3 April 2018
EMA/CHMP/56177/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Minutes of the meeting on 19-22 February 2018

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

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).

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1. Introduction

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

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified as included in the list of participants and restrictions. See (current) February 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 19-22 February 2018 (to be published post March 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 alternate member Mark Ainsworth from Denmark replacing Hanne Lomholt Larsen.

1.2. Adoption of agenda

CHMP agenda for 19-22 February 2018

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 22-25 January 2018

The CHMP adopted the CHMP minutes for 22-25 January 2018. The Minutes of the February 2018 CHMP ORGAM meeting held on 12 February 2018, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. betrixaban - EMEA/H/C/004309

treatment of prophylaxis of venous thromboembolism (VTE)

Scope: Oral explanation

Action: Oral explanation to be held on 20 February 2018 at time 14:00

List of Outstanding Issues adopted on 14.12.2017, 12.10.2017. List of Questions adopted on 21.04.2017.

An oral explanation was held on 20 February 2018 at time 14:00. During the oral explanation, the Applicant presented their answers to the outstanding questions.

2.1.2. andexanet alfa - EMEA/H/C/004108

treatment of direct or indirect factor Xa(FXa) inhibitor when reversal of anticoagulation is needed

Scope: Oral explanation

Action: Oral explanation to be held on 20 February 2018 at time 11:00

List of Outstanding Issues adopted on 09.11.2017. List of Questions adopted on 15.12.2016.

An oral explanation was held on 20 February 2018 at time 11:00.

See 3.2

2.1.3. trastuzumab - EMEA/H/C/004361

treatment of metastatic breast cancer, early breast cancer, metastatic gastric cancer

Scope: Oral explanation

Action: Oral explanation to be held on 21 February 2018 at time 16:00

Oral explanation held on 24.01.2018. List of Outstanding Issues adopted on 09.11.2017. List of Questions adopted on 20.07.2017.

The members were informed about additional analysis submitted by the applicant after the January oral explanation.

The CHMP agreed that an oral explanation was not needed at this time.

See 3.2

2.1.4. metreleptin - Orphan - EMEA/H/C/004218

Aegerion Pharmaceuticals Limited; treatment of leptin deficiency (lipodystrophy)

Scope: Oral explanation

Action: Oral explanation to be held on 21 February 2018 at time 09:00

List of Outstanding Issues adopted on 14.12.2017. List of Questions adopted on 18.05.2017.

An oral explanation was held on 21 February 2018 at time 09:00.

See 3.2

2.1.5. Mylotarg - gemtuzumab ozogamicin - Orphan - EMEA/H/C/004204

Pfizer Limited; combination therapy with daunorubicin (DNR) and cytarabine (AraC) for the treatment of adult patients with previously untreated, de novo acute myeloid leukaemia (AML)

Scope: Oral explanation

Action: Oral explanation to be held on 21 February 2018 at time 14:00

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

List of Outstanding Issues adopted on 14.12.2017. List of Questions adopted on 21.04.2017.

The CHMP agreed that oral explanation was not needed at this time.

See 3.1

2.1.6. ciclosporin - EMEA/H/C/004229

for the treatment of moderate dry eye disease in adults

Scope: Oral explanation

Action: Oral explanation to be held on 21 February 2018 at time 11:00

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 23.03.2017.

An oral explanation was held on 21 February 2018 at time 11:45. During oral explanation, the applicant presented their answers to the outstanding questions.

The Committee discussed the status of this application and its remaining outstanding issues. The Committee discussed the involvement of Ad Hoc Expert Group and agreed that involvement is needed.

See 3.2

2.1.7. rucaparib - Orphan - EMEA/H/C/004272

Clovis Oncology UK Ltd; treatment of ovarian cancer

Scope: Oral explanation/SAG report

Action: Oral explanation to be held on 19 February 2018 at time 16:00

Oral explanation held on 08.11.2017. List of Outstanding Issues adopted on 14.12.2017, 09.11.2017, 14.09.2017. List of Questions adopted on 23.03.2017.

The CHMP noted the report from the SAG Oncology meeting.

An oral explanation was held on 19 February 2018 at time 18:00.

See 3.2

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Repatha - evolocumab - EMEA/H/C/003766/II/0017/G

Amgen Europe B.V.

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Kimmo Jaakkola

“Extension of Indication to include reduction of atherosclerotic cardiovascular disease risk in adults with high cardiovascular risk for Repatha based on the results from Study 20110118 (a category 3 PV activity in the Risk Management Plan, MEA 004); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 5.1 of the SmPC to include important mechanistic information for healthcare professionals based on Study 20120153 (a category 3 PV activity, MEA 006).
Submission of an updated RMP version 2.0 in order to add two category 3 studies in the RMP (Study 20160250 and Study 20150338), as well as to update the milestones of five category 3 studies (20110110, 20110271, 20120138, 20130286, 20130295)”

Scope: Oral explanation

Action: Oral explanation to be held on 20 February 2018 at time 16:00

Request for Supplementary Information adopted on 14.12.2017, 14.09.2017.

An oral explanation was held on 20 February 2018 at time 16:00

See 5.1

2.3.2. Sutent - sunitinib - EMEA/H/C/000687/II/0065

Pfizer Limited

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Carmela Macchiarulo

"Extension of Indication to include adjuvant treatment of patients at high risk of recurrent renal cell carcinoma (RCC) following nephrectomy for Sutent; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated based on the study A6181109 ("a randomized double-blind phase 3 study of adjuvant sunitinib vs. placebo in subjects at high risk of recurrent RCC"). The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the SmPC and Package Leaflet and in addition, to fulfil PAM (FU2 22.5). Furthermore, the PI is brought in line with the latest QRD template version 10. Moreover, updated RMP version 16 has been submitted."

Scope: Oral explanation

Action: Oral explanation to be held on 20 February 2018 at time 09:00

Request for Supplementary Information adopted on 09.11.2017, 20.07.2017.

An Oral explanation was held on 20 February 2018 at time 09:00. The Applicant presented the answers to the questions raised, explained further the B/R balance and gave rationale for restricted indication.

See 5.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Alpivab - peramivir - EMEA/H/C/004299

Biocryst UK Limited; treatment of influenza

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 25.01.2018, 12.10.2017. List of Questions adopted on 18.05.2017.

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

The Committee adopted a positive opinion recommending the granting of marketing

authorisation by consensus together with the CHMP assessment report and translation timetable.

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

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

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

The CHMP noted the letter of recommendation dated 20 February 2018.

The summary of opinion was circulated for information.

3.1.2. Amglidia - glibenclamide - Orphan - EMEA/H/C/004379

Ammtek; treatment of neonatal diabetes

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 14.12.2017, 22.06.2017. List of Questions adopted on 24.01.2017.

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

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

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

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

The summary of opinion was circulated for information.

3.1.3. Riarify - beclometasone dipropionate anhydrous / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004836

Chiesi Farmaceutici S.p.A.; symptomatic treatment and reduction of exacerbations in adult patients with chronic obstructive pulmonary disease (COPD) with airflow limitation and who are at risk of exacerbations

Scope: Opinion

Action: For adoption

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

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

The Committee adopted a positive opinion recommending the granting of 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.

3.1.4. Mylotarg - gemtuzumab ozogamicin - Orphan - EMEA/H/C/004204

Pfizer Limited; combination therapy with daunorubicin (DNR) and cytarabine (AraC) for the treatment of adult patients with previously untreated, de novo acute myeloid leukaemia (AML)

Scope: Oral explanation

Action: Oral explanation to be held on 21 February 2018 at time 14:00

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

List of Outstanding Issues adopted on 14.12.2017. List of Questions adopted on 21.04.2017.

The CHMP agreed that an oral explanation was not needed at this time.

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

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

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

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

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

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

The summary of opinion was circulated for information.

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

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

Scope: Opinion

Action: For adoption

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

Oral explanation held on 23.01.2018. List of Outstanding Issues adopted on 20.07.2017. List of Questions adopted on 15.12.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues. The CHMP considered that a greater proportion of women given Nerlynx in the study lived for 2 years without their disease coming back than women given placebo (around 94% versus 92% respectively). However, it is uncertain that this difference in benefit would be seen in clinical practice. Furthermore, it was noted that Nerlynx causes side effects in the digestive system, particularly diarrhoea, which affected most patients and might be difficult to manage. The Committee therefore concluded that the benefits were not enough to outweigh the risk of side effects and recommended that Nerlynx be refused marketing authorisation.

The CHMP adopted a negative opinion by majority (29 negative out of 30 votes), recommending the refusal of the marketing authorisation application. The CHMP adopted the assessment report.

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

The divergent opinion (Kristina Dunder) was appended to the opinion.

The refusal question and answers document was circulated for information.

3.1.6. Trydonis - beclometasone dipropionate anhydrous / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004702

Chiesi Farmaceutici S.p.A.; symptomatic treatment and reduction of exacerbations in adult patients with chronic obstructive pulmonary disease (COPD) with airflow limitation and who are at risk of exacerbations

Scope: Opinion

Action: For adoption

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

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

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

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

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

The summary of opinion was circulated for information.

