The CHMP adopted the CHMP minutes for 15-18 October 2018. The Minutes of the November 2018 CHMP ORGAM meeting held on 5 November 2018, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. romosozumab - EMEA/H/C/004465

Treatment of osteoporosis

Scope: Oral explanation

Action: Oral explanation to be held on 14 November 2018 at time 11:00

List of Outstanding Issues adopted on 20.09.2018. List of Questions adopted on 26.04.2018.

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

See 3.2

2.1.2. volanesorsen - Orphan - EMEA/H/C/004538

Akcea Therapeutics UK Ltd.; indicated as an adjunct to diet for the treatment of patients with familial chylomicronemia syndrome (FCS)

Scope: Oral explanation

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

List of Outstanding Issues adopted on 20.09.2018, 28.06.2018, 26.04.2018. List of Questions adopted on 14.12.2017.

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

See 3.2

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

AOP Orphan Pharmaceuticals AG; treatment of polycythemia vera

Scope: Oral explanation, SAG report

Action: Oral explanation to be held on 13 November 2018 at time 14:00

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 22.06.2017.

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

See 3.2

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. WS1278
OPDIVO - nivolumab - EMEA/H/C/003985/WS1278/0042
Yervoy - ipilimumab - EMEA/H/C/002213/WS1278/0053

Bristol-Myers Squibb Pharma EEIG

Scope: Oral explanation, SAG report

List of experts for the SAG Oncology meeting on 08 November 2018 adopted via written procedure on 07 November 2018.

Action: Oral explanation to be held on 13 November 2018 at time 09:00

See 5.3.

The CHMP noted the report from SAG held on 8th November 2018.

An oral explanation was held on 13 November 2018 at time 09:00. During the oral explanation the applicant presented evidence for a relevant contribution of ipilimumab to the superior efficacy of the combination in comparison with system organ class.

Participation of patient representative

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

Amgen Europe B.V.

Scope: Oral explanation, Similarity assessment report

List of experts for the SAG Oncology meeting on 08 November 2018 adopted via written procedure on 07 November 2018.

Action: Oral explanation to be held on 13 November 2018 at time 11:00

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

See 5.3

2.4. Referral procedure oral explanations

2.4.1. Diclofenac Sodium Spray Gel 4% cutaneous spray, solution and associated names– EMEA/H/A-29(4)/1467

MAHs: various

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Martina Weise

Scope: Opinion

Action: For adoption

An oral explanation via TC was held on 14 November 2018 at 11:00. During the oral explanation, the company presented the favourable B/R balance based on published literature data.

See 10.4

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Erleada - apalutamide - EMEA/H/C/004452

Janssen-Cilag International N.V.; treatment of non-metastatic castration resistant prostate cancer (NM CRPC)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 20.09.2018. List of Questions adopted on 28.06.2018.

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

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

Furthermore, the CHMP considered that apalutamide 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 15 November 2018.

3.1.2. Fexinidazole Winthrop - fexinidazole - Article 58 - EMEA/H/W/002320

sanofi-aventis groupe; treatment of human African trypanosomiasis (HAT)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 20.09.2018, 26.06.2018. List of Questions adopted on 24.04.2018.

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

The CHMP noted the report from SAG meeting held on 25 September 2018 (WHO was involved).

The Committee adopted a positive opinion recommending the granting of a scientific opinion 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 14 November 2018.

3.1.3. Macimorelin Aeterna Zentaris - macimorelin - EMEA/H/C/004660

Aeterna Zentaris GmbH; Diagnosis of Adult growth hormone deficiency (AGHD)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 20.09.2018. List of Questions adopted on 22.03.2018.

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

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

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

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

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

The summary of opinion was circulated for information.

3.1.4. Silodosin Recordati - silodosin - EMEA/H/C/004964

Recordati Ireland Ltd; treatment of prostatic hyperplasia (BPH)

Scope: Opinion

Action: For adoption

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

List of Questions adopted on 28.06.2018.

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

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

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

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

The summary of opinion was circulated for information.

3.1.5. Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171

Sanofi Pasteur SA; indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4 in individuals 9 to 45 years of age with prior dengue virus infection and living in endemic areas (see sections 4.2, 4.4 and 4.8). The use of Dengvaxia should be in accordance with official recommendations

Scope: Corrected opinion documents

Action: For information

Opinion adopted on 18.10.2018. List of Outstanding Issues adopted on 20.09.2018, 26.04.2018, 23.03.2017. List of Questions adopted on 21.07.2016.

The CHMP noted the corrected opinion documents.

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

3.2.1. fremanezumab - EMEA/H/C/004833

prevention of episodic and chronic migraine

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 31.05.2018.

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

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

3.2.2. atazanavir - EMEA/H/C/004859

treatment of HIV-1 infection

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 26.07.2018.

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

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

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

AOP Orphan Pharmaceuticals AG; treatment of polycythemia vera

Scope: SAG report, List of outstanding issues

Action: Oral explanation to be held on 13 November 2018 at time 14:00

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 22.06.2017.

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

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

See 2.1

The CHMP noted the SAG report.

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

3.2.4. bevacizumab - EMEA/H/C/004697

Treatment of adult patients with metastatic carcinoma of the colon or rectum, metastatic breast cancer, unresectable advanced, metastatic or recurrent non-small cell lung cancer, advanced and/or metastatic renal cell cancer, persistent, recurrent, or metastatic carcinoma of the cervix

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.06.2018.

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.

3.2.5. cannabidiol - Orphan - EMEA/H/C/004675

GW Research Ltd; Adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 31.05.2018.

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 ≤100,000 /µL).

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 09.11.2017.

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

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

3.2.7. 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 outstanding issues

Action: For adoption

List of Questions adopted on 26.07.2018.

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

The Committee adopted a list of outstanding issues.

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

3.2.8. romosozumab - EMEA/H/C/004465

Treatment of osteoporosis

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 20.09.2018. List of Questions adopted on 26.04.2018.

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

See 2.1

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 an ad-hoc expert group and adopted a list of questions to this group.

3.2.9. hydroxycarbamide - EMEA/H/C/004837

prevention of complications of Sickle Cell disease

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.06.2018.

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. adalimumab - EMEA/H/C/004475

treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

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.

3.2.11. - adalimumab - EMEA/H/C/005158

treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

Scope: List of outstanding issues

Action: For adoption

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

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

3.2.12. 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 outstanding issues

Action: For adoption

List of Questions adopted on 26.07.2018.

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 adopted the similarity assessment report.

3.2.13. buprenorphine - EMEA/H/C/004743

Substitution treatment for opioid drug dependence

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.

3.2.14. dacomitinib - EMEA/H/C/004779

first-line treatment of adults with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR)-activating mutations.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.06.2018.

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.

3.2.15. canakinumab - EMEA/H/C/004754

prevention of major cardiovascular events

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 31.05.2018.

The Committee was reminded of the status of this application and its remaining outstanding issues. The Biostatistical Working Party has been consulted.

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

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

3.2.16. volanesorsen - Orphan - EMEA/H/C/004538

Akcea Therapeutics UK Ltd.; indicated as an adjunct to diet for the treatment of patients with familial chylomicronemia syndrome (FCS)

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 20.09.2018, 28.06.2018, 26.04.2018. List of Questions adopted on 14.12.2017.

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

See 2.1

The Committee was reminded of the status of this application and its remaining outstanding issuesThe Committee adopted a 4th list of outstanding issues with a specific timetable.

3.2.17. 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 outstanding issues, Final list of experts to Ad Hoc Expert Group

Action: For adoption

List of Questions adopted on 26.07.2018.

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 adopted the final list of experts to the ad-hoc expert Group.

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

3.3.1. sodium oxybate - EMEA/H/C/004962

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

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

Post-meeting note: The final list of questions was adopted after the Plenary via written procedure on 20.11.2018.

3.3.2. 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.

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. deferasirox - EMEA/H/C/005014

treatment of chronic iron overload

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. ravulizumab - Orphan - EMEA/H/C/004954

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

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. paclitaxel - EMEA/H/C/004441

treatment of metastatic breast cancer

Scope: Letter from the applicant dated 31 October 2018 requesting an extention to the clock stop to respond to the second list of outstanding issues adopted on 26 July 2018.

Action: For adoption

List of Outstanding Issues adopted on 26.07.2018, 31.05.2018. List of Questions adopted on 14.12.2017.

The CHMP agreed to the request by the applicant for an extention to the clock stop to respond to the second list of outstanding issues adopted on 26 July 2018.

3.4.2. cabazitaxel - EMEA/H/C/004951

treatment of prostate cancer

Scope: Letter from third party

Action: For information

List of Questions adopted on 20.09.2018

The CHMP noted the letter from the third party.

3.4.3. rituximab - EMEA/H/C/004807

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

Scope: letter by the applicant requesting an extension of the clock stop to respond to the list of questions adopted on 18.10.2018

Action: For adoption

List of Questions adopted on 18.10.2018

The CHMP agreed to the request by the applicant for an extension of the clock stop to respond to the list of questions adopted on 18.10.2018.

3.4.4. dapivirine - Article 58 - EMEA/H/W/002168

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

Scope: List of experts for the SAG HIV Viral Diseases meeting.

Action: For adoption

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

The CHMP discussed the list of experts for the SAG HIV Viral Diseases. The final list will be adopted after the Plenary via written procedure. Furthermore the CHMP noted the final list of outstanding issues adopted at the October Plenary.

Post-meeting note: the final list of experts was adopted via written procedure on 26th November 2018.

3.4.5. pegfilgrastim - EMEA/H/C/005008

treatment of neutropenia

Scope: Request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018

Action: For adoption

List of Questions adopted on 28.06.2018.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018

3.4.6. pegfilgrastim - EMEA/H/C/004789

treatment of neutropenia

Scope: Request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018

Action: For adoption

List of Questions adopted on 28.06.2018.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/X/0034/G

Vertex Pharmaceuticals (Europe) Ltd.

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur:

Rhea Fitzgerald

Scope: “The MAH applied for an addition of a new pharmaceutical form (granules) and an addition of two new strengths (100/125 mg and 150/188 mg) for paediatric use (2 to 5 years).

In addition, the MAH updated sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.3, 6.3 and 6.4 of the SmPC of the tablets formulation to bring it in line with the safety updates proposed with the new paediatric granules formulation and its extension for use in 2-5 years old. Annex II, the PL and RMP v5.4 have been updated accordingly.”

Action: For adoption

List of Outstanding Issues adopted on 20.09.2018. List of Questions adopted on 28.06.2018.

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

The Committee adopted a positive opinion 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 adopted the similarity assessment report for Orkambi.

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. 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

List of Questions adopted on 26.07.2018.

The Committee discussed the issues identified in this application, which related to the

indication wording and the observed differences in bioequivalence PFP/PFS.

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

No items

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

Eli Lilly Nederland B.V.

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Kolbeinn Gudmundsson , PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include Cyramza indicated as monotherapy for the treatment of adult patients with hepatocellular carcinoma who have an alpha fetoprotein (AFP) of ≥ 400 ng/mL, after prior sorafenib therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.11 and 5.2 of the SmPC are updated in accordance. The Package Leaflet is updated in accordance. RMP version 8.1 has been submitted."

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

Action: For adoption

The Committee discussed the issues identified in this application. It was noted that there were questions remaining regarding the benefit-risk balance for ramucirumab in the treatment of adult patients with hepatocellular carcinoma who have an alpha fetoprotein (AFP) of ⩾400 ng/mL, after prior sorafenib therapy.

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

5.1.2. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0060

Merck Sharp & Dohme B.V.

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

Scope: "Extension of Indication to include, in combination with carboplatin and either paclitaxel or nab-paclitaxel, for the first-line treatment of metastatic squamous NSCLC in adults for Keytruda.
As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Additionally, editorial corrections to section 5.1 of the SmPC are introduced (concerning the procedure EMEA/H/C/003820/II/0052). The RMP version 20.1 has also been submitted."

Action: For adoption

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

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

5.1.3. Kisqali - ribociclib - EMEA/H/C/004213/II/0004

Novartis Europharm Limited

Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver

Scope: "Extension of Indication to include treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant. In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist for Kisqali. The proposed extension to the indication is based upon data from study CLEE011E2301 (A Phase III randomized, double-blind, placebo-controlled study of LEE011 or placebo in combination with tamoxifen and goserelin or a non-steroidal aromatase inhibitor (NSAI) and goserelin for the treatment of premenopausal women with hormone receptor positive, HER2- negative, advanced breast cancer) and study CLEE011F2301 (A randomized double-blind, placebo-controlled study of ribociclib in combination with fulvestrant for the treatment of men and postmenopausal women with hormone receptor positive, HER2 negative, advanced breast cancer who have received no or only one line of prior endocrine treatment).
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC have been updated and the Package Leaflet has been updated accordingly.
In addition, the MAH took the opportunity to make some editorial changes in the SmPC and to make an administrative update to the Estonian and Latvian local representatives addresses in the Package Leaflet.
An updated RMP version 2.0 was submitted as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 20.09.2018.

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

The Committee adopted a positive opinion 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 noted the letter of recommendation dated 14 November 2018.

5.1.4. MabThera - rituximab - EMEA/H/C/000165/II/0149

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver

Scope: "Extension of indication in the treatment of adult patients with severe, active granulomatosis with polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA) for MabThera; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package leaflet is updated accordingly. In addition, the MAH took the opportunity to implement a terminology change in Annex II.D.
The RMP (v17.1) has been also updated and includes the changes of the approved variation II/144.
The variation leads to amendments to the Summary of Product Characteristics, Annex II and Package Leaflet and to the Risk Management Plan (RMP)."

Action: For adoption

Request for Supplementary Information adopted on 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.

5.1.5. MabThera - rituximab - EMEA/H/C/000165/II/0150

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Doris Stenver

Scope: "Extension of indication to include the treatment of patients with moderate to severe pemphigus vulgaris (PV) for MabThera; 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 is updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018.

The Committee discussed the issues identified in this application. The main remaining issues discussed concerned the wording of the indication and the supportive data. The members concluded that with the available data the indication in patients with established pemphigus vulgaris could not be justified. Further data from the ongoing study WA29330 was requested from the MAH.

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

5.1.6. Ravicti - glycerol phenylbutyrate - Orphan - EMEA/H/C/003822/II/0019

Horizon Pharma Ireland Limited

Rapporteur: Greg Markey, Co-Rapporteur: Jayne Crowe

Scope: "C.I.6 - Extension of indication to include in the authorised indication the new paediatric population from 0 to 2 months for RAVICTI based on the final results from study HPN-100-009, an Open Label Study of the Safety, Efficacy and Pharmacokinetics of Glycerol Phenylbutyrate in Pediatric Subjects under Two Years of Age with Urea Cycle Disorders (UCDs); 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.
This submission covers as well the requirement to submit clinical studies in the paediatric population in accordance with Article 46 of Regulation (EC) No 1901/2006 (the 'Paediatric Regulation') for study HPN-100-009."

Action: For adoption

Request for Supplementary Information adopted on 20.09.2018.

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

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

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

The summary of opinion was circulated for information.

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

Celgene Europe BV

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension of indication to include treatment with Revlimid in combination with bortezomib and dexamethasone of adult patients with previously untreated multiple myeloma. As a consequence, the MAH submitted a request to add 7-capsule pack sizes for the 7.5 mg, 20 mg and 25 mg strengths of Revlimid (lenalidomide) to support the proposed posology and lenalidomide dose modification. Sections 4.1, 4.2, 4.4, 4.8, 5.1, 6.5 and 8 of the SmPC are updated; the Package Leaflet is updated in accordance. Additionally, minor editorial changes have been introduced throughout the PI and annex II key elements of the RMM have been updated to include information on timing of blood and semen donation in line with the SmPC section 4.4.

An updated RMP (version 36.1) has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application, concerning the study population with particular view of subgroups and limitations of the clinical trial data in support of part of the new indication.

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

5.1.8. 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

Request for Supplementary Information adopted on 26.07.2018.

The Committee discussed the issues identified in this application, mainly relating to uncertainties regarding the contribution of Revolade to the oberved effect on top of immunosuppressive therapy and the limited data in the paediatric population and some safety data from the SOAR study.

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

5.1.9. Xyrem - sodium oxybate - EMEA/H/C/000593/II/0076

UCB Pharma S.A.

Rapporteur: Bruno Sepodes, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension of Indication to include adolescents and children older then 7 years for Xyrem; As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance.
The updated version (9.0) of the RMP was submitted."

Action: For adoption

The Committee discussed the issues identified in this application, mainly concerning the suitability of the formulation (in particular the dosing device) for children older than 7 years.

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

5.1.10. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0047

Merck Sharp & Dohme B.V.

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

Scope: "Extension of Indication to include (as monotherapy) adjuvant treatment of melanoma of adults with Stage III melanoma and 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."

Corrected opinion was adopted via written procedure on 30.10.2018

Action: For information

Opinion was adopted on 18.10.2018. Request for Supplementary Information adopted on 26.07.2018.

The CHMP noted the corrected opinion which was adopted via written procedure on 30.10.2018.

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

5.2.1. WS1344
Edistride - dapagliflozin - EMEA/H/C/004161/WS1344/0025
Forxiga - dapagliflozin - EMEA/H/C/002322/WS1344/0044

AstraZeneca AB

Lead Rapporteur: Kristina Dunder, Lead Co-Rapporteur: Martina Weise, PRAC Rapporteur: Annika Folin

Scope: "Extension of Indication to include new indication for the treatment of insufficiently controlled type 1 diabetes mellitus as an adjunct to insulin, when insulin does not provide adequate glycaemic control, for Forxiga and Edistride; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The updated RMP version 16 has also been submitted.
In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor editorial changes to SmPC and Package Leaflet."

Final list of experts to Ad Hoc Expert Group

Action: For adoption

Request for Supplementary Information adopted on 18.10.2018, 31.05.2018.

The CHMP adopted the final list of experts to Ad Hoc Expert Group.

5.2.2. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0057

Merck Sharp & Dohme B.V.

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

Scope: "Extension of Indication to include 1st line treatment of locally advanced or metastatic non-small cell lung cancer tumours expressing PD-L1 with a ≥ 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 ≥ 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 ≥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."

Request by the MAH for an extension to the clockstop to respond to RSI.

Action: For adoption

Request for Supplementary Information adopted on 18.10.2018.

The CHMP agreed to the request by the applicant for an extension to the clockstop to respond to RSI adopted on 18.10.2018.

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

5.3.1. WS1278
OPDIVO - nivolumab - EMEA/H/C/003985/WS1278/0042
Yervoy - ipilimumab - EMEA/H/C/002213/WS1278/0053

Bristol-Myers Squibb Pharma EEIG

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."

List of experts for the SAG Oncology meeting on 08 November 2018 adopted via written procedure on 07 November 2018.

Action: For adoption

Report from the SAG-Oncology meeting held 08 November 2018.

Opinion adopted on 26.07.2018.
Request for Supplementary Information adopted on 31.05.2018, 22.02.2018.

See 2.3.

The CHMP noted the report from SAG held 08 November 2018. The SAG considered the benefit-risk balance of the combination positive despite the fact that quantification of the individual contributions in the combination cannot be quantified precisely. The experts thought that further investigation on the optimal dosing and the patient population more likely to respond to this combination might be appropiate. The majority of the SAG members found the methodological principles advocating a fully factorial design unwarrented based on the observed benefit for the combination with deviations from general principles and guidelines justifiable.

The CHMP was reminded of the available data.

An oral explanation was held on 13 November 2018 at time 09:00.

The CHMP considered that the results from the main study comparing Opdivo and Yervoy with sunitinib showed a clinically important increase in patients' survival with the combination, and side effects were considered acceptable. Although the precise contribution of Yervoy was not clear, the CHMP re-assessed data from other non-clinical and clinical studies, including studies with the combination in relevant other cancer types, and considered that the benefit of Yervoy in the combination has been sufficiently demonstrated. The CHMP was of the opinion that the benefits of the combination largely outweigh its risks and therefore recommended granting the change to the marketing authorisation. However, the company must conduct a study to determine the precise contribution of Yervoy in the combination and if the risks could be further minimised.

Participation of patient representative

The CHMP adopted a positive opinion by majority (24 out of 31 votes) together with the CHMP Assessment Report and translation timetable.

The Icelandic member was in agreement with the CHMP recommendation, the Norwegian member was not in agreement.

The divergent position (Alexandre Moreau, Bruno Sepodes, Concepcion Prieto Yerro, Constantinos Markopoulos, Johann Lodewijk Hillege, Robert James Hemmings, Sol Ruiz, Svein Rune Andersen*)* was appended to the opinion.

The summary of opinion was circulated for information.

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

Amgen Europe B.V.

Scope: "Extension of indication to include the treatment of adults with Philadelphia chromosome-negative CD19 positive B precursor ALL in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1% for BLINCYTO monotherapy; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. In addition, the Marketing authorisation holder took the opportunity to update the contact details of the Portuguese and Irish local representatives in the Package Leaflet."

List of experts for the SAG Oncology meeting on 08 November 2018 adopted via written procedure on 07 November 2018.

Similarity assessment report.

Action: For adoption

Opinion adopted on 26.07.2018.

See 2.3

The CHMP noted the report from SAG held 08 November 2018.

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

The CHMP agreed with the SAG conclusion that, although there is no strong evidence of patients living longer, the available data from the main study indicate a good response to Blincyto, with around 78% of patients not having measurable residual cancer cells after treatment. The Committee also considered that patients with minimal residual disease are at high risk of the disease coming back and have few treatment options.

Therefore, the CHMP concluded that the benefits of Blincyto outweigh its risks and recommended granting the change to the marketing authorisation. However, the CHMP requested the company to provide further data from ongoing studies once available.

The Committee adopted a positive opinion by majority (29 out of 31 votes) together with the CHMP Assessment Report and translation timetable.

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

The divergent position (Alexandre Moreau, Daniela Melchiorri) was appended to the opinion.

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report for Blincyto.

The CHMP noted the letter of recommendation dated 15 November 2018.

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. osilodrostat – Orphan - H0004821

Novartis Europharm Limited; Treatment of Cushing's syndrome

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. tagraxofusp - Orphan - H0005031

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

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

Action: For adoption

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

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

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 7 recommendations for eligibility to PRIME: All 7 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. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0014

Roche Registration GmbH

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

Scope: "Extension of Indication to include Tecentriq in combination with bevacizumab, indicated for the first-line treatment of patients with unresectable locally advanced or metastatic renal cell carcinoma (RCC) whose tumours have a PD-L1 expression ≥ 1%. As a consequence, section 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated in order to add updated safety and efficacy information. The Package Leaflet is updated in accordance. RMP version 5.0 has been submitted."

Letter by the MAH dated 22.10.2018 informing the EMA about the withdrawal of the variation application

Action: For information

The CHMP noted the letter from the applicant dated 22 October 2018 informing EMA about the withdrawal of the variation application.

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

Amgen Europe B.V.

Rapporteur: Jorge Camarero Jiménez,

Scope: "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 to add a once-weekly dose regimen for carfilzomib (Kyprolis) at 20/70 mg/m2 in combination with dexamethasone (Kd) for the treatment of the currently indicated patient population. The MAH took the opportunity to implement editorial changes to the SmPC and Patient Information Leaflet (PIL) due to the revised excipients guideline (EMA/CHMP/302620/2017). The PIL is updated accordingly."

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to the PK data in relation to the new dosing regime.

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

9.1.3. Kyprolis - carfilzomib - EMEA/H/C/003790, Orphan

Amgen Europe B.V.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Alexandre Moreau

Action: For discussion

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

9.1.4. Adenuric - febuxostat - EMEA/H/C/000777/II/0051

Menarini International Operations Luxembourg S.A.,

Rapporteur: Andrea Laslop

Scope: "Update of section 5.1 of the SmPC in order to include the results of the clinical safety study CARES (TMX-67_301), to compare the cardiovascular outcomes of febuxostat and allopurinol in subjects with gout and cardiovascular comorbidities; this is a Multicenter, Randomized, Active-Control, Phase 3B Study.
In addition, the Marketing authorisation holder (MAH) took the opportunity to provide a consolidated Module 2.7.6 in order to list all the synopsis of individual studies in a unique tabular format."