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

3.2.1. erenumab - EMEA/H/C/004447

indicated for prophylaxis of migraine in adults

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 12.10.2017.

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

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

3.2.2. bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449

treatment of adults infected with human immunodeficiency virus-1 (HIV-1)

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 09.11.2017.

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

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

3.2.3. carmustine - EMEA/H/C/004326

treatment of brain tumors, multiple myeloma, Hodgkin's disease and non-Hodgkin’s lymphomas

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 12.10.2017, 20.07.2017. List of Questions adopted on 13.10.2016.

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

The Committee adopted a 3rd list of outstanding issues with a specific timetable.

3.2.4. sufentanil - EMEA/H/C/004335

management of acute moderate to severe pain

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 20.07.2017.

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.

3.2.5. adalimumab - EMEA/H/C/004866

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, uveitis, paediatric uveitis

Scope: List of outstanding issue

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.

3.2.6. adalimumab - EMEA/H/C/004865

treatment of juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa (HS), uveitis, paediatric uveitis

Scope: List of outstanding issue

Action: For adoption

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

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

3.2.7. adalimumab - EMEA/H/C/004320

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa (HS), Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis, paediatric uveitis.

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.09.2017.

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

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

3.2.8. trastuzumab - EMEA/H/C/004361

treatment of metastatic breast cancer, early breast cancer, metastatic gastric cancer

Scope: List of outstanding issue

Action: Oral explanation to be held on 21 February 2018 at time 16:00

Oral explanation held on 24.01.2018. List of Outstanding Issues adopted on 09.11.2017. List of Questions adopted on 20.07.2017.

The members were informed about additional analysis submitted by the applicant after the January oral explanation.

The CHMP agreed that an oral explanation was not needed at this time.

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

3.2.9. vestronidase alfa - Orphan - EMEA/H/C/004438

Ultragenyx Germany GmbH; indicated for the treatment of Mucopolysaccharidosis VII (MPS VII; Sly syndrome) for patients of all ages

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.09.2017.

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

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

3.2.10. metreleptin - Orphan - EMEA/H/C/004218

Aegerion Pharmaceuticals Limited; treatment of leptin deficiency (lipodystrophy)

Scope: List of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 14.12.2017. List of Questions adopted on 18.05.2017.

An oral explanation was held on 21 February 2018 at time 09:00.

The Committee adopted a 2nd list of outstanding issues.

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

3.2.11. nitisinone - EMEA/H/C/004582

treatment of hereditary tyrosinemia type 1

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 22.06.2017.

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

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

3.2.12. andexanet alfa - EMEA/H/C/004108

treatment of direct or indirect factor Xa(FXa) inhibitor when reversal of anticoagulation is needed

Scope: List of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 09.11.2017. List of Questions adopted on 15.12.2016.

An oral explanation was held on 20 February 2018 at time 11:00.

The Committee adopted a 2nd 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.

3.2.13. prasugrel - EMEA/H/C/004644

prevention of atherothrombotic events

Scope: List of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 14.12.2017. List of Questions adopted on 14.09.2017.

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

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

3.2.14. sodium benzoate - Orphan - EMEA/H/C/004150

Lucane Pharma; treatment of non ketotic hyperglycinemia, urea cycle disorders including carbamoyl-phosphate synthase-1 deficiency, ornithine transcarbamylase deficiency,

citrullinaemia type 1, argininosuccinic aciduria, hyperargininaemia, n-acetylglutamate synthase deficiency, ornithine translocase deficiency and lysinuric protein intolerance

Scope: List of outstanding issue,
Letter from applicant dated 15 February 2018 requesting for an extension of clock stop to respond to the list of outstanding issue

Action: For adoption

List of Questions adopted on 22.06.2017.

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

The Committee adopted a list of outstanding issues.

The CHMP did not agree to the request by the applicant for extension to the clock stop, but agreed on clock stop to respond to the list of outstanding issues with a specific timetable.

3.2.15. ciclosporin - EMEA/H/C/004229

for the treatment of moderate dry eye disease in adults

Scope: List of outstanding issue

Action: Oral explanation to be held on 21 February 2018 at time 11:00

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 23.03.2017.

An oral explanation was held on 21 February 2018 at time 11:45. During oral explanation, the applicant presented their answers to the outstanding questions.

The Committee discussed the status of this application and its remaining outstanding issues. The Committee discussed the involvement of Ad Hoc Expert Group and agreed that involvement is needed.

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

Post-meeting note: draft list of questions to the Ad Hoc Expert Group were adopted via written procedure on 8 March 2018.

3.2.16. naldemedine - EMEA/H/C/004256

treatment of opioid-induced constipation (OIC) in adult patients

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 20.07.2017.

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

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

3.2.17. rucaparib - Orphan - EMEA/H/C/004272

Clovis Oncology UK Ltd; treatment of ovarian cancer

Scope: List of outstanding issue/SAG report

Action: Oral explanation to be held on 19 February 2018 at time 16:00

Oral explanation held on 08.11.2017. List of Outstanding Issues adopted on 14.12.2017, 09.11.2017, 14.09.2017. List of Questions adopted on 23.03.2017.

The CHMP noted the report from the SAG Oncology meeting.

Oral explanation was held on 19 February 2018 at time 18:00.

The Committee discussed a 4th list of outstanding issues.

Post-meeting note: The final LoOI with a specific timetable was adopted via written procedure after the plenary on 23 February 2018.

3.2.18. infliximab - EMEA/H/C/004647

treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, psoriasis and ulcerative colitis

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.09.2017.

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

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

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

3.3.1. entolimod - Orphan - EMEA/H/C/004656

TMC Pharma Services Ltd; treatment of acute radiation syndrome

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.2. inotersen - Orphan - EMEA/H/C/004782

Accelerated assessment

Ionis USA Ltd; treatment of transthyretin amyloidosis (hATTR)

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

Kyowa Kirin Limited; treatment of cutaneous T-cell lymphoma

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. daunorubicin / cytarabine - Orphan - EMEA/H/C/004282

Accelerated assessment

Jazz Pharmaceuticals Ireland Limited; treatment of adults with high-risk acute myeloid leukaemia (AML)

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.5. pegfilgrastim - EMEA/H/C/004802

treatment of neutropenia

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. brigatinib - EMEA/H/C/004248

treatment of anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC)

Scope: Request for an extension of clock stop to respond to the List of Outstanding Issues adopted in January 2018.

Action: For adoption

List of Outstanding Issues adopted on 25.01.2018, 12.10.2017. List of Questions adopted on 22.06.2017.

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

3.4.2. glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004245

indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD)

Scope: Request for an extension of clock stop to respond to the List of Questions adopted in November 2017.

Action: For adoption

List of Questions adopted on 09.11.2017.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted in November 2017.

3.4.3. buprenorphine - EMEA/H/C/004651

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

Scope: Request for an extension of clock stop to respond to the List of questions adopted in January 2018.

Action: For adoption

List of Questions adopted on 25.01.2018

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

3.4.4. abaloparatide - EMEA/H/C/004157

treatment of osteoporosis

Scope: Updated list of questions and draft list of experts for the ad-hoc expert group meeting.

Action: For adoption

Oral explanation held on 13.12.2017. List of Outstanding Issues adopted on 14.12.2017, 20.07.2017, 15.12.2016. List of Questions adopted on 01.04.2016.

The CHMP adopted the updated list of questions and list of experts for the ad-hoc expert group meeting.

3.4.5. pegfilgrastim - EMEA/H/C/004413

treatment of neutropenia

Scope: Request for an extension of clock stop to respond to the List of Outstanding Issues adopted in December 2017

Action: For adoption

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

The CHMP agreed to the request by the applicant for an additional extension of clock stop to respond to the List of Outstanding Issues adopted in December 2017.

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

3.5.1. Aplidin - plitidepsin - Orphan - EMEA/H/C/004354

Pharma Mar, S.A.; treatment of multiple myeloma

Scope: final re-examination timetable, draft list of question to the SAG

Action: For adoption

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

Opinion 14.12.2017

The CHMP adopted the list of experts for the SAG Oncology meeting to be held on 7 March 2018 and adopted a list of questions to this group.

The CHMP adopted final re-examination timetable.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Daxas - roflumilast - EMEA/H/C/001179/X/0035

AstraZeneca AB

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension application to add a new strength of 250 µg in a PVC/PVDC/Alu blister of 28 tablets."

Action: For adoption

List of Outstanding Issues adopted on 14.12.2017. List of Questions adopted on 20.07.2017.

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

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

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

4.1.2. Lynparza - olaparib - Orphan - EMEA/H/C/003726/X/0016/G

AstraZeneca AB

Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Carmela Macchiarulo

Scope: "Extension application to add a new pharmaceutical form associated with a new strength (100mg and 150 mg film-coated tablets) including an extension of the indication to treat patients with platinum-sensitive relapsed ovarian tumours. The extension application is grouped with a type II variation to align the PI for the currently authorised capsule licence with the safety updates proposed for the tablet formulation."

Action: For adoption

List of Outstanding Issues adopted on 14.12.2017. List of Questions adopted on 14.09.2017.