Request by the MAH for an extension to the clock stop to respond to the RSI adopted on 04.10.2018

Action: For adoption
Request for Supplementary Information adopted on 04.10.2018.

The CHMP did not agree to the requested clock stop extension.

The MAH should submit the responses as per the agreed timetable.

10. Referral procedures

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

No items

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

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

MAHs: various

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

Scope: Opinion

Action: For adoption

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

The CHMP adopted an opinion by consensus, recommending that the interim limit approved in the current CEP for gentamicin sulphate should be reduced to as low as reasonably practicable in line with manufacturing capability and batch data. A limit of 8 ppm is considered to be within the current manufacturing capability of the API manufacturer based on current batch data and is also within the validated range of the analytical method.

The CHMP adopted the assessment report.

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

The CHMP agreed to the public health communication.

10.3. 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. Diotop 75mg/20mg modified-release capsules, hard - Diclofenac/Omeprazole – EMEA/H/A29(4)/1474

MAH: Temmler Pharma GmbH

Rapporteur: Greg Markey, Co-Rapporteur: Martina Weise

Scope: Opinion

Action: For adoption

MRP Procedure number: UK/H/6135/001/E/001, notification by the Medicines and Healthcare products Regulatory Agency dated 28 September 2018 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC.

The CHMP discussed the available data.

The CHMP adopted an opinion by consensus, recommending that the marketing authorisation should be granted.

The CHMP adopted the assessment report.

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

The CHMP agreed to the public health communication.

10.4.2. Diclofenac Sodium Spray Gel 4% cutaneous spray, solution and associated names– EMEA/H/A-29(4)/1467

MAHs: various

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Martina Weise

Scope: Opinion

Action: For adoption

An oral explanation via TC was held on 14 November 2018 at 11:00. During the oral explanation, the company presented the favourable B/R balance based on published literature data.

See 2.4

The members further discussed the available data.

The CHMP adopted an opinion by a majority (20 out of 31 votes), recommending that the marketing authorisation(s) should be granted.

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

The divergent position (Alexandre Moreau, Blanka Hirschlerova, Concepcion Prieto Yerro, Constantinos Markopoulos, Jan Mueller-Berghaus, Johann Lodewijk Hillege, Martina Weise, Ondrej Slanar, Rajko Kenda, Sinan B. Sarac and Sol Ruiz) was appended to this opinion.

The CHMP agreed to the public health communication.

10.4.3. Perlinring 0.120mg/0.015mg per 24 hours Vaginal Delivery System - Etonogestrel and Ethinylestradiol - EMEA/H/A-29/1473

MAH: Actavis Group PTC EHF

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

Scope: Corrected opinion

Action: For information

UK/H/6234/001/DC; Disagreement on the proposed deviations from the recommended posology

Opinion adopted on 18.10.2018

The CHMP noted the corrected opinion.

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

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

MAH Septodont group of companies and associated companies

Rapporteur: Romaldas Maciulaitis, Co-rapporteur: Fatima Ventura

Scope: List of outstanding issues

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 discussed the available data.

The CHMP adopted a list of outstanding issues .

Note: The final timetable was adopted via written procedure on 23.11.2018 after the CHMP plenary meeting.

Submission of responses: 07.02.2019

Re-start of the procedure: 28.02.2019

Rapporteur/co-rapporteur joint assessment report(s) circulated to CHMP: 08.03.2019

Comments: 15.03.2019

Updated Rapporteur/co-rapporteur joint assessment report(s) circulated to CHMP: 21.03.2019

CHMP LoOI/opinion: March 2019 CHMP

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

10.6.1. Angiotensin-II-receptor antagonists (sartans) containing a tetrazole group - EMEA/H/A-31/1471

MAHs: various

Rapporteur: Martina Weise

Scope: Final list of questions to SWP adopted via written procedure on 29 October 2018. Addendum to CHMP rapporteurs' joint assessment on risk.

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 noted the final list of questions to the SWP adopted via written procedure on 29 October 2018 and adopted the addendum to the CHMP rapporteurs' joint assessment on risk. This addendum aims to provide clarity on the currently agreed acceptable daily intakes of the two detected nitrosamines (NDEA, NDMA) for each of the sartans that are part of the referral.

10.6.2. Fluoroquinolones and Quinolones for systemic and inhalation use (EMEA/H/A-31/1452) – QUINSAIR (CAP) - EMEA/H/A-31/1452/C/002789/0010

Chiesi Farmaceutici S.p.A. (Quinsair)

Lead CHMP Rapporteur: Martina Weise, Referral PRAC Rapporteur: Eva Jirsová; PRAC Co-rapporteur: Martin Huber,
Quinsair Rapporteur: Robert James Hemmings, Co-Rapporteur: Ondrej Slanar

Scope: "PRAC recommendation to CHMP"
Review of the benefit-risk balance following notification by Germany of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Action: For adoption

Having considered the PRAC recommendation, the CHMP adopted an opinion by consensus, recommending the following:

The marketing authorisation(s) for medicinal products containing nalidixic acid, flumequine, pipemidic acid and cinoxacin should be suspended.

The marketing authorisations for medicinal products containing pefloxacin, lomefloxacin, ciprofloxacin, levofloxacin, ofloxacin, moxifloxacin, norfloxacin, prulifloxacin, rufloxacin should be varied.

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

The CHMP adopted the DHPC and communication plan.

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

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

MAHs: Galderma Nordic AB

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

Scope: Appointment of rapporteurs, Timetable

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

Action: For adoption

The CHMP appointed Filip Josephson as Rapporteur (interest level 1) and Johann Lodewijk Hillege as Co-Rapporteur (interest level 1).

The CHMP adopted the specific timetable.

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 28.11.2018

Comments: 03.12.2018

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 06.12.2018

List of questions or CHMP opinion: December 2018 CHMP

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

The CHMP noted the ENS.

12. Inspections

12.1. GMP inspections

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

Scope: Results of the 2015 EMA Sampling and Testing Programme for Centrally Authorised Products

Action: For adoption

The CHMP adopted the results of the 2015 sampling and testing programme.

Scope: Results of the 2016 EMA Sampling and Testing Programme for Centrally Authorised Products

Action: For adoption

The CHMP adopted the results of the 2016 sampling and testing programme.

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

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

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Area of expertise of CHMP Co-opted Member

Discussion on area of expertise in light of the expiry of the mandate of co-opted member Koenraad Norga on 24 January 2019.

The area of expertise of Koenraad Norga is Pharmacology.

Action: For discussion

The CHMP discussed the area of expertise and agreed on the two areas:

1) Pharmacoepidemiology.

2) Statistics for clinical trials and observational studies.

Nominations may include persons who have been nominated as alternates in the Committee. Nominations should be accompanied by a recommendation specifying the competence. Where possible, a detailed CV to support the specific expertise required should be included, although reference may also be made to the information held by the EMA with respect to the European Expert List, which includes information on areas of expertise and a CV for each expert.

Nominations should be sent by **January 23rd 2019, end of business.**

The CHMP agreed for the election to take place during the January 2019 CHMP Plenary meeting.

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 29-31 October 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 November 2018

Action: For adoption

The CHMP adopted the EURD list.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 07-09 November 2018

Action: For information

The CHMP noted the minutes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Draft agenda for HMPC meeting to be held on 19-22 November 2018

Action: For information

The CHMP noted the draft agenda.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at November 2018 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 13-16 November 2018

Action: For information

The CHMP noted the report.

Joint PDCO/CHMP session

Action: For discussion

The Joint CHMP-PDCO session was held.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 06-08 November 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 12-14 November 2018

Action: For information

The CHMP noted the report.

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

14.3.1. Scientific Advice Working Party (SAWP)

Nomination of new SAWP delegates

Action: For adoption

The CHMP appointed the following new members:

Alternate: Elina Ronnemaa (SE)

Alternate: Joerg Zinserling (DE)

Alternate: Flora Musuamba Tshinanu (BE)

Alternate: Finbarr Leacy (IE)

Report from the SAWP meeting held on 29-31 October 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.

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 November 2018 meeting to CHMP for adoption:

- 12 reports on products in scientific advice and protocol assistance
- 8 reports on products in pre-authorisation procedures
- 1 report on products in post-authorisation procedures
- 5 reports on products in plasma master file

Action: For adoption

The CHMP adopted the BWP reports.

14.3.4. Antimicrobial Advice ad hoc Expert Group (AMEG)

Scope: Draft scientific advice by the Antimicrobial Advice Ad Hoc Expert Group (AMEG) on the categorisation of antimicrobials and the preliminary risk profiling for new antimicrobials; Background information: request from the European Commission for the update of the AMEG advice on the impact on public health and animal health of the use of antibiotics in animals (link)

Action: For discussion

The CHMP noted the update. Further discussion is expected at the December meeting.

14.3.5. Respiratory Drafting Group (RDG)

Chair: Karolina Törneke

Scope: Election of chair
Action: For adoption

The CHMP re-elected Karolina Törneke as chair.

14.3.6. Safety Working Party (SWP)

Scope: Response from SWP to PRAC on list of questions on dolutegravir

Action: For adoption

Post-meeting note: The SWP response was adopted via written procedure on 23 November 2018.

14.3.1. Vaccines Working Party (VWP)

Scope: List of questions from CMDh to VWP on the use of Influenza vaccines for passive protection of infants via maternal immunisation

Action: For adoption

The CHMP adopted the List of questions from CMDh to VWP.

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

14.7.1. CHMP 2019 Draft Work Plan

CHMP: Harald Enzmann

Action: For discussion

The CHMP noted that feedback from topic leaders and contributors on work plan topics is awaited. Further discussions are expected to take place next ORGAM and Plenary meeting.

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Report on antimicrobial resistance in Europe

Report published under http://www.encepp.eu/encepp/viewResource.htm?id=26035

Action: For information

The CHMP noted the published report.

15.1.2. Preparedness of the system and capacity increase

Action: For adoption

The CHMP noted the results.

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 12 – 15 November 2018 meeting

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Harald Enzmann	Chair	Germany	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Bart Van der Schueren	Member	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Katarina Vučić	Member	Croatia	No interests declared	
Selma Arapovic Dzakula	Alternate	Croatia	No interests declared	
Loizos Panayi	Alternate	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Tomas Boran	Alternate	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Mark Ainsworth	Alternate	Denmark	No participation in final deliberations and voting on:	3.2.7. turoctocog alfa pegol - Orphan - EMEA/H/C/004883
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	
Martina Weise	Member	Germany	No restrictions applicable to this meeting	
Janet Koenig	Alternate	Germany	No interests declared	
Constatinos Markopoulos	Member	Greece	No interests declared	
Agnes Gyurasics	Member	Hungary	No interests declared	
Kolbeinn	Member	Iceland	No interests	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Gudmundsson			declared	
Jayne Crowe	Member	Ireland	No interests declared	
Peter Kiely	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No restrictions applicable to this meeting	
Juris Pokrotnieks	Member	Latvia	No restrictions applicable to this meeting	
Natalja Karpova	Alternate	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No participation in final deliberations and voting on:	5.1.4. MabThera - rituximab - EMEA/H/C/000165/II/0149 5.1.5. MabThera - rituximab - EMEA/H/C/000165/II/0150 9.1.1. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0014
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Svein Rune Andersen	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No restrictions applicable to this meeting	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Bruno Sepodes	Vice-Chair	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Dana Gabriela Marin	Alternate	Romania	No interests declared	
Frantisek Drafi	Member	Slovakia	No interests declared	
Rajko Kenda	Member	Slovenia	No participation in final deliberations and voting on:	3.2.2. atazanavir - EMEA/H/C/004859
Concepcion Prieto Yerro	Member	Spain	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jorge Camarero Jiménez	Alternate	Spain	No participation in final deliberations and voting on:	5.1.4. MabThera - rituximab - EMEA/H/C/000165/II/0149 5.1.5. MabThera - rituximab - EMEA/H/C/000165/II/0150 9.1.1. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0014
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	
Koenraad Norga	Co-opted member	Belgium	No restrictions applicable to this meeting	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Blanka Hirschlerova	Co-opted member	Czech Republic	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Patricia Diaz Ramos	Expert - in person*	Spain	No restrictions applicable to this meeting	
Valerie Lescrainier	Expert - in person*	Belgium	No interests declared	
Nele Steens	Expert - in person*	Belgium	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Kairi Rooma	Expert - in person*	Estonia	No interests declared	
Martin Gore	Expert in person	United Kingdom	No restrictions applicable to this meeting	
Ingrid Wang	Expert - via telephone*	Norway	No interests declared	
Hilde Roshol	Expert - via telephone*	Norway	No interests declared	
Elina Rönnemaa	Expert - via telephone*	Sweden	No interests declared	
Barbara Bannister	Expert - via telephone*	United Kingdom	No interests declared	
Bjørn Oddvar Strøm	Expert - via telephone*	Norway	No restrictions applicable to this meeting	
Martijn van Gils	Expert - via telephone*	Netherlands	No interests declared	
Frank Holtkamp	Expert - via telephone*	Netherlands	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Angelina Doriguzzi	Expert - via telephone*	Austria	No restrictions applicable to meetings	
Norbert Benda	Expert - via telephone*	Germany	No interests declared	
Eva Jirsová	Expert - via telephone*	Czech Republic	No interests declared	
Nele Steens	Expert - via Adobe*	Belgium	No interests declared	
Christoph Unkrig	Expert - via Adobe*	Germany	No interests declared	
Clemens Mittmann	Expert - via Adobe*	Germany	No interests declared	
Elmer Schabel	Expert - via Adobe*	Germany	No interests declared	
Julia Katharina Maier	Expert - via Adobe*	Germany	No interests declared	
Miranda Vroenhove	Expert - via Adobe*	Belgium	No interests declared	
Jan Neuhauser	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)*

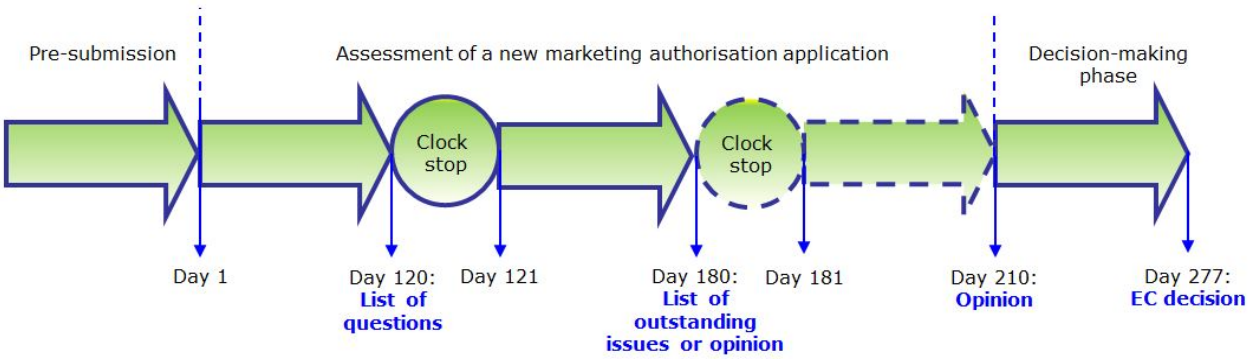
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures (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 *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

medicine or class of medicines on behalf of the EU. Further information on such procedures can be found here.

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

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

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 December 2018
EMA/CHMP/800490/2018

Annex to Minutes 12-15 November 2018 CHMP

Pre submission and post authorisation issues

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
Send a question via our website www.ema.europa.eu/contact

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

Final Outcome of Rapporteurship allocation for November 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

Atriance - nelarabine - EMEA/H/C/000752/S/0044 Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark	Positive Opinion adopted by consensus together with the CHMP assessment report. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
Brineura - cerliponase alfa - EMEA/H/C/004065/S/0009, Orphan BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga	Positive Opinion adopted by consensus together with the CHMP assessment report. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
IMVANEX - modified vaccinia ankara virus - EMEA/H/C/002596/S/0037 Bavarian Nordic A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams	Positive Opinion adopted by consensus together with the CHMP assessment report. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
Lojuxta - lomitapide - EMEA/H/C/002578/S/0032 Amryt Pharmaceuticals DAC, Rapporteur: Johann	Request for Supplementary Information adopted with a specific timetable.

Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 15.11.2018.	
Naglazyme - galsulfase - EMEA/H/C/000640/S/0073 BioMarin International Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty Request for Supplementary Information adopted on 15.11.2018.	Request for Supplementary Information adopted with a specific timetable.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - EMEA/H/C/002450/R/0021, Orphan, ATMP Chiesi Farmaceutici S.p.A., Rapporteur: Egbert Flory, PRAC Rapporteur: Julie Williams Request for Supplementary Information adopted on 12.10.2018.	The CHMP, having considered the application as set out in the assessment report and on the basis of the evidence of compliance with the specific obligations submitted by the marketing authorisation holder, is of the opinion that the risk-benefit balance of the above mentioned medicinal product remains favourable, and therefore recommends by consensus, the renewal of the conditional marketing authorisation in accordance with Article 6(3) of Regulation (EC) No 507/2006 for the above mentioned medicinal product for which the draft Summary of Product Characteristics is set out in Annex I. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Adempas - riociguat - EMEA/H/C/002737/R/0026, Orphan Bayer AG, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Julie Williams Request for Supplementary Information adopted on 20.09.2018.	Positive Opinion adopted by consensus together with the CHMP assessment report. 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.
Anoro Ellipta - umeclidinium / vilanterol - EMEA/H/C/002751/R/0022 Glaxo Group Ltd, Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Peter Kiely, PRAC	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of

Rapporteur: Amelia Cupelli	the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Hemangiol - propranolol - EMEA/H/C/002621/R/0018 PIERRE FABRE DERMATOLOGIE, Rapporteur: Joseph Emmerich, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Eva A. Segovia	Positive Opinion adopted by consensus together with the CHMP assessment report. 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.
Incruse Ellipta - umeclidinium bromide - EMEA/H/C/002809/R/0021 Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Amelia Cupelli	Positive Opinion adopted by consensus together with the CHMP assessment report. 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.
Laventair Ellipta - umeclidinium / vilanterol - EMEA/H/C/003754/R/0025 GlaxoSmithKline (Ireland) Limited, Duplicate, Duplicate of Anoro Ellipta, Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Amelia Cupelli	Positive Opinion adopted by consensus together with the CHMP assessment report. 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.
Qutenza - capsaicin - EMEA/H/C/000909/R/0047 Grunenthal GmbH, Rapporteur: Bruno Sepodes, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Ana Sofia Diniz Martins Request for Supplementary Information adopted on 15.11.2018.	Request for Supplementary Information adopted with a specific timetable.
Renvela - sevelamer carbonate - EMEA/H/C/000993/R/0046 Genzyme Europe BV, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Laurence de Fays Request for Supplementary Information adopted on 15.11.2018.	Request for Supplementary Information adopted with a specific timetable.
Ulunar Breezhaler - indacaterol / glycopyrronium -	Positive Opinion adopted by consensus together

EMEA/H/C/003875/R/0028 Novartis Europharm Limited, Rapporteur: Mark Ainsworth, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Anette Kirstine Stark Request for Supplementary Information adopted on 18.10.2018.	with the CHMP assessment report. 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

Caprelsa - vandetanib - EMEA/H/C/002315/R/0032 Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni Request for Supplementary Information adopted on 18.10.2018.	Positive Opinion adopted by consensus together with the CHMP assessment report. 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.
Cometriq - cabozantinib - EMEA/H/C/002640/R/0029, Orphan Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 15.11.2018.	Request for supplementary adopted with a specific timetable.
CRYSVITA - burosumab - EMEA/H/C/004275/R/0002, Orphan Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski	Positive Opinion adopted by consensus together with the CHMP assessment report. 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.
SIRTURO - bedaquiline - EMEA/H/C/002614/R/0031, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga	Positive Opinion adopted by consensus together with the CHMP assessment report. 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 29-31 October 2018 PRAC:	
Signal of hepatitis E infection	Adopted.
Tacrolimus	
TACFORIUS – EMEA/H/C/004435 Teva B.V., Rapporteur: Milena Stain	
ADVAGRAF – EMEA/H/C/000712 Astellas Pharma Europe B.V., Rapporteur: Jayne Crowe, Co- Rapporteur: Romaldas Mačiulaitis	
MODIGRAF – EMEA/H/C/000954 Astellas Pharma Europe B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Romaldas Mačiulaitis	
ENVARSUS – EMEA/H/C/002655 Chiesi Farmaceutici S.p.A., Rapporteur: John Joseph Borg	
PRAC recommendation on a variation**: For adoption**	
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its November 2018 meeting:	
EMEA/H/C/PSUSA/00000413/201803 (bimatoprost) CAPS: **Lumigan** (EMEA/H/C/000391) (bimatoprost), Allergan Pharmaceuticals Ireland, Rapporteur: Mark Ainsworth NAPS: **AET, DE** - BIMATOPROST AET **BIMADOC** - DOC GENERICI S.R.L **BIMAGAN** - S.C. ROMPHARM COMPANY S.R.L. **BIMAROZ** - ADAMED **BIMATO-VISION** - OMNIVISION GMBH **BIMATOPROST** - SANDOZ B.V. **BIMATOPROST 1 A PHARMA** - 1 A PHARMA GMBH **BIMATOPROST ASPIRE** - ASPIRE PHARMA LIMITED **BIMATOPROST GENOPTIM** - SYNOPTIS PHARMA SP Z O O **BIMATOPROST HEXAL** - HEXAL AG **BIMATOPROST MYLAN** - MYLAN S.A.S, MYLAN	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following change(s): Bimatoprost 0.1 mg/ml eye drops, solution (0.01%) Update of section 4.8 of the SmPC to add the adverse reactions dizziness, hypertension, photophobia, ocular discomfort and skin discoloration (periocular). The package leaflet is updated accordingly. Bimatoprost 0.3 mg/ml eye drops, solution (0.03%)

S.P.A., MYLAN B.V., MYLAN, LDA, GENERICS [UK] LIMITED **BIMATOPROST MYLAN PHARMA** - MYLAN S.A.S **BIMATOPROST PHARMATHEN** - PHARMATHEN S.A. **BIMATOPROST PHARMATHEN** - ASPIRE PHARMA LIMITED **BIMATOPROST RATIOPHARM** - TEVA B.V, RATIOPHARM GMBH **BIMATOPROST SANDOZ** - SANDOZ FARMACÊUTICA LDA., SANDOZ B.V., SANDOZ, SANDOZ N.V., SANDOZ GMBH, S.C. SANDOZ S.R.L., SANDOZ PHARMACEUTICALS D.D. **BIMATOPROST SANDOZ** - SANDOZ FARMACÊUTICA LDA., SANDOZ A/S, SANDOZ S.P.A., SANDOZ FARMACÉUTICA, S.A., SANDOZ, SANDOZ N.V., SANDOZ GMBH, SANDOZ PHARMACEUTICALS D.D., SANDOZ LTD **BIMATOPROST STADA** - AET, DE **BIMATOPROST TEVA** - TEVA NEDERLAND B.V., TEVA UK LIMITED **BIMATOPROST TEVA** - TEVA SANTÉ, TEVA ITALIA S.R.L., TEVA PHARMA **BIMATOPROST TEVA UK** - TEVA UK LIMITED **BIMICAN** - ZAKLADY FARMACEUTYCZNE "POLPHARMA" SPOLKA AKCYJNA, MEDANA PHARMA SPOLKA AKCYJNA, WARSZAWSKIE ZAKLADY FARMACEUTYCZNE POLFA S.A. **BIMICAN NEO** - ZAKLADY FARMACEUTYCZNE "POLPHARMA" SPOLKA AKCYJNA **BIMIFRE** - ZAKLADY FARMACEUTYCZNE "POLPHARMA" SPOLKA AKCYJNA **BIMIFREE** - ZAKLADY FARMACEUTYCZNE "POLPHARMA" SPOLKA AKCYJNA, WARSZAWSKIE ZAKLADY FARMACEUTYCZNE POLFA S.A. **BIPROEYE** - GENERICS [UK] LIMITED **BIRMOST** - RAFARM SA. **BITOPRIX** - GENETIC SPA **BRINUS** - GENETIC SPA **BRITNYA** - PHARMATHEN HELLAS S.A. **BRITNYA** - PHARMATHEN S.A. **BROSTIMAB** - GENETIC SPA **EYREIDA** - ASPIRE PHARMA LIMITED **GLAROST** - DELORBIS PHARMACEUTICALS LTD **SANDOZ GMBH** - BIMATOPROST SANDOZ GMBH **STURIBAN** - ACTAVIS GROUP PTC EHF **TREPROVIST** - SANDOZ B.V., SANDOZ GMBH **UP-46** - UNI-PHARMA KLEON TSETIS PHARMACEUTICAL LABORATORIES S.A **VIZIBIM** - DR. GERHARD MANN CHEM.-PHARM.	Update of section 4.8 of the SmPC to add the adverse reactions ocular discomfort and skin discoloration (periocular). The Package leaflet is updated accordingly. Bimatoprost 0.3 mg/ml eye drops, solution in a single-dose container (0.03% PF) Update of section 4.8 of the SmPC to add the adverse reactions dizziness, eye discharge, ocular discomfort and hypertension. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