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

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

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

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

4.2.1. Sprycel - dasatinib - EMEA/H/C/000709/X/0056/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Doris Stenver

Scope: "Extension application to introduce a new pharmaceutical form (powder for oral suspension) associated with a new strength (10 mg/ml)

2. C.I.6.a(type II) to include the treatment of children and adolescents aged 1 year to 18 years with Ph+ chronic phase CML for Sprycel. Sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, to add a warning on effects on growth and development in the paediatric population and to update the safety information. The Package Leaflet is updated in accordance."

Action: For adoption

List of Questions adopted on 14.09.2017.

The Committee discussed the issues identified in this application.

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

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

4.3.1. Imbruvica - ibrutinib - Orphan - EMEA/H/C/003791/X/0037

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty

Scope: "Extension application to introduce a new pharmaceutical form (film-coated tablets)

associated with new strengths (140 mg, 280 mg, 420 mg and 560 mg)."

Action: For adoption

The Committee noted the issues identified in this application.

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

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

Genzyme Europe BV

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

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

Action: For adoption

The Committee noted the issues identified in this application.

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

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

Genzyme Europe BV

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

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

Action: For adoption

The Committee discussed the issues identified in this application.

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

4.4. Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008

No items

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

No items

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

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

5.1.1. Bosulif - bosutinib - Orphan - EMEA/H/C/002373/II/0025/G

Pfizer Limited

Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber

Scope: "Extension of Indication to include treatment of adult patients with newly diagnosed Philadelphia Chromosome positive (Ph+) Chronic Phase (CP) Chronic Myelogenous Leukaemia (CML) for Bosulif based on study AV001. In addition, the MAH updated SmPC with safety and efficacy date from studies B1871006 and B1871008. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. Moreover, the updated RMP version 4.0 has been submitted, as part of this application. Furthermore, the Annex IIIA is brought in line with the latest QRD template version 10."

Action: For adoption

Request for Supplementary Information adopted on 09.11.2017.

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

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

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

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report

The CHMP noted the letter of recommendation dated 22 February 2018.

5.1.2. Feraccru - ferric maltol - EMEA/H/C/002733/II/0010

Shield TX (UK) Ltd

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension of indication to widen the indication for Feraccru from the treatment "in adults with Iron deficiency anaemia in patients with IBD" to the treatment of "adults with Iron deficiency"; As a consequence, sections 4.1, 4, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet has been updated accordingly.

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

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017.

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

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

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

The summary of opinion was circulated for information.

5.1.3. Isentress - raltegravir - EMEA/H/C/000860/II/0064/G

Merck Sharp & Dohme Limited

Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams

Scope: "Extension of indication to include treatment of HIV-1 exposed neonates (under the age of 4 weeks) based on safety and PK data from one pivotal Phase 1 study, IMPAACT P1110 (Protocol 080), in a total of 42 HIV-1 exposed full-term infants (defined as ≥37 weeks gestational age and ≥2000 g), who received either 2 single doses of oral suspension, within 48 hours of birth and Day 7-10 of age (Cohort I), or a multiple-dose regimen of raltegravir over the first 6 weeks of age (Cohort II). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly. Further, the suspension volume has been updated from 5 mL to 10 mL for a final suspension concentration of 10 mg/mL to facilitate accurate measurement of the smaller doses required for neonates. As a consequence, the 5 mL syringe previously supplied in the presentation for granules for oral suspension is replaced with 3 new oral dosing syringes of various sizes (1 mL, 3 mL, and 10 mL), from a different (new) supplier. As a consequence, sections 6.5 and 6.6 of the SmPC have been updated and the labelling and instructions for use in the Package Leaflet have been updated accordingly. An updated RMP version 14.0 was agreed during the procedure."

Action: For adoption

Request for Supplementary Information adopted on 09.11.2017.

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

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

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

The summary of opinion was circulated for information.

5.1.4. Kineret - anakinra - EMEA/H/C/000363/II/0056

Swedish Orphan Biovitrum AB (publ)

Rapporteur: Mark Ainsworth, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Doris Stenver

Scope: "Extension of indication to include a new indication for Kineret 100 mg/0.67 ml solution for injection in pre-filled syringe for the treatment of Still's disease, including Systemic Juvenile Idiopathic Arthritis and Adult-Onset Still's Disease. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.6, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet and the RMP (version 4.4) are updated accordingly. Furthermore, the product information is brought in line with the latest QRD template version 10. In addition, the marketing authorisation holder took the opportunity to make some editorial changes in the SmPC and Package leaflet."

Action: For adoption

Request for Supplementary Information adopted on 25.12.2017, 09.11.2017, 20.07.2017.

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

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

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

The summary of opinion was circulated for information.

5.1.5. Lenvima - lenvatinib - Orphan - EMEA/H/C/003727/II/0011/G

Eisai Europe Ltd.

Rapporteur: Bart Van der Schueren, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include treatment of hepatocellular carcinoma (HCC) based on pivotal Study 304. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1, and 5.2 of the SmPC are being updated and the package leaflet is updated accordingly. In addition, section 4.2 of the SmPC is being updated to add that the product can be administered as a suspension in water or apple juice. In addition, the labelling is updated to include the unique identifier. An updated RMP version 10 was provided a part of the application."

Action: For adoption

Request for Supplementary Information adopted on 09.11.2017.

The Committee discussed the issues identified in this application. The Committee discussed the proposed indication and agreed that further clarifications should be asked from the applicant.

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

5.1.6. Repatha - evolocumab - EMEA/H/C/003766/II/0017/G

Amgen Europe B.V.

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of Indication to include reduction of atherosclerotic cardiovascular disease risk in adults with high cardiovascular risk for Repatha based on the results from Study 20110118 (a category 3 PV activity in the Risk Management Plan, MEA 004); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 5.1 of the SmPC to include important mechanistic information for healthcare professionals based on Study 20120153 (a category 3 PV activity, MEA 006).
Submission of an updated RMP version 2.0 in order to add two category 3 studies in the RMP (Study 20160250 and Study 20150338), as well as to update the milestones of five category 3 studies (20110110, 20110271, 20120138, 20130286, 20130295)"

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017, 14.09.2017.

See 2.3

An oral explanation was held on 20 February 2018 at time 16:00

The oral explanation focused on the wording of the indication.

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

5.1.7. RoActemra - tocilizumab - EMEA/H/C/000955/II/0072

Roche Registration Limited

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include "the treatment of juvenile idiopathic polyarthritis (pJIA; rheumatoid factor positive or negative and extended oligoarthritis) in patients 2 years of age and older, who have responded inadequately to previous therapy with methotrexate" for RoActemra; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add information on posology, warnings, safety, efficacy and pharmacokinetics. The Package Leaflet is updated accordingly. The Risk Management Plan version 23.1 is adopted."

Action: For adoption

Request for Supplementary Information adopted on 09.11.2017.

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

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

Assessment Report and translation timetable.

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

The summary of opinion was circulated for information.

5.1.8. Sutent - sunitinib - EMEA/H/C/000687/II/0065

Pfizer Limited

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Carmela Macchiarulo

Scope: "Extension of Indication to include adjuvant treatment of patients at high risk of recurrent renal cell carcinoma (RCC) following nephrectomy for Sutent; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated based on the study A6181109 ("a randomized double-blind phase 3 study of adjuvant sunitinib vs. placebo in subjects at high risk of recurrent RCC"). The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the SmPC and Package Leaflet and in addition, to fulfil PAM (FU2 22.5). Furthermore, the PI is brought in line with the latest QRD template version 10. Moreover, updated RMP version 16 has been submitted."

Action: For adoption

Request for Supplementary Information adopted on 09.11.2017, 20.07.2017.

An oral explanation was held on 20 February 2018 at time 09:00. The Applicant presented the answers to the questions raised, explained further the B/R balance and gave rationale for restricted indication.

The CHMP considered that the evidence that Sutent delays the return of the cancer was not convincing. When data from those patients at highest risk of cancer returning were looked at separately, the benefits of Sutent were still not convincing.

Given the known side effects of the medicine, the Committee concluded that the benefits did not outweigh the risks and recommended that the change to the marketing authorisation of Sutent be refused.

The CHMP adopted a negative opinion by majority (25 negative out of 30 votes) recommending the refusal of the extension of indication. The CHMP adopted the assessment report.

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

The divergent opinions *(*Tuomo Lapvetelainen*,* Daniela Melchiorri, Agnes Gyurasics, Sinan B. Sarac, Mila Vlaskovska) were appended to the opinion.

The refusal question and answers document was circulated for information.

5.1.9. Tagrisso - osimertinib - EMEA/H/C/004124/II/0019

AstraZeneca AB

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer whose tumours have epidermal growth factor receptor exon 19 deletions or exon 21 (L858R) substitution mutations, based on data from the FLAURA study (D5160C00007); a phase III, double-blind, randomised study to assess the efficacy and safety of AZD9291 versus a standard of care epidermal growth factor receptor-Tyrosine Kinase Inhibitor as first-line treatment in patients with epidermal growth factor receptor mutation-positive, locally-advanced or metastatic non-small-cell lung cancer.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly.
In addition, the MAH took the opportunity to implement editorial changes in the SmPC and Package Leaflet.
As part of this application the MAH is requesting an additional year of market protection.
An updated RMP version 8 was submitted as part of the application."