FABRIK GMBH, PHARMASWISS ČESKÁ REPUBLIKA S.R.O. **ZAKLADY FARMACEUTYCZNE "POLPHARMA" SPOLKA AKCYJNA** - BIMATOPROST POLPHARMA **БИМАГАН** - S.C. ROMPHARM COMPANY S.R.L. **ВИЗИБИМ** - PHARMASWISS ČESKÁ REPUBLIKA S.R.O. , PRAC Rapporteur: Anette Kirstine Stark, "08 Mar 2015 – 07 Mar 2018"	
EMEA/H/C/PSUSA/00000998/201803 (dexmedetomidine) CAPS: **Dexdor** (EMEA/H/C/002268) (dexmedetomidine), Orion Corporation, Rapporteur: Greg Markey NAPS: **NAPs** - EU , PRAC Rapporteur: Julie Williams, "Update of sections 4.4 of the SmPC to add to add a warning on hyperthermia and 4.9 of the SmPC to include the adverse reaction of hypertension and respiratory depression. The Package leaflet to be updated accordingly."	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following change(s): Update of sections 4.4 of the SmPC to add to add a warning on hyperthermia and 4.9 of the SmPC to include the adverse reaction of hypertension and respiratory depression. The Package leaflet to be updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00002980/201804 (tocilizumab) CAPS: **RoActemra** (EMEA/H/C/000955) (tocilizumab), Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "11.04.2017 to 10.04.2018"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation for the above-mentioned medicinal product, concerning the following changes: Update of sections 4.8 and 5.1 of the SmPC to add the adverse reaction "Hypofibrinogenaemia" with a frequency "common". The introductory wording to the adverse drug reaction (ADR) tables is updated to reflect the ADRs are based on clinical trials and/or post-marketing experience. Section 5.1 is updated to indicate that during clinical studies with tocilizumab rapid decrease in fibrinogen was observed. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned

	recommendation of the CHMP.
EMEA/H/C/PSUSA/00010250/201804 (propranolol (centrally authorised product)) CAPS: **Hemangiol** (EMEA/H/C/002621) (propranolol), PIERRE FABRE DERMATOLOGIE, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Eva A. Segovia, "Update of section 4.8 of the SmPC to add the adverse reactions of "dermatitis psoriasiform" with a frequency not known and "dermatitis diaper" with a frequency common. The Package leaflet is updated accordingly."	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 4.8 of the SmPC to add the adverse reactions of "dermatitis psoriasiform" with a frequency not known and "dermatitis diaper" with a frequency common. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010534/201804 (irinotecan (liposomal formulations)) CAPS: **Onivyde** (EMEA/H/C/004125) (irinotecan hydrochloride trihydrate), Baxalta Innovations GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: David Olsen, "23Oct2017 – 22Apr2018"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 of the SmPC to add a warning on the risk of vascular disorders. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010591/201804 (parathyroid hormone) CAPS: **Natpar** (EMEA/H/C/003861) (parathyroid hormone), Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Rhea Fitzgerald, "Update of section 4.4 of the SmPC to add a warning on urolithiasis. The Package leaflet is updated accordingly."	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 of the SmPC to add a warning on urolithiasis. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

B.4. EPARs / WPARs

Bevespi Aerosphere - glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004245 AstraZeneca AB, indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD), Fixed combination application (Article 10b of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171 Sanofi Pasteur, prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4, 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.
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814, Article 28 Seqirus Netherlands B.V., prophylaxis of influenza in adults and children from 4 years of age, 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.
Luxturna - voretigene neparvovec - EMEA/H/C/004451, Orphan, ATMP Spark Therapeutics Ireland Ltd, treatment of patients with vision loss due to Leber congenital amaurosis or retinitis pigmentosa inherited retinal dystrophy, 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.
Namuscla - mexiletine hcl - EMEA/H/C/004584, Orphan Lupin Europe GmbH, treatment of non-dystrophic myotonic disorders, 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.
Ogivri - trastuzumab - EMEA/H/C/004916 MYLAN S.A.S, treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC), Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
TAKHZYRO - lanadelumab - EMEA/H/C/004806, Orphan Shire Pharmaceuticals Ireland Limited, treatment of angioedema attacks, prevention of angioedema attacks, 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

BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/II/0026 Teva Pharma B.V., Duplicate, Duplicate of DuoResp Spiromax, Rapporteur: Nithyanandan Nagercoil Opinion adopted on 08.11.2018.	Positive Opinion adopted by consensus on 08.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Bortezomib Hospira - bortezomib - EMEA/H/C/004207/II/0008 Pfizer Europe MA EEIG, Generic, Generic of VELCADE, Rapporteur: Milena Stain Opinion adopted on 08.11.2018. Request for Supplementary Information adopted on 13.09.2018.	Positive Opinion adopted by consensus on 08.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cinryze - C1 esterase inhibitor (human) - EMEA/H/C/001207/II/0064 Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 25.10.2018.	Request for supplementary information adopted with a specific timetable.
Darzalex - daratumumab - EMEA/H/C/004077/II/0018/G, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 08.11.2018.	Request for supplementary information adopted with a specific timetable.
DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/II/0026 Teva Pharma B.V., Rapporteur: Nithyanandan Nagercoil Opinion adopted on 08.11.2018.	Positive Opinion adopted by consensus on 08.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Dupixent - dupilumab - EMEA/H/C/004390/II/0006/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 25.10.2018, 19.07.2018.	Request for supplementary information adopted with a specific timetable.
Entyvio - vedolizumab - EMEA/H/C/002782/II/0029 Takeda Pharma A/S, Rapporteur: Greg Markey Opinion adopted on 25.10.2018. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 25.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 12.07.2018, 17.05.2018.	
Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0108/G Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 15.11.2018.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Fasenra - benralizumab - EMEA/H/C/004433/II/0008 AstraZeneca AB, Rapporteur: Nithyanandan Nagercoil Request for Supplementary Information adopted on 08.11.2018.	Request for supplementary information adopted with a specific timetable.
Foclivia - influenza virus surface antigens (inactivated) of strain A/Vietnam/1194/2004 (H5N1) - EMEA/H/C/001208/II/0038/G Seqirus S.r.l, Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 08.11.2018.	Request for supplementary information adopted with a specific timetable.
Gliolan - aminolevulinic acid - EMEA/H/C/000744/II/0015 medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Bruno Sepodes Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 20.09.2018, 28.06.2018.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Herzuma - trastuzumab - EMEA/H/C/002575/II/0012 Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 15.11.2018.	Request for supplementary information adopted with a specific timetable.
Kentera - oxybutynin - EMEA/H/C/000532/II/0047 Nicobrand Limited, Rapporteur: Bart Van der Schueren Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 13.09.2018.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kovaltry - octocog alfa - EMEA/H/C/003825/II/0017/G Bayer AG, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 15.11.2018.	Request for Supplementary Information adopted with a specific timetable.
Levemir - insulin detemir -	Positive Opinion adopted by consensus on

EMEA/H/C/000528/II/0089 Novo Nordisk A/S, Rapporteur: Sinan B. Sarac Opinion adopted on 08.11.2018. Request for Supplementary Information adopted on 27.09.2018.	08.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Metalyse - tenecteplase - EMEA/H/C/000306/II/0057 Boehringer Ingelheim International GmbH, Rapporteur: Harald Enzmann Opinion adopted on 25.10.2018.	Positive Opinion adopted by consensus on 25.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Miglustat Gen.Orph - miglustat - EMEA/H/C/004366/II/0003 Gen.Orph, Generic, Generic of Zavesca, Rapporteur: Milena Stain Request for Supplementary Information adopted on 08.11.2018.	Request for supplementary information adopted with a specific timetable.
Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0070 Roche Registration GmbH, Rapporteur: Concepcion Prieto Yerro Opinion adopted on 25.10.2018.	Positive Opinion adopted by consensus on 25.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Obizur - susoctocog alfa - EMEA/H/C/002792/II/0021 Baxalta Innovations GmbH, Rapporteur: Nithyanandan Nagercoil Opinion adopted on 15.11.2018.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PREVYMIS - letermovir - EMEA/H/C/004536/II/0005, Orphan Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson Opinion adopted on 08.11.2018.	Positive Opinion adopted by consensus on 08.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0136/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 13.09.2018.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0140 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 15.11.2018.	Request for supplementary information adopted with a specific timetable.
Revolade - eltrombopag / eltrombopag	Positive Opinion adopted by consensus on

olamine - EMEA/H/C/001110/II/0052/G Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 20.09.2018.	15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Sancuso - granisetron - EMEA/H/C/002296/II/0053/G Kyowa Kirin Holdings B.V., Rapporteur: Romaldas Mačiulaitis Request for Supplementary Information adopted on 15.11.2018.	Request for supplementary information adopted with a specific timetable.
SIRTURO - bedaquiline - EMEA/H/C/002614/II/0030, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson Request for Supplementary Information adopted on 08.11.2018.	Request for supplementary information adopted with a specific timetable.
Somavert - pegvisomant - EMEA/H/C/000409/II/0086/G Pfizer Europe MA EEIG, Rapporteur: Joseph Emmerich Opinion adopted on 08.11.2018. Request for Supplementary Information adopted on 13.09.2018.	Positive Opinion adopted by consensus on 08.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Trazimera - trastuzumab - EMEA/H/C/004463/II/0002 Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 08.11.2018.	Request for supplementary information adopted with a specific timetable.
Ucedane - carglumic acid - EMEA/H/C/004019/II/0002/G Lucane Pharma, Generic, Generic of Carbaglu, Rapporteur: Eleftheria Nikolaidi Request for Supplementary Information adopted on 15.11.2018.	Request for Supplementary Information adopted with a specific timetable.
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0040 MCM Vaccine B.V., Rapporteur: Bart Van der Schueren Opinion adopted on 08.11.2018.	Positive Opinion adopted by consensus on 08.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Voncento - human coagulation factor VIII / human von willebrand factor -	Positive Opinion adopted by consensus on 15.11.2018.