Action: For adoption

The Committee discussed the issues identified in this application. There were questions related to overall survival analysis identified, which should be addressed by the applicant.

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

5.1.10. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0037

PTC Therapeutics International Limited

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include a new population (children from 2 to less than 5 years of age) for Translarna; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and RMP (version 7.1) is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017.

The Committee discussed the issues identified in this application. The Committee noted the remaining uncertainties with dose- and time dependency, which should be resolved.

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

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

Bayer AG

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

Scope: "Extension of Indication to include the prevention of stroke, myocardial infarction and cardiovascular death, and for the prevention of acute limb ischaemia and mortality in adult patients with coronary artery disease (CAD) or peripheral artery disease (PAD) for Xarelto 2.5 mg co-administered with acetylsalicylic acid; as a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance.
In addition, section 4.8 of the SmPC is updated for all other dose strengths (10/15/20 mg) of Xarelto with relevant exposure information based on the provided clinical data.
The updated RMP version 11.1 has also been submitted."

Action: For adoption

The Committee noted the issues identified in this application.

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

5.1.12. Xgeva - denosumab - EMEA/H/C/002173/II/0055

Amgen Europe B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of Indication to include prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with advanced malignancies involving bone (see section 5.1); as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 09.11.2017, 20.07.2017.

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

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

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

The summary of opinion was circulated for information.

5.1.13. Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/II/0023

Novo Nordisk A/S

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

Scope: "Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety information based on cardiovascular outcomes studies conducted a for each of the monocomponents of Xultophy: LEADER (Liraglutide Cardiovascular Outcomes Trial) and DEVOTE (Insulin Degludec Cardiovascular Outcomes Trial).

The MAH is also proposing to reorganise parts of section 5.1 to improve the reader friendliness and to remove Xultophy from the list of medicines under additional monitoring.

The Package Leaflet is updated accordingly.

The RMP version 7.0 has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application, which related to the indication, where further justification is expected on LEADER trial.

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

5.1.14. Zydelig - idelalisib - EMEA/H/C/003843/II/0032/G

Gilead Sciences International Limited

Rapporteur: Filip Josephson, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Patrick Batty

Scope: "C.I.13: Submission of the final report from study 101-08, a phase 2, single-arm study evaluated idelalisib monotherapy and in combination with rituximab in elderly subjects with previously untreated CLL or small lymphocytic lymphoma. Inclusion of this report provides additional safety data to support the evaluation of the use of idelalisib in patients with CLL. Submission of this report is also made in fulfilment of PAM008.

C.I.13: Submission of the final report from study GS-US-312-0123, a phase 3 randomized study evaluated idelalisib in combination with bendamustine and rituximab in subjects with previously untreated CLL. Inclusion of this report is supportive of a complete safety evaluation concerning the use of this combination in patients with CLL."

Action: For adoption

Request for Supplementary Information adopted on 09.11.2017, 18.05.2017.

The CHMP noted the letter from the applicant informing the EMA of the withdrawal of the extension of indication part of the grouped variation (to include its use in combination with bendamustine and rituximab based on the results of the primary analysis of pivotal Study GS-US-312-0115).

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

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

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

The summary of opinion was circulated for information.

5.1.15. WS1274
Tafinlar - dabrafenib - EMEA/H/C/002604/WS1274/0031 & Mekinist - trametinib - EMEA/H/C/002643/WS1274/0023

Novartis Europharm Limited

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

Scope: "Extension of indication to include the combination adjuvant treatment with trametinib and dabrafenib of adult patients with stage III melanoma with a BRAF V600 mutation, following complete resection. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the Mekinist and Tafinlar SmPCs are updated. The Package Leaflet and the Risk Management plan (version 14.0 for Mekinist and version 9.0 for Tafinlar, according to GVP module V revision 2) are updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to correct some typos throughout the Mekinist and Tafinlar product information, to include a cross reference to the Mekinist SmPC in section 4.6 of the Tafinlar SmPC regarding fertility, to update the list of local representatives for Bulgaria, Hungary, Estonia, Latvia and Lithuania in the Package Leaflet of both products."

Action: For adoption

The Committee discussed the issues identified in this application, which related to the uncertainties of clinical effect.

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

5.1.16. WS1278
Yervoy - ipilimumab - EMEA/H/C/2213/WS1278/0053 & Opdivo - nivolumab - EMEA/H/C/3985/WS1278/0042

Bristol-Myers Squibb Pharma EEIG

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

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

Action: For adoption

The Committee discussed the issues identified in this application. It was noted that further clarification is needed regarding the clinical efficacy of the combination therapy.

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

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

5.2.1. Rapamune - sirolimus - EMEA/H/C/000273/II/0164

Pfizer Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include the treatment of patients with lymphangioleiomyomatosis. As a consequence section 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 6.0) are updated in accordance. In addition the MAH took the opportunity to make very minor formatting changes in the Labelling."

Action: For information

Request for Supplementary Information adopted on 25.01.2018, 20.07.2017.

The Committee adopted a revised 2nd request for supplementary information via written procedure on 27 February 2018.

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

No items

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

7. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

7.1. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. regn2810 - H0004844

Metastatic Cutaneous Squamous Cell Carcinoma (CSCC) indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma (mCSCC), or with locally advanced cutaneous squamous cell carcinoma (laCSCC) who are not candidates for surgery

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. lanadelumab – Orphan - H0004806

Shire Pharmaceuticals Ireland Limited, Routine prevention of angioedema attacks and the control of symptoms of hereditary angioedema (HAE) in patients aged 12 years and older

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 6 recommendations for eligibility to PRIME: 1 was accepted to PRIME at the *proof of principle* stage and 5 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. Deltyba - delamanid - Orphan - EMEA/H/C/002552/R/0027

Otsuka Novel Products GmbH

Rapporteur: Greg Markey, Co-Rapporteur: Koenraad Norga, PRAC Rapporteur: Julie Williams

Scope: Renewal

Action: For discussion

Request for Supplementary Information adopted on 25.01.2018.

The renewal of the conditional marketing authorisation was recommended, subject to the conditions and obligations as detailed in this assessment report.

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable, recommending the renewal of the conditional marketing authorisation.

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

9.1.2. WS1316 - Glyxambi-EMEA/H/C/003833/WS1316/0011; Jardiance-EMEA/H/C/002677/WS1316/0037; Synjardy-EMEA/H/C/003770/WS1316/0032

Boehringer Ingelheim International GmbH

Lead Rapporteur: Johann Lodewijk Hillege

Scope: “Update of section 5.1 of the SmPC for Jardiance, Synjardy and Glyxambi in order to add clinically relevant information on hear failure and microvascular endpoints based on the results from trial 1245.25 (EMPA-REG OUTCOME study). The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to update section 4.4 of the SmPC to align the statement regarding diabetic ketoacidosis for all SGLT-2 Inhibitors.”

Action: For adoption

The Committee discussed the issues identified in this application, which related to an update of several sections of the SmPC and PIL.

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

9.1.3. Nulojix - belatacept - EMEA/H/C/002098

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Filip Josephson, Co - Rapporteur: Romaldas Mačiulaitis

Scope: Update on DHPC on shortage and communication plan was adopted via written procedure on 5 February 2018.

Action: For information

The CHMP noted the DHPC and communication plan.

9.1.4. Opdivo - nivolumab - EMEA/H/C/003985/II/0036/G

Bristol-Myers Squibb Pharma EEIG

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

Scope: “C.I.4 (Type II) - Update of sections 4.2, 5.1, 5.2 and 6.6 of the SmPC in order to introduce new dosing regimens and schedule.

C.I.4 (Type II) - Update of sections 4.2, 5.1, 5.2 and 6.6 of the SmPC in order to introduce change the infusion time from 60 minutes to 30 minutes

These changes are based on interim results from study CA209153; this is a phase IIIb/IV safety trial of nivolumab in subjects with advanced or metastatic non-small cell Lung cancer who have progressed during or after receiving at least one prior systemic regimen; The Package Leaflet is updated accordingly. The RMP version 10.0 has also been submitted.”

Action: For adoption

Request for Supplementary Information adopted on 14.09.2017.

The Committee discussed the issues identified in this application. The Committee noted the proposed changes to posology, however the applicant is asked to further discuss the safety of the 30-minute infusion time.

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

9.1.5. Tafinlar - dabrafenib - EMEA/H/C/002604/R/0030

Novartis Europharm Limited

Rapporteur: Filip Josephson, Co-Rapporteur: Bjorg Bolstad,
PRAC Rapporteur: Ulla Wändel Liminga

Scope: Renewal

Action: For discussion

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

Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

9.1.6. Cerdelga - eliglustat - EMEA/H/C/003724/II/0015/G, Orphan

Genzyme Europe BV

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Update of sections 4.2., 4.3., 4.4, 4.5. and 5.2. of the SmPC based on the final data from studies POP13777 "Pharmacokinetics of Oral Single-Dose eliglustat in Subjects with Hepatic Impairment" (MEA003.3) and POP13778 "Pharmacokinetics of Oral Single-Dose eliglustat in Subjects with Renal Impairment" (MEA004.3). Annex II D - Conditions Or Restrictions With Regard To The Safe And Effective Use Of The Medicinal Product of the Product Information, additional risk minimisation measures has likewise been amended. The Package Leaflet is updated accordingly. The RMP version 5.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017.

The Committee discussed the issues identified in this application. The Committee noted the proposed SmPC texts, but further clarifications were asked regarding contraindications.

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

10. Referral procedures

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

No items

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

No items

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

No items

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

No items

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

10.5.1. Scandonest and associated names – mepivacaine - EMEA/H/A-30/1455

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 Scandonest and associated names. Summary of Product Characteristics and Module 3 harmonisation was triggered by the MAH.

List of Questions adopted at October 2017 CHMP

The Committee was reminded of the status of this referral and its remaining outstanding issues. The main issue discussed was related to the current indication wording especially the use of the product in case a vasoconstrictor is contraindicated. The members also reflected on the best way to include the information in the SmPC if deleted from the section 4.1.

The Committee adopted a list of outstanding issues and agreed to a new timetable with a 2-months clock stop.

Submission of responses: 19.04.2018

Re-start of the procedure: 03.05.2018

Rapporteur/co-rapporteur JAR: 16.05.2018

Comments: 21.05.2018

Updated Rapporteur/co-rapporteur JAR circulated to CHMP: 24.05.2018

LoOI/ CHMP opinion: May 2018 CHMP

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

The CHMP noted the February 2018 Early Notification System.

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

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

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Election of Co-opted member

Election of CHMP co-opted member in Quality (non-biologicals) and Pharmacokinetics

Action: For adoption

The CHMP elected Blanka Hirschlerová (CZ) as new CHMP co-opted member.

14.1.2. Joint CHMP-PDCO-CAT Strategic review and Learning meeting to be held in Oslo, Norway under the Bulgarian Presidency of the Council of the European Union

Scope: Discussion on topics to be added on the agenda of the upcoming Strategic Review and Learning meeting 7-9 May 2018

Action: For discussion

The CHMP noted the potential topics to be covered during the meeting in Oslo.

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 5-8 February 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 February 2018

Action: For adoption

The CHMP adopted the list.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 14-16 February 2018

Action: For information

The CHMP noted the CAT draft minutes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 29-30 January 2018

Action: For information

The CHMP noted the report.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at February 2018 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 20-23 February 2018

Action: For information

The CHMP noted the report.

Joint CHMP/PDCO session

Agenda for joint 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 13-15 February 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 19-21 February 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)

Report from the SAWP meeting held on 5-8 February 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. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP February 2018 meeting to CHMP for adoption:

- 11 reports on products in scientific advice and protocol assistance
- 11 reports on products in pre-authorisation procedures
- 00 reports on products in post-authorisation procedures
- 05 reports on products in plasma master file

Action: For adoption

The CHMP adopted the BWP reports

14.3.3. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 21 February 2018.

Action: For adoption

The CHMP adopted the Table of Decisions of the NRG meeting held on 21 February 2018.

Furthermore the CHMP adopted additional names by written procedure on 27 February 2018.

14.3.4. Central Nervous System Working Party (CNSWP)

Chair: Karl Broich/André Elferink

Scope: Guideline on the clinical investigation of medicines for the treatment of Alzheimer's disease and other dementias (CPMP/EWP/553/95 Rev.2)

Action: For adoption

The CHMP adopted the guideline.

14.3.5. Vaccines Working Party (VWP)

Chair: Mair Powell/Svein Rune Andersen

Nomination of additional assessor (observer) to VWP

Action: For adoption

Postponed

14.3.6. Cardiovascular Working Party (CVSWP)

Chair: Kristina Dunder

Vice-chair election – deadline for nominations have been extended.

Nominations should be sent **by 13 April 2018.**

Action: For information

The CHMP noted the extension of the deadline to submit nominations.

14.3.7. Discussion on additional assessors (so called observers) to working parties and drafting groups

CHMP: Tomas Salmonson

Action: For discussion

The CHMP continued the discussion on whether the number of additional assessors nominated to temporary working parties should be limited. The majority of the Chairs who responded to the survey did not consider the number of additional assessors as a problem for the functioning of their working party. The discussion is expected to be concluded at the March CHMP. It was agreed to send the full composition of temporary working parties to CHMP for information.

14.3.8. Composition of drafting groups and temporary working parties in view of goals to be achieved in 2018

CHMP: Tomas Salmonson

Action: For discussion

No other requests to change the composition of the groups have been received since the February CHMP ORGAM. The only request relates to RIWP.

14.3.9. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

SWP response to CMDh Question - Acceptability of statement on potential residues of latex in the Product information of products packed in containers with synthetic rubber stopper (EMA/CHMP/SWP/652246/2017)

Action: For adoption

The SWP position was discussed and minor amendments were proposed. Namely it was agreed not to include the reference to QWP and PRAC as initially proposed in the response, as it will be in CMDh's remit to decide whether formal consultation of these groups is warranted. An updated version will be circulated for adoption via written procedure.

Post-meeting note: SWP final response was adopted via written procedure on 16.03.2018.

14.3.10. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Henrike Potthast

Ibuprofen 200 - 800 mg oral use immediate release formulations product-specific bioequivalence guidance (EMA/CHMP/356876/2017)

Action: For adoption

Postponed

14.3.11. Pharmacogenomics Working Party (PGWP)

Chair: Krishna Prasad/Markus Paulmichl

Guideline on good pharmacogenomic practice (EMA/CHMP/268544/2016)

Rapporteur: Krishna Prasad

Action: For adoption

The CHMP adopted the guideline.

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 2018 Work Plan

Action: For adoption

The CHMP adopted the CHMP 2018 Work Plan.

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Preparedness of the system and capacity increase

Action: For information

The CHMP noted the information.

16. List of participants

List of participants including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the 19 – 22 February 2018 meeting

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Bart Van der Schueren	Member	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Katarina Vučić	Member	Croatia	No interests declared	
Emilia Mavrokordatou	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Mark Ainsworth	Alternate	Denmark	No participation in final deliberations and voting on:	5.1.13. Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/II/0023
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Joseph Emmerich	Alternate	France	No interests declared	
Harald Enzmann	Member (Vice-Chair)	Germany	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Eleftheria Nikolaidi	Member	Greece	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Agnes Gyurasics	Member	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	
Peter Kiely	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No restrictions applicable to this meeting	
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:	5.1.7. RoActemra - tocilizumab - EMEA/H/C/000955/II/0072;
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	Member	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Simona Badoi	Member	Romania	No interests declared	
Dana Gabriela Marin	Alternate	Romania	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Francisek Drafi	Member	Slovakia	No interests declared	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Jorge Camarero Jiménez	Alternate	Spain	No participation in final deliberations and voting on:	5.1.7. RoActemra - tocilizumab - EMEA/H/C/000955/II/0072;
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Greg Markey	Member	United Kingdom	No interests declared	
Nithyanandan Nagercoil	Alternate	United Kingdom	No restrictions applicable to this meeting	
Robert James Hemmings	Co-opted member	United Kingdom	No restrictions applicable to this meeting	
Koenraad Norga	Co-opted member	Belgium	No restrictions applicable to this meeting	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Maria Escudero Galindo	Expert - in person*	Spain	No restrictions applicable to this meeting	3.2.13. prasugrel - EMEA/H/C/004644;
Anne Hasle Buur	Expert - in person*	Denmark	No interests declared	
Hanne Lomholt Larsen	Expert - in person*	Denmark	No interests declared	
Barbara Spruce	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Valerie Lescrainier	Expert - in person*	Belgium	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Anabel Cortés Blanco	Expert - via telephone*	Spain	No interests declared	
Cândida Silva	Expert - via telephone*	Portugal	No interests declared	
Jan Willem van der Laan	Expert - via telephone*	Netherlands	No interests declared	
Cecilia Chisholm	Expert - via telephone*	United Kingdom	No interests declared	
Aghadiuno Olaperi	Expert - via telephone*	United Kingdom	No interests declared	
Dominik Karres	Expert - via telephone*	United Kingdom - MHRA	No interests declared	
Anna Vikerfors	Expert - via telephone*	Sweden	No interests declared	
Jonas Bergh	Expert - via telephone*	Sweden	No restrictions applicable to meetings	
Leon van Aerts	Expert - via telephone*	Netherlands	No interests declared	
Frauke Naumann-Winter	Expert - via telephone*	Germany	No interests declared	
Diana van Riet-Nales	Expert - via telephone*	Netherlands	No interests declared	
Fernando Mendez Hermida	Expert - via telephone*	Spain	No interests declared	
Martina Schussler-Lenz	Expert - via telephone*	Germany	No interests declared	
Niall Fanning	Expert - via telephone*	Ireland	No restrictions applicable to meetings	
Steffen Gross	Expert - via Adobe*	Germany	No interests declared	
Kendra Schafti	Expert - via Adobe*	Germany	No interests declared	
Benjamin Hofner	Expert - via Adobe*	Germany	No restrictions applicable to meetings	
Olga Kholmanskikh	Expert - via Adobe*	Belgium	No interests declared	
George Aislaitner	Expert - via Adobe*	Germany	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Christine Greiner	Expert - via Adobe*	Germany	No interests declared	
Christine Vaculik	Expert - via Adobe*	Austria	No restrictions applicable to meetings	
Representative from the European Commission attended the meeting Meeting run with support from relevant 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)*