EMEA/H/C/002493/II/0035/G CSL Behring GmbH, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 15.11.2018.	The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1420 **Ambirix-EMEA/H/C/000426/WS1420/0092** **Twinrix Adult-EMEA/H/C/000112/WS1420/0126** **Twinrix Paediatric-EMEA/H/C/000129/WS1420/0127** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 08.11.2018.	Request for supplementary information adopted with a specific timetable.
WS1427 **Nuwiq-EMEA/H/C/002813/WS1427/0024** **Vihuma-EMEA/H/C/004459/WS1427/0007** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 25.10.2018. Request for Supplementary Information adopted on 20.09.2018.	Positive Opinion adopted by consensus on 25.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1432 **Ambirix-EMEA/H/C/000426/WS1432/0093** **Twinrix Adult-EMEA/H/C/000112/WS1432/0127** **Twinrix Paediatric-EMEA/H/C/000129/WS1432/0128** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Robert James Hemmings Request for Supplementary Information adopted on 08.11.2018.	Request for supplementary information adopted with a specific timetable.
WS1456 **Infanrix hexa-EMEA/H/C/000296/WS1456/0247** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 08.11.2018.	Positive Opinion adopted by consensus on 08.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Brilique - ticagrelor - EMEA/H/C/001241/II/0041	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP

AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, “Update of section and 4.4 of the SmPC in order to update safety information in relation to an increased frequency of mostly asymptomatic ventricular pauses during treatment with ticagrelor compared with clopidogrel, and to introduce “stroke” as a possible event in case of premature discontinuation, based on already assessed studies and post-marketing use (clinical trials PLATO (D5130C05262), PEGASUS (D5132C00001), SOCRATES (D5134C00001) and EUCLID (D5135C00001)).” Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 20.09.2018.	Members were in agreement with the CHMP recommendation.
Bronchitol - mannitol - EMEA/H/C/001252/II/0034, Orphan Pharmaxis Pharmaceuticals Limited, Rapporteur: Nithyanandan Nagercoil, “Update of sections 4.8 and 5.1 of the SmPC in order to update the frequency of certain adverse events and to update the clinical safety and efficacy information based on the results of the clinical data from Study CF 303. This is a phase 3 safety and efficacy clinical trial in adult cystic fibrosis subjects. The package leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in the product information and correct the Annex A.” Request for Supplementary Information adopted on 08.11.2018.	Request for supplementary information adopted with a specific timetable.
Dacogen - decitabine - EMEA/H/C/002221/II/0035, Orphan Janssen-Cilag International N.V., Rapporteur: Alexandre Moreau, “Update of section 4.4, and 4.8 of the SmPC in order to add the adverse events "Hepatic Function abnormal" with the frequency very common and "Hyperbilirubinaemia" with the frequency common, as well as to include clinical recommendations in patients developing signs or symptoms of hepatic impairment based on a cumulative review of post-marketing data and clinical literature; the Package Leaflet is updated accordingly. Moreover, the existing wording for the warning of patients with renal impairment has been revised in alignment with recommendation on patients with hepatic impairment.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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." Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 20.09.2018, 26.07.2018.	
Darzalex - daratumumab - EMEA/H/C/004077/II/0019, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "Update of sections 4.2, 4.8 and 5.2 of the SmPC in order to include the possibility for a split first dose for the treatment of patients with multiple myeloma, based on the Phase 1b open-label, non-randomised, multicentre Study 54767414MMY1001. The package leaflet is updated accordingly." Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 18.10.2018.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ferriprox - deferiprone - EMEA/H/C/000236/II/0126/G Apotex Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update safety information on the use of Ferriprox in patients with renal or hepatic impairment, based on the final results of two clinical studies LA39-0412 (An Open-Label Study to Compare the Pharmacokinetic Profiles of a Single Dose of Ferriprox in Subjects with Impaired Renal Function and Healthy Volunteers) and LA40-0412 (An Open-Label Study to Compare the Pharmacokinetic Profiles of a Single Dose of Ferriprox in Subjects with Impaired Hepatic Function and Healthy Volunteers). The studies are listed as category 3 study in the RMP. The Package leaflet and labelling are updated accordingly. The RMP version 13.1 has also been submitted to include consequential changes regarding these two clinical studies minor changes requested to be addressed at the next regulatory procedure, as well as the RMP format is updated to conform to GVP Module V Rev 2	Request for supplementary information adopted with a specific timetable.

template. In addition, the Marketing authorisation holder (MAH) took the opportunity to make some minor edits in the PI." Request for Supplementary Information adopted on 15.11.2018.	
Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0084 AstraZeneca AB, Rapporteur: Bart Van der Schueren, "Update of section 4.6 of the SmPC to include new information from a publication on breast-feeding. (Brady et al., 2018). The variation also includes recommendations from the Renewal procedure (EMEA/H/C/002617/0079) which included removal of the additional monitoring section, as well as updates from recommendations in the new EMA Guidelines for Vaccines. The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to introduce minor editorial changes to the Product Information." Request for Supplementary Information adopted on 08.11.2018.	Request for supplementary information adopted with a specific timetable.
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0097/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to reflect the final results from the study IgPro20_3004: Multi-centre, open-label extension study to investigate the long-term safety and efficacy of IgPro20 in maintenance treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) in subjects completing Study IgPro20_3003. The Package Leaflet is updated accordingly. Update of sections 4.2, 5.1 and 5.2 of the SmPC with the total number of patients with primary immunodeficiency (PID) based on the data from 7 previously submitted clinical trials in PID patients. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes in the PI and to bring the Labelling in line with the latest QRD template version 10."	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 15.11.2018.	
Instanyl - fentanyl - EMEA/H/C/000959/II/0047/G Takeda Pharma A/S, Rapporteur: Alexandre Moreau, “Update of section 4.4. to revised the risks of respiratory depression and the risks in patients with Chronic Obstructive Pulmonary Disease based on cumulative saftey data respectively. Update of section 4.5 with regards interactions with others CNS depressants and skeletal muscle relaxants based on literature data. Update of section 4.8 to add loss of consciousness. PL is updtaed accordingly. the MAH took this opportunity to update the labelling in line with QRD latest templates.” Request for Supplementary Information adopted on 15.11.2018.	Request for supplementary information adopted with a specific timetable.
Keytruda - pembrolizumab - EMEA/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.” Opinion adopted on 08.11.2018. Request for Supplementary Information adopted on 13.09.2018.	Positive Opinion adopted by consensus on 08.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0031, Orphan Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, “Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 to add a once-weekly dose regimen for carfilzomib (Kyprolis) at 20/70 mg/m2 in combination with dexamethasone (Kd) for the treatment of the currently indicated patient population. The MAH took the opportunity to implement editorial changes to the SmPC and Patient Information Leaflet (PIL) due to the revised excipients guideline (EMA/CHMP/302620/2017). The PIL is updated accordingly.” Request for Supplementary Information adopted on 15.11.2018.	Request for supplementary information adopted with a specific timetable.

Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0067 Roche Registration GmbH, Rapporteur: Concepcion Prieto Yerro, “Submission of the final study results from 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 paediatric patients with chronic kidney disease on hemodialysis; listed in the paediatric investigation plan (PIP).” Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 20.09.2018.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Otezla - apremilast - EMEA/H/C/003746/II/0021 Celgene Europe BV, Rapporteur: Peter Kiely, “Update of sections 4.2 and 5.1 of Otezla SmPC with information up to 5 years of treatment following the long-term extension phases of 2 pivotal Phase 3 studies of apremilast in the treatment of moderate to severe plaque psoriasis and 3 pivotal and 1 supportive Phase 3 studies in the treatment of active Psoriatic Arthritis (CC-10004-PSA-002, -003, -004, -005 and CC-10004-PSOR-008, - 009) listed as a category 3 study in the RMP (MEA 002).” Opinion adopted on 08.11.2018. Request for Supplementary Information adopted on 13.09.2018.	Positive Opinion adopted by consensus on 08.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Praluent - alirocumab - EMEA/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.” Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 13.09.2018.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Remicade - infliximab - EMEA/H/C/000240/II/0217 Janssen Biologics B.V., Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC in order to add the adverse drug reaction “acute	Request for supplementary information adopted with a specific timetable.

generalised exanthematous pustulosis (AGEP)" with a frequency rare. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet." Request for Supplementary Information adopted on 15.11.2018.	
Revestive - teduglutide - EMEA/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 15.11.2018, 20.09.2018, 26.07.2018, 31.05.2018.	Request for supplementary information adopted with a specific timetable.
Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0053 Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, "Update of section 4.4 and 4.8 of the SmPC in order to extend the warning on cytogenetic abnormalities to reflect the incidence of new genetic abnormalities following data from study ELT116826 (AUS18T) – An open-label, single center, non-randomized, Phase 2, dose modification study Pilot Study of a Thrombopoietin-Receptor Agonist (TPO-R Agonist), Eltrombopag, in Aplastic Anemia Patients With Immunosuppressive-Therapy Refractory Thrombocytopenia. listed as a category 3 study in the RMP" Request for Supplementary Information adopted on 15.11.2018.	Request for supplementary information adopted with a specific timetable.
Rubraca - rucaparib - EMEA/H/C/004272/II/0003, Orphan Clovis Oncology UK Limited, Rapporteur: Jorge Camarero Jiménez, "To update section 5.2 of the SmPC based on final results from Part 1 of study CO-338-45; this is a Phase 1, single-dose study of the disposition of [14C]-radiolabelled rucaparib in patients with advanced solid tumours"	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 15.11.2018.	
Sprycel - dasatinib - EMEA/H/C/000709/II/0064 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Sinan B. Sarac, "Submission of results from existing and new PK analyses together with the review of the literature data on the dasatinib PK profile in fasted conditions to assess implications arising for the recommendation for administration, as requested by the CHMP." Request for Supplementary Information adopted on 15.11.2018.	Request for supplementary information adopted with a specific timetable.
Sutent - sunitinib - EMEA/H/C/000687/II/0070 Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include paediatric study results (from studies A6181196 and ACNS1021) performed in compliance with a paediatric investigation plan (PIP)." Request for Supplementary Information adopted on 08.11.2018, 27.09.2018.	Request for supplementary information adopted with a specific timetable.
Tivicay - dolutegravir - EMEA/H/C/002753/II/0041/G ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of sections 4.4, 4.8 and 5.1 of the SmPC based on week 24 data (secondary analysis) from the pivotal Phase III studies, 204861 [GEMINI-1] and 205543 [GEMINI-2] in ART-naïve adult subjects. Further, SmPC section 4.1 has been updated to include a cross reference to section 4.4 regarding the use of Tivicay in combination with lamivudine as a two-drug regimen. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the SmPC." Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 26.07.2018.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Translarna - ataluren - EMEA/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	Request for Supplementary Information adopted with a specific timetable.

on study PTC124-GD-042-HV (MEA016). The package leaflet is updated accordingly." Request for Supplementary Information adopted on 15.11.2018, 13.09.2018.	
Trulicity - dulaglutide - EMEA/H/C/002825/II/0032 Eli Lilly Nederland B.V., Rapporteur: Greg Markey, "Update of section 4.4 of the SmPC, following a cumulative review of Acute Kidney Injury events undertaken upon request by PRAC (EPITT No 19204), to add information regarding the potential for dulaglutide to possibly contribute to the volume depletion event, which could indirectly contribute to the occurrence of AKI. The Package Leaflet has been updated accordingly." Request for Supplementary Information adopted on 15.11.2018.	Request for Supplementary Information adopted with a specific timetable.
Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0011 Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to add a warning about an increased risk of invasive disease caused by Neisseria meningitidis serogroup B in persons with complement deficiencies or using concomitant treatments inhibiting terminal complement activation." Opinion adopted on 08.11.2018.	Positive Opinion adopted by consensus on 08.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0005, Orphan Ipsen Pharma, Rapporteur: Martina Weise, "Update of section 5.2 of the SmPC in order to add information from an in vivo drug interaction study (study identifier: LX1606.1-110-NRM) to evaluate the effect of multiple doses of concomitant gastric acid reducers such as PPIs on the PK of telotristat ethyl, LP-778902." Request for Supplementary Information adopted on 15.11.2018.	Request for supplementary information adopted with a specific timetable.
Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0067 Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the long-term safety and efficacy data obtained from the open-label extensions (parts II to V) of the phase III study BIA-2093-305. The study was assessed in	Request for supplementary information adopted with a specific timetable.

procedure EMA/H/C/988/P46 025." Request for Supplementary Information adopted on 15.11.2018.	
Zostavax - shingles (herpes zoster) vaccine (live) - EMEA/H/C/000674/II/0120 MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to add the adverse reactions Guillain-Barré syndrome and facial paralysis with frequency "very rare" following a review post-marketing cases; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 08.11.2018.	Request for supplementary information adopted with a specific timetable.
WS1444 **Kisplyx-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 amend the existing warnings on proteinuria and non-gastro-intestianl fistula and to add pneumothorax and nephrotic syndrome as new adverse drug reactions (ADRs) with uncommon frequency. The PL is updated accordingly." Opinion adopted on 25.10.2018. Request for Supplementary Information adopted on 13.09.2018.	Positive Opinion adopted by consensus on 25.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1477 **Lixiana-EMEA/H/C/002629/WS1477/0019** **Roteas-EMEA/H/C/004339/WS1477/0007** Daiichi Sankyo Europe GmbH, Lead Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.4, 4.8 and 5.1 of the SmPC for Lixiana and Roteas to update the clinical efficacy and safety information based on the final results from study DUI176b-D-U311, a phase IIIB prospective, randomised, open-label, blinded evaluator study to evaluate the efficacy and safety of low molecular weight heparin/edoxaban versus dalterparin in venous thromboembolism associated with cancer. In addition, the Worlsharing applicant (WSA) took the opportunity to combine the 15 mg, 30 mg and 60 mg strengths SmPCs, to delete 'aspirin' from section 2 of the Package Leaflet, to update the contact details of the Portuguese local representative in the Package Leaflet for Lixiana	Request for supplementary information adopted with a specific timetable.

only, and to make some corrections to the German, Finnish, Italian, Lithuanian, Maltese and Portuguese translations." Request for Supplementary Information adopted on 08.11.2018.	