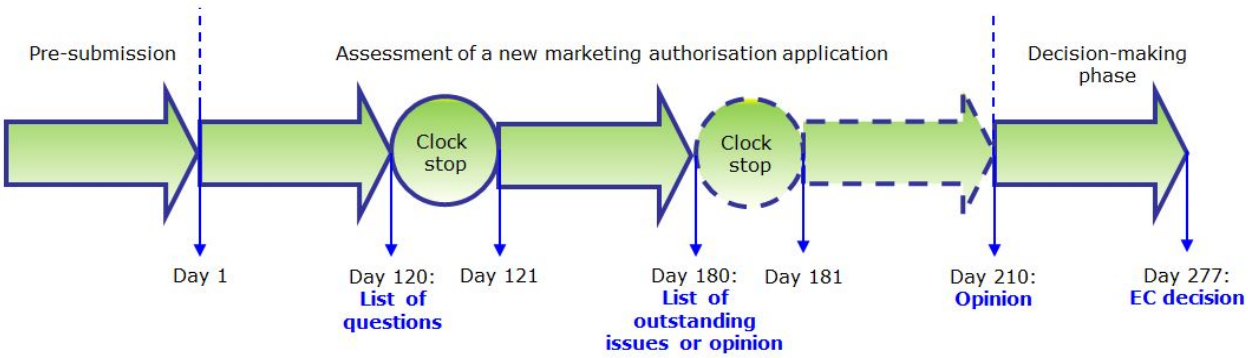
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

3 April 2018
EMA/CHMP/56176/2018

Annex to 19-22 February 2018 CHMP Minutes

Pre submission and post authorisation issues

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
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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 February 2018: **For adoption**	Adopted.

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

Final Outcome of Rapporteurship allocation for February 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

Increlex - mecasermin - EMEA/H/C/000704/S/0050 Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka	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.
Obizur - susoctocog alfa - EMEA/H/C/002792/S/0016 Baxalta Innovations GmbH, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Brigitte Keller-Stanislawski	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.
Orphacol - cholic acid - EMEA/H/C/001250/S/0022, Orphan Laboratoires CTRS, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Patrick Batty	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.
Raxone - idebenone - EMEA/H/C/003834/S/0009, Orphan	Positive Opinion adopted by consensus together with the CHMP assessment report.

Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Carmela Macchiarulo Request for Supplementary Information adopted on 25.01.2018.	The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
Vedrop - tocofersolan - EMEA/H/C/000920/S/0027 Orphan Europe SARL, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty	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.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Lojuxta - lomitapide - EMEA/H/C/002578/R/0029 Aegerion Pharmaceuticals Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Menno van der Elst	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that an additional five-year renewal was required. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Lonquex - lipegfilgrastim - EMEA/H/C/002556/R/0039 Sicor Biotech UAB, Rapporteur: Greg Markey, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Patrick Batty	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that an additional five-year renewal was required. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Atosiban SUN - atosiban - EMEA/H/C/002329/R/0012 Sun Pharmaceutical Industries Europe B.V., Generic, Generic of Tractocile, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary adopted with a specific timetable.

Imatinib Accord - imatinib - EMEA/H/C/002681/R/0020 Accord Healthcare Limited, Generic, Generic of Glivec, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia Request for Supplementary Information adopted on 25.01.2018.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that 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.
Imatinib medac - imatinib - EMEA/H/C/002692/R/0008 medac Gesellschaft fur klinische Spezialpraparate mbH, Generic, Generic of Glivec, Rapporteur: John Joseph Borg, PRAC Rapporteur: Eva A. Segovia,	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Imnovid - pomalidomide - EMEA/H/C/002682/R/0028, Orphan Celgene Europe Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Patrick Batty Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary adopted with a specific timetable.
Imvanex - modified vaccinia ankara virus - EMEA/H/C/002596/R/0032 Bavarian Nordic A/S, Rapporteur: Greg Markey, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Julie Williams	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.
Inflectra - infliximab - EMEA/H/C/002778/R/0056 Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Patrick Batty Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary adopted with a specific timetable.
Memantine ratiopharm - memantine - EMEA/H/C/002671/R/0011 ratiopharm GmbH, Generic, Generic of Ebixa,	Positive Opinion adopted by consensus together with the CHMP assessment report and

Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Dolores Montero Corominas Request for Supplementary Information adopted on 14.12.2017.	translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Nexium Control - esomeprazole - EMEA/H/C/002618/R/0021 Pfizer Consumer Healthcare Limited, Rapporteur: Romaldas Mačiulaitis, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Simona Kudeliene Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary adopted with a specific timetable.
Ovaleap - follitropin alfa - EMEA/H/C/002608/R/0023 Teva B.V., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary adopted with a specific timetable.
Remsima - infliximab - EMEA/H/C/002576/R/0047 Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Patrick Batty Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary adopted with a specific timetable.
Spedra - avanafil - EMEA/H/C/002581/R/0029 Menarini International Operations Luxembourg S.A., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Dolores Montero Corominas Request for Supplementary Information adopted on 14.12.2017.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Stivarga - regorafenib - EMEA/H/C/002573/R/0025 Bayer AG, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary adopted with a specific timetable.

Stribild - elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil - EMEA/H/C/002574/R/0086 Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Julie Williams Request for Supplementary Information adopted on 14.12.2017.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Tafinlar - dabrafenib - EMEA/H/C/002604/R/0030 Novartis Europharm Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ulla Wändel Liminga	See agenda 9.1
Voncento - human coagulation factor VIII / human von willebrand factor - EMEA/H/C/002493/R/0032 CSL Behring GmbH, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Sabine Straus	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

B.2.3. Renewals of Conditional Marketing Authorisations

Deltyba - delamanid - EMEA/H/C/002552/R/0027, Orphan Otsuka Novel Products GmbH, Rapporteur: Greg Markey, Co-Rapporteur: Koenraad Norga, PRAC Rapporteur: Julie Williams Request for Supplementary Information adopted on 25.01.2018.	See agenda 9.1
Natpar - parathyroid hormone - EMEA/H/C/003861/R/0007, Orphan Shire Pharmaceuticals Ireland Ltd, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Almath Spooner Request for Supplementary Information adopted on 25.01.2018.	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.
Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (H5N1) (live attenuated, nasal) -	Positive Opinion adopted by consensus together with the CHMP assessment report.

EMEA/H/C/003963/R/0011 **AstraZeneca AB,** Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Daniela Philadelphy	Based on the review of the available information, the CHMP was of the opinion that an additional five-year renewal was required. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection PRAC recommendations on signals adopted at the PRAC meeting held on 5-8 February 2018 PRAC:	Noted.
Signal of pneumonia: **Olumiant - Baricitinib - EMEA/H/C/004085** Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart Van der Schueren PRAC recommendation on a variation: **For adoption**	Adopted.
Signal of aortitis: **Accofil – Filgrastim – EMEA/H/C/003956** Accord Healthcare Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Sol Ruiz **Filgrastim Hexal – Filgrastim – EMEA/H/C/000918** Hexal AG, Rapporteur: Greg Markey, Co-Rapporteur: Johann Lodewijk Hillege **Grastofil – Filgrastim – EMEA/H/C/002150** Apotex Europe BV, Rapporteur: Robert James Hemmings, Co-Rapporteur: Sol Ruiz **Nivestim– Filgrastim – EMEA/H/C/001142** Hospira UK Limited, Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Ondrej Slanar **Ratiograstim – Filgrastim – EMEA/H/C/000825** ratiopharm GmbH, Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Filip Josephson **Lonquex– lipegfilgrastim – EMEA/H/C/002556** Sicor Biotech UAB, Rapporteur: Greg Markey,	Adopted.

Co-Rapporteur: Johann Lodewijk Hillege **Neulasta – pegfilgrastim – EMEA/H/C/000420** Amgen Europe B.V., Rapporteur: Robert James Hemmings, Co-Rapporteur: Johann Lodewijk Hillege PRAC recommendation on a variation: **For adoption**	
Signal of cutaneous lupus erythematosus: **Siklos - Hydroxycarbamide – EMEA/H/C/000689** Addmedica, Rapporteur: Koenraad Norga, Co-Rapporteur: Eleftheria Nikolaidi PRAC recommendation on a variation: **For adoption**	Adopted.
Signal of interaction possibly leading to decreased levothyroxine efficacy and hypothyroidism: **Norvir - Ritonavir – EMEA/H/C/000127** AbbVie Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Jacqueline Genoux-Hames **Kaletra – Lopinavir/Ritonavir – EMEA/H/C/000368** AbbVie Limited, Rapporteur: Joseph Emmerich, Co-Rapporteur: Jacqueline Genoux-Hames PRAC recommendation on a variation: **For adoption**	Adopted.
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its February 2018 meeting:	
EMEA/H/C/PSUSA/00000428/201706 (botulinum toxin b) CAPS: **NeuroBloc** (EMEA/H/C/000301) (botulinum b toxin), Eisai Ltd, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ana Sofia Diniz Martins, "1 July 2014 – 30 June 2017"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change: Update of Annex II.D to remove the educational materials. In addition, the MAH took the opportunity to implement some minor editorial changes and to update the product information in line with the latest QRD template (version

	10). The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00001369/201704 (fentanyl (transmucosal route of administration)) CAPS: **Effentora** (EMEA/H/C/000833) (fentanyl), Teva B.V., Rapporteur: Martina Weise **Instanyl** (EMEA/H/C/000959) (fentanyl), Takeda Pharma A/S, Rapporteur: Alexandre Moreau **PecFent** (EMEA/H/C/001164) (fentanyl), Kyowa Kirin Services Limited, Rapporteur: Martina Weise NAPS: **NAPS** – EU, PRAC Rapporteur: Ghania Chamouni, "01 May 2014 - 30 April 2017"	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 authorisations for the medicinal products containing the above referred active substance, concerning the following changes: Update of section of 4.2 and 4.4 of the SmPC to add a warning on hyperalgesia and absence of adequate pain control. The Package leaflet is updated accordingly. Update of section 5.1 to introduce information on the possible mechanistic effects of fentanyl on the hypothalamic-pituitary-adrenal or –gonadal axes. The Package leaflet is updated accordingly. Update of section 4.4 to modify the warning on iatrogenic addiction following opioid abuse from rare to known to occur and inclusion of this adverse reaction in section 4.8. In addition, drug abuse and neonatal withdrawal syndrome have been included in section 4.8. The package leaflet has been updated accordingly.
EMEA/H/C/PSUSA/00001714/201707 (icatibant) CAPS: **Firazyr** (EMEA/H/C/000899) (icatibant), Shire Orphan Therapies GmbH, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "12-Jul-2016 to 11-Jul-2017"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended , recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8. of the SmPC to add "urticaria" as an adverse reaction with frequency "unknown". The package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00002886/201707 (temozolomide)	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004

CAPS: **Temodal** (EMEA/H/C/000229) (temozolomide), Merck Sharp & Dohme Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, “13 July 2014 to 12 July 2017”	the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change: Update of section 4.8 of the SmPC to add sepsis (frequency uncommon). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the SmPC and in the package leaflet. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00009255/201707 (perampanel) CAPS: **Fycompa** (EMEA/H/C/002434) (perampanel), Eisai Europe Ltd., Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams, “23 Jan 2017 to 22 Jul 2017”	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 and 4.8 of the SmPC to add a warning on severe cutaneous adverse reactions (SCARs) including drug reaction with eosinophilia and systemic symptoms (DRESS), and to add the same adverse reaction with a frequency not known. 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/00010303/201707 (idelalisib) CAPS: **Zydelig** (EMEA/H/C/003843) (idelalisib), Gilead Sciences International Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, “23-Jan-17 to 22-Jul-17”	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 SPC to add a warning on reported cases of progressive multifocal leukoencephalopathy. 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/00010448/201707 (carfilzomib) CAPS: **Kyprolis** (EMEA/H/C/003790) (carfilzomib), Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Nikica Mirošević Skvrce, "20 January 2017 – 19 July 2017"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 to include herpes zoster infection and confusional state as adverse drug reactions both with a frequency common. Section 4.2 is also aligned with this new information included in section 4.8. 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

Balimek - binimetinib - EMEA/H/C/004052 Pierre Fabre Medicament, treatment of unresectable or metastatic melanoma, Article 3(1) - Indent 3 - New active substance for mandatory CP indication of Regulation (EC) No 726/2004 **WPAR**	For information only. Comments can be sent to the EPL in case necessary.
EnCyzix - enclomifene - EMEA/H/C/004198 Renable Pharma Limited, treatment of hypogonadotrophic hypogonadism, 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.
Hemlibra - emicizumab - EMEA/H/C/004406 Roche Registration Limited, routine prophylaxis to prevent bleeding or reduce the frequency of bleeding episodes in patients with haemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors, 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.
Lamzede - velmanase alfa - EMEA/H/C/003922, Orphan Chiesi Farmaceutici S.p.A., indicated for long-term enzyme replacement therapy in patients with alpha-mannosidosis, New active substance	For information only. Comments can be sent to the EPL in case necessary.

(Article 8(3) of Directive No 2001/83/EC)	
Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029 AstraZeneca AB, for the treatment of hyperkalaemia, 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.
Semglee - insulin glargine - EMEA/H/C/004280 Mylan S.A.S, treatment of diabetes mellitus, 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.
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336 GlaxoSmithkline Biologicals SA, prevention of herpes zoster (HZ) and HZ-related complications, 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.
Vitrolife IVF media - recombinant human albumin solution - EMEA/H/D/004693 DNV Nemko Presafe AS, human assisted reproductive techniques including in-vitro fertilisation procedures, Ancillary medicinal substance/blood derivative substance (Article 1(4)/1(4a) of both Directives No 93/42/EEC and 90/385/EEC)	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

Aloxi - palonosetron - EMEA/H/C/000563/II/0045/G Helsinn Birex Pharmaceuticals Ltd, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
ATryn - antithrombin alfa - EMEA/H/C/000587/II/0033/G Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 15.02.2018.	Request for supplementary information adopted with a specific timetable.
Axumin - fluciclovine (18F) -	Positive Opinion adopted by consensus on

EMEA/H/C/004197/II/0001/G Blue Earth Diagnostics Ltd, Rapporteur: Harald Enzmann Opinion adopted on 15.02.2018. Request for Supplementary Information adopted on 14.12.2017.	15.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Axumin - fluciclovine (18F) - EMEA/H/C/004197/II/0002/G Blue Earth Diagnostics Ltd, Rapporteur: Harald Enzmann Opinion adopted on 15.02.2018. Request for Supplementary Information adopted on 14.12.2017.	Positive Opinion adopted by consensus on 15.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Benepali - etanercept - EMEA/H/C/004007/II/0031/G Samsung Bioepis UK Limited, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
Daptomycin Hospira - daptomycin - EMEA/H/C/004310/II/0006/G Hospira UK Limited, Generic, Generic of Cubicin, Rapporteur: Kolbeinn Gudmundsson Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
Erelzi - etanercept - EMEA/H/C/004192/II/0005/G Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 01.02.2018.	Positive Opinion adopted by consensus on 01.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/II/0053 Omrix Biopharmaceuticals N. V., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 08.02.2018.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Eylea - aflibercept - EMEA/H/C/002392/II/0040/G Bayer AG, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
Eylea - aflibercept - EMEA/H/C/002392/II/0041/G Bayer AG, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
Flixabi - infliximab -	Request for Supplementary Information adopted

EMEA/H/C/004020/II/0020 Samsung Bioepis UK Limited, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 08.02.2018.	with a specific timetable.
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0091 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 15.02.2018. Request for Supplementary Information adopted on 14.12.2017.	Positive Opinion adopted by consensus on 15.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Inflectra - infliximab - EMEA/H/C/002778/II/0057 Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey Opinion adopted on 15.02.2018.	Positive Opinion adopted by consensus on 15.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
NovoSeven - eptacog alfa / eptacog alfa (activated) - EMEA/H/C/000074/II/0101/G Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 15.02.2018.	Request for supplementary information adopted with a specific timetable.
Nucala - mepolizumab - EMEA/H/C/003860/II/0012 GlaxoSmithKline Trading Services Limited, Rapporteur: Nithyanandan Nagercoil Opinion adopted on 01.02.2018.	Positive Opinion adopted by consensus on 01.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Opatanol - olopatadine - EMEA/H/C/000407/II/0035/G Novartis Europharm Limited, Rapporteur: Peter Kiely Opinion adopted on 01.02.2018. Request for Supplementary Information adopted on 19.10.2017.	Positive Opinion adopted by consensus on 01.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0098/G Roche Registration Limited, Rapporteur: Filip Josephson Opinion adopted on 22.02.2018.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0099/G Roche Registration Limited, Rapporteur: Filip Josephson Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 22.02.2018.	
Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/II/0054/G Merck Serono Europe Limited, Rapporteur: Nithyanandan Nagercoil Opinion adopted on 22.02.2018.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0040 Biogen Idec Ltd, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 18.01.2018.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Procysbi - mercaptamine - EMEA/H/C/002465/II/0018, Orphan Chiesi Orphan B.V., Rapporteur: Kristina Dunder Opinion adopted on 15.02.2018.	Positive Opinion adopted by consensus on 15.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Protopic - tacrolimus - EMEA/H/C/000374/II/0072/G LEO Pharma A/S, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 15.02.2018.	Request for supplementary information adopted with a specific timetable.
Remsima - infliximab - EMEA/H/C/002576/II/0048 Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey Opinion adopted on 15.02.2018.	Positive Opinion adopted by consensus on 15.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0020 CSL Behring GmbH, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 08.02.2018.	Request for Supplementary Information adopted with a specific timetable.
Vimizim - elosulfase alfa - EMEA/H/C/002779/II/0022/G, Orphan BioMarin Europe Ltd, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
WS1232 **Infanrix hexa-** **EMEA/H/C/000296/WS1232/0232** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 15.02.2018. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 15.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 14.12.2017.	
WS1233/G **Hexacima-** **EMEA/H/C/002702/WS1233/0070/G** **Hexaxim-** **EMEA/H/W/002495/WS1233/0075/G** **Hexyon-** **EMEA/H/C/002796/WS1233/0074/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 01.02.2018. Request for Supplementary Information adopted on 16.11.2017.	Positive Opinion adopted by consensus on 01.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1237/G **Ambirix-** **EMEA/H/C/000426/WS1237/0089/G** **Fendrix-** **EMEA/H/C/000550/WS1237/0061/G** **Infanrix hexa-** **EMEA/H/C/000296/WS1237/0233/G** **Twinrix Adult-** **EMEA/H/C/000112/WS1237/0123/G** **Twinrix Paediatric-** **EMEA/H/C/000129/WS1237/0124/G** GlaxoSmithKline Biologicals, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 18.01.2018.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1275/G **Filgrastim Hexal-** **EMEA/H/C/000918/WS1275/0038/G** **Zarzio-** **EMEA/H/C/000917/WS1275/0039/G** Hexal AG, Duplicate, Duplicate of Zarzio, Lead Rapporteur: Greg Markey Opinion adopted on 22.02.2018.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1303/G **Hexacima-** **EMEA/H/C/002702/WS1303/0077/G** **Hexaxim-** **EMEA/H/W/002495/WS1303/0082/G** **Hexyon-** **EMEA/H/C/002796/WS1303/0081/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 22.02.2018.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1311/G	Request for Supplementary Information adopted