B.5.3. CHMP-PRAC assessed procedures

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 (dated 01 Nov 2018) is approved." Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 20.09.2018.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Dificlir - fidaxomicin - EMEA/H/C/002087/II/0033 Astellas Pharma Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of an updated RMP in order to reflect the final outcome (Year 5) of the ClosER study (study AG2012-3459, Clostridium difficile European Resistance surveillance study). The ClosER study was a prospective, longitudinal, pan-European, in vitro sentinel surveillance study of susceptibility of Clostridium difficile to fidaxomicin and other antibiotics. The study is an additional pharmacovigilance activity (Category 3, MEA 002.4) included in the Dificlir RMP. The RMP is also brought in line with the new format requirements in accordance with GVP Module V on risk management systems (Rev 2) and guidance on the format of the risk management plan (RMP) in the EU (Rev 2). RMP version 10.1 is approved with this variation." Opinion adopted on 31.10.2018.	Positive Opinion adopted by consensus on 31.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant,	Request for supplementary information adopted with a specific timetable.

adjuvanted) - EMEA/H/W/002300/II/0036 GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné, “Update of section 4.4 of the SmPC in order to modify the warning related to the waning of protection against Plasmodium falciparum malaria over time. This update is based on final results from study MALARIA-076 listed as a category 3 study in the RMP. This was an open extension to the phase III, multi-centre study MALARIA-055 PRI (110021) to evaluate long-term efficacy, safety and immunogenicity of the GSK Biologicals’ candidate malaria vaccine in infants and children. The RMP version 4.1 has also been submitted.” Request for Supplementary Information adopted on 31.10.2018.	
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0029/G Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber, “Group of variations consisting of the: 2) C.I.3.b: to update section 4.8 on the list of adverse drug reactions and their corresponding frequencies following the PRAC outcome on PSUR procedure (PSUSA/10366/201709). 2) C.I.4: to update sections 4.2,4.4 and 5.2 of the SmPC to add results from a phase I open label parallel study to evaluate the pharmacokinetics of a single oral dose of extended-release combination of naltrexone and bupropion in subjects with normal hepatic function or varying degrees of impaired hepatic function and remove the recommendation to not use naltrexone/bupropion in patients with mild hepatic impairment. The existing warning has also been updated accordingly. The warning related to contraindications has also been aligned to section 4.3 to add end-stage renal failure patients. Consequentially an updated RMP (version 11) has also been submitted. In addition, the MAH takes the opportunity to update the warning on lactose to be in accordance with EC guideline on Guideline on "Excipients in the labelling and package leaflet of medicinal products for human use".”	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 15.11.2018.	
NovoMix - insulin aspart - EMEA/H/C/000308/II/0095 Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "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)" Request for Supplementary Information adopted on 15.11.2018, 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0002 Roche Registration GmbH, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Julie Williams, "Update of sections 4.4, 4.5, 4.6 and 5.1 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 2.3 has also been submitted. Furthermore, the MAH took the opportunity to implement a minor editorial change in section 6.6 of the SmPC with regards to instructions for dilution." Opinion adopted on 31.10.2018. Request for Supplementary Information adopted on 06.09.2018, 12.07.2018, 17.05.2018.	Positive Opinion adopted by consensus on 31.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
OFEV - nintedanib - EMEA/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 6.3 (in revision 2 of the template) is also updated accordingly." Opinion adopted on 31.10.2018. Request for Supplementary Information adopted on 06.09.2018.	Positive Opinion adopted by consensus on 31.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Onivyde - irinotecan hydrochloride trihydrate - EMEA/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." Request for Supplementary Information adopted on 15.11.2018, 18.10.2018, 20.09.2018.	Request for supplementary information adopted with a specific timetable.
SIRTURO - bedaquiline - EMEA/H/C/002614/II/0028, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.4 of the SmPC in order to update the safety information with inclusion of a statement on bedaquiline resistance, further to a request by the PRAC in the context of the assessment of PSUR procedure EMEA/H/C/PSUSA/00010074/201709 (LEG 011). The RMP version 3.0 has also been submitted, updated based on the data triggering the SmPC update and to reflect completion of studies which were assessed in previous procedures. 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 31.10.2018.	Request for supplementary information adopted with a specific timetable.
TAGRISSO - osimertinib - EMEA/H/C/004124/II/0026 AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst, "C.I.11: Submission of an updated RMP version 12.0 following the completion of study D6030C00001 (BLOOM) (A Phase I, Open-label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Anti-Tumour Activity of AZD9291 in Patients with EGFR Mutation Positive Advanced Stage Non-Small Cell Lung Cancer [NSCLC]; BLOOM in order to remove the following safety concerns included as missing information: Use in patients with ECOG performance status≥2" and "Use in patients with symptomatic brain metastases."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 15.11.2018.	
Tamiflu - oseltamivir - EMEA/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." Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 20.09.2018.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tarceva - erlotinib - EMEA/H/C/000618/II/0058 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Update of sections 4.2, 4.5 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 7.1 has been agreed, 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, 4.8, 5.1 and 5.2 of the SmPC. Moreover, Annex II has been updated, as additional risk minimisation measures (educational material) have been deleted." Opinion adopted on 15.11.2018. Request for Supplementary Information adopted on 26.07.2018.	Positive Opinion adopted by consensus on 15.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Toujeo - insulin glargine - EMEA/H/C/000309/II/0106 Sanofi-Aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Submission of the final report from a	Positive Opinion adopted by consensus on 31.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

completed Phase 3b study, EFC13799: "A randomized, open-label, 2-arm, parallel-group, multicenter, 26-week study assessing the safety and efficacy of HOE901-U300 versus Lantus (insulin glargine 100 U/mL) in patients ≥ 65 years with treatment of diabetes mellitus type II (T2DM) inadequately controlled on antidiabetic regimens either including no insulin, or with basal insulin as their only insulin". The RMP (version 5) is updated to reflect the exposure data in elderly patients." Opinion adopted on 31.10.2018.	
Varuby - rolapitant - EMEA/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 (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." Opinion adopted on 31.10.2018. Request for Supplementary Information adopted on 06.09.2018, 12.07.2018.	Positive Opinion adopted by consensus on 31.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Volibris - ambrisentan - EMEA/H/C/000839/II/0054 GlaxoSmithKline (Ireland) Limited, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "Update of sections 4.2 and 5.2 of the SmPC based on results of a juvenile nonclinical toxicology study. The Risk Management Plan version 7.5 (in version 2 of the RMP template) has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct typographical errors	Positive Opinion adopted by consensus on 31.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

including the rash frequency in section 4.8 of the SmPC and the date of renewal; and to introduce minor update in the braille section. Moreover, the MAH took the opportunity to combine version of the SmPCs for the different strengths." Opinion adopted on 31.10.2018. Request for Supplementary Information adopted on 14.06.2018.	

B.5.4. PRAC assessed procedures

PRAC Led **Abraxane - paclitaxel - EMEA/H/C/000778/II/0092** Celgene Europe BV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 17.0 in order to propose the reclassification and/or renaming of known safety concerns associated with the use of paclitaxel in accordance with the new Guideline on Good Pharmacovigilance Practices (GVP) Module V version 2" Request for Supplementary Information adopted on 31.10.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0072** UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP (version 14.0) in order to revise the distribution's list of educational materials (addition of dermatologists) and to revise the RMP in line with the new RMP template (GVP Module V rev.2) including the update of the important identified risks and important potential risks. The PASS protocol for Study UP0038 designed to assess the effectiveness of the educational material is updated to add dermatologists to the healthcare professional study population, to remove Italy and Spain from study participation and to make additional administrative changes. In addition, the MAH took the opportunity to make some administrative changes in the RMP." Request for Supplementary Information adopted on 31.10.2018.	Request for supplementary information adopted with a specific timetable.

PRAC Led **Colobreathe - colistimethate sodium - EMEA/H/C/001225/II/0039** Teva B.V., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, “Submission of the final report from study CLB-MD-08, a Category 3, non-interventional PASS. This is a Safety, Cross-sectional survey study to evaluate the effectiveness of the Colobreathe risk minimisation educational programme among healthcare professionals and patients. This submission also fulfils MEA 012.1.” Request for Supplementary Information adopted on 31.10.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Eurartesim - piperaquine tetraphosphate / artenimol - EMEA/H/C/001199/II/0032** Alfasigma S.p.A., Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, “Submission of an updated RMP version 15.2 (in line with the revision 2 of the RMP template) in order to close the Pregnancy Registry. In addition, the Marketing authorisation holder (MAH) took the opportunity to: - Distribution of a new version of the educational material. - Addition of two important potential risks: `Delayed haemolytic anaemia’ and `Severe skin reactions´, such as Stevens- Johnson syndrome and Toxic Epidermal Necrolysis. - Limitation of the reproductive risk to the first trimester of pregnancy. - Update on several studies. - Inclusion of Eurartesim into the WHO Essential Medicines List. - Update the MAH details.” Request for Supplementary Information adopted on 31.10.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Herceptin - trastuzumab - EMEA/H/C/000278/II/0147** Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “Submission of the final report from the pregnancy registry (H4621g, MotHER), study listed as a category 3 study in the RMP. This is an observational study of pregnancy and	Positive Opinion adopted by consensus on 31.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

pregnancy outcome in women with breast cancer treated with trastuzumab, pertuzumab in combination with trastuzumab, or ADO-trastuzumab emtansine during pregnancy or within 7 months prior to conception. The RMP is being updated accordingly (version 20.0) and in response to comments discussed and received in procedure EMEA/H/C/000278/II/140." Opinion adopted on 31.10.2018.	
PRAC Led **Humira - adalimumab -** **EMEA/H/C/000481/II/0173** AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from of BSRBR-RA (British Society for Rheumatology Biologics Registers Rheumatoid Arthritis); this is a registry in the UK, a prospective observational cohort study, with the primary aim to monitor the long-term safety of new drugs for RA. No changes to the PI are proposed." Opinion adopted on 31.10.2018. Request for Supplementary Information adopted on 08.03.2018.	Positive Opinion adopted by consensus on 31.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Humira - adalimumab -** **EMEA/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 14.2 in order to update the list of safety concerns in relation to prior assessments and in line with GVP Module V. In addition and as a consequence of the RMP update, the Annex II of the Product Information is updated in relation to the additional minimisation measure of the Patient Reminder Card. Consequential minor changes to the SmPC and PL are also made." Opinion adopted on 31.10.2018. Request for Supplementary Information adopted on 06.09.2018.	Positive Opinion adopted by consensus on 31.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **MabThera - rituximab -** **EMEA/H/C/000165/II/0144** Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver,	Positive Opinion adopted by consensus on 31.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC-CHMP liaison: Sinan B. Sarac, “Update the RMP to remove the additional risk minimisation measure of Educational Outreaches for the important identified risk of Infusion Related Reactions and Acute Infusion Related Reactions (IRR). In addition, the RMP has been updated in line with the GVP module V guideline (rev 2). The finally agreed RMP version is 16.1.” Opinion adopted on 31.10.2018. Request for Supplementary Information adopted on 12.07.2018, 12.04.2018.	
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.” Request for Supplementary Information adopted on 31.10.2018, 06.09.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Nulojix - belatacept - EMEA/H/C/002098/II/0050/G** Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, “Submission of the final report from studies (IM103074 and IM103077) listed as category 3 studies in the RMP. Study IM103074 is an observational study designed to assess the pattern of use of balatacept in US transplant recipients in routine clinical practice. Study IM103077 is an observational study designed to assess the patterns of use of belatacept in renal transplantation using the collaborative transplant study. An updated RMP (version 16.0) is submitted in order to reflect the results of the above studies. In addition, the MAH took the opportunity to update the RMP in line with the new RMP template (GVP Module V rev.2), to reflect minor editorial changes and to reflect the earlier completion dates for two remaining studies (IM103075 and IM103076) listed as category 3 studies in the RMP.” Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 31.10.2018.	
PRAC Led **Otezla - apremilast -** **EMEA/H/C/003746/II/0023** Celgene Europe BV, Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Submission of an updated RMP version 11.0 in order to reclassify and/or rename the known safety concerns associated with the use of apremilast in accordance with the new Guideline on GVP Module V. In addition, the RMP is converted to the RMP template Revision 2." Request for Supplementary Information adopted on 31.10.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Tasmar - tolcapone -** **EMEA/H/C/000132/II/0061** Meda AB, Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "Submission of an updated RMP version 7 in order to: - reflect currently available data from post-marketing experience and patient exposure data; - align the RMP with the new GVP RMP template rev.2; - remove the important identified risk 'dopaminergic effects due to increased bioavailability of co-administered levodopa (e.g. dyskinesia)' and the potential risk 'drug interactions with significant clinical consequence including sudden sleep onset'." Request for Supplementary Information adopted on 31.10.2018.	Request for supplementary information adopted with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

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

WS1409 **Keppra-EMEA/H/C/000277/WS1409/0172** UCB Pharma S.A., Lead Rapporteur: Koenraad Norga, Request for Supplementary Information adopted on 13.09.2018.	Positive Opinion adopted by consensus on 08.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation

WS1469 **Glyxambi-EMEA/H/C/003833/WS1469/0016** **Jentadueto-EMEA/H/C/002279/WS1469/0046** **Trajenta-EMEA/H/C/002110/WS1469/0034** Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 15.11.2018.	Request for supplementary information adopted with a specific timetable.
WS1486 **Aluvia-EMEA/H/W/000764/WS1486/0106** **Kaletra-EMEA/H/C/000368/WS1486/0173** **Norvir-EMEA/H/C/000127/WS1486/0151** AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Joseph Emmerich, "To update sections 4.4 Special warnings and precautions for use and 4.8 Undesirable effects of the SmPC with the risk of autoimmune hepatitis as recommended by PRAC (EPITT no: 18956)." Opinion adopted on 25.10.2018.	Positive Opinion adopted by consensus on 25.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hexacima-EMEA/H/C/002702/WS1455/0084/G **Hexaxim-EMEA/H/W/002495/WS1455/0089/G** **Hexyon-EMEA/H/C/002796/WS1455/0088/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 08.11.2018.	Request for supplementary information adopted with a specific timetable.

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

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

Bortezomib Accord - bortezomib - EMEA/H/C/003984/II/0014 Accord Healthcare Limited, Generic, Generic of VELCADE, Rapporteur: Milena Stain Request for Supplementary Information adopted on 13.09.2018.	CHMP agreed to an extension to the clockstop to respond to the RSI adopted on 13.09.2018.
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0084 Pfizer Europe MA EEIG, Rapporteur: Greg	CHMP agreed to an extension to the clockstop to respond to the RSI adopted on 18.10.2018.

Markey, “Update of section 4.2 of the SmPC in order to update the posology information in infants, following the final results from study MenACWY-TT-087 (Study 087); this is a phase IIIb, controlled, randomised, open study aimed to demonstrate the immunogenicity and safety of Nimenrix in healthy infants, given on a 3+1 primary and booster (2, 4, 6 and 15-18 months of age), a 1+1 primary and booster (6 and 15-18 months of age) or as a single dose at 15-18 months of age. The Package Leaflet is updated accordingly. The MAH took the opportunity to include editorial changes in sections 4.4 and 4.8 of the SmPC.” Request for Supplementary Information adopted on 18.10.2018.	

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

esketamine - EMEA/H/C/004535, treatment-resistant depression	
quizartinib - EMEA/H/C/004468, Orphan Daiichi Sankyo Europe GmbH, treatment of acute myeloid leukaemia	Accelerated review
plazomicin - EMEA/H/C/004457, treatment of Complicated urinary tract infection (cUTI), including pyelonephritis; treatment of Bloodstream infection (BSI); treatment of infections due to Enterobacteriaceae	
onasemnogene abeparvovec - EMEA/H/C/004750, Orphan, ATMP AveXis Netherlands B.V., treatment of treatment of spinal muscular atroophy (SMA)	Accelerated review

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

tobramycin - EMEA/H/C/005086, management of chronic pulmonary infection due to Pseudomonas aeruginosa in patients aged 6 years and older with cystic fibrosis (CF). List of Questions adopted on 18.10.2018.	

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

idebenone - EMEA/H/C/003834/S/0012, Orphan
Santhera Pharmaceuticals (Deutschland) GmbH

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

Afinitor - everolimus - EMEA/H/C/001038/R/0060
Novartis Europharm Limited, Rapporteur: Harald Enzmann, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber

BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/R/0027
Teva Pharma B.V., Duplicate, Duplicate of DuoResp Spiromax, Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Anette Kirstine Stark

DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/R/0027
Teva Pharma B.V., Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Anette Kirstine Stark

Envarsus - tacrolimus - EMEA/H/C/002655/R/0014
Chiesi Farmaceutici S.p.A., Rapporteur: John Joseph Borg, PRAC Rapporteur: Ronan Grimes

Gazyvaro - obinutuzumab - EMEA/H/C/002799/R/0031, Orphan
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty

Instanyl - fentanyl - EMEA/H/C/000959/R/0049
Takeda Pharma A/S, Rapporteur: Alexandre Moreau, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Ghania Chamouni

Nuwiq - simoctocog alfa - EMEA/H/C/002813/R/0027
Octapharma AB, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Ulla Wändel Liminga

Plegridy - peginterferon beta-1a - EMEA/H/C/002827/R/0051
Biogen Netherlands B.V., Rapporteur: Johann

Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Julie Williams

Velphoro - mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches - EMEA/H/C/002705/R/0018
Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Julie Williams

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

B.6.7. Type II Variations scope of the Variations: Extension of indication

Dupixent - dupilumab - EMEA/H/C/004390/II/0012
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Kimmo Jaakkola, “Extension of Indication to extend the adult atopic dermatitis indication to the paediatric, 12 years to 17 years (adolescent) patients under Article 8 of the Paediatric Regulation (1901/2006). This study is submitted in accordance with the requirement of Article 46.”

Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0012
Les Laboratoires Servier, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin, “Extension of Indication to include Lonsurf indicated for the treatment of adult patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction, who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, platinum-, and either a taxane- or irinotecan-based chemotherapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
RMP version 6.1 has also been submitted and updated in accordance with Template Rev 2.”

Lucentis - ranibizumab - EMEA/H/C/000715/II/0074/G
Novartis Europharm Limited, Rapporteur:

Kristina Dunder, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Ulla Wändel Liminga, “Extension of Indication to include new indication for Lucentis vial presentation: treatment of retinopathy of prematurity (ROP) in preterm infants; as a consequence, sections 2, 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. In addition, RMP version 18.0 is also submitted. B.IV.1.a.1 – To introduce a low volume high accuracy syringe, as a stand-alone medical device for the administration of the Lucentis 0.2mg paediatric dose (corresponding to 0.02 ml of the Lucentis 10 mg/ml solution for injection in vial presentations).”	
SIRTURO - bedaquiline - EMEA/H/C/002614/II/0033/G, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Ulla Wändel Liminga, “Grouping of an Extension of Indication to include patients 12 years of age and older for SIRTURO and a Type II variation to change the safety information in Section 4.9 of the SmPC. The extension of indication is supported by the Week 24 analysis of Cohort 1 (adolescent subjects aged ≥12 to <18 years) of Study TMC207-C211. Based on these data, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated version of the RMP (version 3.2) was included in the submission.”	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0018 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Extension of Indication to include Tecentriq, in combination with carboplatin and etoposide, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) for Tecentriq; as a consequence, sections sections 4.1, 4.2, 4.8 and 5.1 of the SmPC of the SmPC are updated. The Package Leaflet is updated in accordance. RMP version 8.0 has been submitted”	

Tecentriq - atezolizumab -
EMEA/H/C/004143/II/0019
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Extension of Indication to include Tecentriq, in combination with nab-paclitaxel and carboplatin, indicated for the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC) who do not have EGFR mutant or ALK-positive NSCLC; as a consequence, sections sections 4.1, 4.2, 4.8 and 5.1 of the SmPC of the SmPC are updated. The Package Leaflet is updated in accordance. RMP version 9.0 has been submitted.”

WS1501
Anoro
Ellipta-EMEA/H/C/002751/WS1501/0024
Laventair
Ellipta-EMEA/H/C/003754/WS1501/0027
Glaxo Group Ltd, Lead Rapporteur: Peter Kiely, Lead Co-Rapporteur: Ewa Balkowiec Iskra, “Update of sections 4.1. and 5.1 of the SmPC in order to update the efficacy information regarding the benefit on disease exacerbations of Umeclidinium and Umeclidinium/vilanterol from the CTT116855 study (InforMing the PAthway of COPD Treatment [IMPACT]) and the benefit on disease exacerbations of Vilanterol from the HZC113782 study (Study to Understand Mortality and Morbidity [SUMMIT]).
The Package Leaflet is updated in accordance.”

WS1505
Incruse
Ellipta-EMEA/H/C/002809/WS1505/0023
Rolufta
Ellipta-EMEA/H/C/004654/WS1505/0008
Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead Co-Rapporteur: Peter Kiely, “Update of sections 4.1. and 5.1 of the SmPC in order to update the efficacy information regarding the benefit of Umeclidinium and Umeclidinium/vilanterol from the CTT116855 study (InforMing the PAthway of COPD Treatment [IMPACT]).
The Package Leaflet is updated in accordance.”

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Entyvio - vedolizumab -
EMEA/H/C/002782/II/0037
Takeda Pharma A/S, Rapporteur: Greg Markey

Myalepta - metreleptin -
EMEA/H/C/004218/II/0003, Orphan
Aegerion Pharmaceuticals B.V., Rapporteur: Bart Van der Schueren

Natpar - parathyroid hormone -
EMEA/H/C/003861/II/0013/G, Orphan
Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren

Zinplava - bezlotoxumab -
EMEA/H/C/004136/II/0014
Merck Sharp & Dohme B.V., Rapporteur: Jan Mueller-Berghaus

WS1538
Aflunov-EMEA/H/C/002094/WS1538/0046
Foclivia-EMEA/H/C/001208/WS1538/0041
Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri

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

B.6.10. CHMP-PRAC assessed procedures

B.6.11. PRAC assessed procedures

B.6.12. CHMP-CAT assessed procedures

tisagenlecleucel -
EMEA/H/C/004090/II/0001, Orphan, ATMP
Novartis Europharm Limited

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

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

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

G. ANNEX G

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

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

G.2. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 12-15 November 2018 CHMP plenary

G.3.2. List of procedures starting in November 2018 for December 2018 CHMP adoption of outcomes

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