Aflunov- **EMEA/H/C/002094/WS1311/0040/G** **Foclivia-** **EMEA/H/C/001208/WS1311/0034/G** Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 01.02.2018.	with a specific timetable.
WS1314 **Abasaglar-** **EMEA/H/C/002835/WS1314/0017** **Humalog-** **EMEA/H/C/000088/WS1314/0162** **Liprolog-** **EMEA/H/C/000393/WS1314/0124** Eli Lilly Nederland B.V., Lead Rapporteur: Robert James Hemmings Opinion adopted on 01.02.2018.	Positive Opinion adopted by consensus on 01.02.2018. 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

Afstyla - lonoctocog alfa - **EMEA/H/C/004075/II/0007** CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.4 and 4.8 of the SmPC in order to include information on inhibitor development in Previously Untreated Patients (PUPs), based on the ongoing Phase III study CSL627_3001, evaluating the long-term safety and efficacy of rVIII-Single Chain for routine prophylaxis and on-demand treatment of bleeding episodes in children, adolescents and adults with severe haemophilia A and the outcome of the Referral EMEA/H/A-31/1448. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make editorial changes related to the secondary packaging in section 6.5 and 6.6 of the SmPC, in section 4 of the Labelling and sections 3 and 6 of the Package leaflet. Moreover, the MAH took the opportunity to update the list of local representatives (for Bulgaria) in the Package Leaflet." Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 25.01.2018, 14.12.2017.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Bexsero - meningococcal group B vaccine (rDNA, component, adsorbed) -	Request for supplementary information adopted with a specific timetable.

EMEA/H/C/002333/II/0059 GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, “Update of section 4.2 of the SmPC to update the dosing schedule for infants (2 months to 5 months of age) to allow for 2 primary doses plus 1 booster dose in the second year of life based on the results from study V72_28 and its extension V72_28E1 and to update the intervals between primary doses for children (2 years to 10 years of age) to not less than 1 month based on the results from the extension study V72_28E1. Update of section 4.8 of the SmPC to include the number of subjects exposed to at least 1 dose based on the results from the studies V72_28 and V72_28E1. Update of section 5.1 of the SmPC to update the information about immunogenicity in infants and children based on the results from the studies V72_28 and V72_28E1. The Package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the SmPC and labelling.” Request for Supplementary Information adopted on 22.02.2018, 12.10.2017.	
Caprelsa - vandetanib - EMEA/H/C/002315/II/0029 Genzyme Europe BV, Rapporteur: Alexandre Moreau, “Update of section 5.3 of the SmPC to reflect the results from pre-clinical study titled “ZD6474: A 104 Week Carcinogenicity Study by Oral Gavage in Rats”, study number 521826.” Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
Caprelsa - vandetanib - EMEA/H/C/002315/II/0030 Genzyme Europe BV, Rapporteur: Alexandre Moreau, “Update of section 5.1 of the SmPC to add information on overall survival based on the addendum to clinical study report from the study D4200C00058 (cut-off date 2015): An International, Phase III, Randomized, Double-Blinded, Placebo-Controlled, Multi-Center Study to Assess the Efficacy of ZD6474 versus Placebo in Subjects with Unresectable Locally Advanced or Metastatic Medullary Thyroid Cancer. In addition, the Marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet.”	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 22.02.2018.	
DuoTrav - travoprost / timolol - EMEA/H/C/000665/II/0052 Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, “Update of sections 4.8 of the SmPC in order to add “lid sulcus deepened” and “iris hyperpigmentation” as new adverse drug reactions with frequency not known and to upgrade the frequency of “skin hyperpigmentation (periocular)” from rare to uncommon based on the post-approval review of the safety data. In addition, section 4.8 of SmPC has been updated to align Adverse Drug Reactions table for the travoprost monotherapy. Based on the same safety review, section 4.6 of SmPC has been modified. In addition, the MAH took the opportunity to align the Product information with the currently approved travoprost EU SmPC and QRD version 10 and to update the list of local representatives.” Opinion adopted on 15.02.2018. Request for Supplementary Information adopted on 14.12.2017.	Positive Opinion adopted by consensus on 15.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Eliquis - apixaban - EMEA/H/C/002148/II/0051 Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, “Update of section 4.8 of the SmPC in order to reflect a frequency of all adverse drug reactions for each indication based on clinical trials data. The package leaflet is updated accordingly.” Request for Supplementary Information adopted on 15.02.2018.	Request for supplementary information adopted with a specific timetable.
Humira - adalimumab - EMEA/H/C/000481/II/0170 AbbVie Limited, Rapporteur: Kristina Dunder, “Update of section 4.6 of the SmPC in order to update information on pregnancy and lactation based on results from pregnancy registry (OTIS; study number M03-604) and supported by relevant published literature. The Package Leaflet is updated accordingly.” Request for Supplementary Information adopted on 22.02.2018, 30.11.2017.	Request for supplementary information adopted with a specific timetable.
Humira - adalimumab - EMEA/H/C/000481/II/0172 AbbVie Limited, Rapporteur: Kristina Dunder,	Request for Supplementary Information adopted with a specific timetable.

"Update of sections 5.1 and 5.2 of the SmPC for 40mg/0.8ml and 40mg/0.4 ml Prefilled pen and prefilled syringe in order to add information on non-radiographic axial spondyloarthritis following final results from Humira remission-withdrawal-retreatment study (M13-375) listed in the RMP." Request for Supplementary Information adopted on 01.02.2018.	
Infanrix hexa - diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and Haemophilus influenzae type b (Hib) conjugate vaccine (adsorbed) - EMEA/H/C/000296/II/0234 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 5.1 of the SmPC in order to update the safety information regarding the long term immunity persistence to Hepatitis B at 12/13 years based on the final study CSR DTPa-HBV-IPV-114 in the framework of art. 46 submission (procedure number EMEA/H/C/000296/P46/117). In addition, minor editorial updates are included in section 4.4 of the SmPC to improve clarity." Opinion adopted on 08.02.2018.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Infanrix hexa - diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and Haemophilus influenzae type b (Hib) conjugate vaccine (adsorbed) - EMEA/H/C/000296/II/0235 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 4.5 of the SmPC in order to update the interactions section with additional data on the co-administration with Meningococcal serogroup B vaccine (MenB) in order to facilitate the administration of Infanrix hexa and Bexsero to infants and toddlers based on final results from clinical studies V72P12, V72P13 and V72P16." Request for Supplementary Information adopted on 08.02.2018.	Request for Supplementary Information adopted with a specific timetable.
Invirase - saquinavir - EMEA/H/C/000113/II/0122 Roche Registration Limited, Rapporteur: Milena Stain, "Update of sections 4.2, 4.3, and 4.5 of the SmPC following an update to the Company Core Data Sheet in order to include a cross-	Positive Opinion adopted by consensus on 15.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

reference to a new contraindication against switching from rilpivirine to invirase/ritonavir (section 4.2), to include lurasidone in the contraindications section (section 4.3) and to add information on additional interactions regarding lurasidone, rilpivirine, and tyrosine kinase inhibitors (section 4.5). The existing information regarding the interaction with alfuzosin has been updated to include a warning that co-administration may also cause potentially life-threatening cardiac arrhythmia. The existing information regarding interaction with medicines listed in the section 'neuroleptics' has been moved to the section 'antipsychotics' (section 4.5). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct formatting and minor typographical errors in the PI." Opinion adopted on 15.02.2018. Request for Supplementary Information adopted on 07.12.2017.	
Isentress - raltegravir - EMEA/H/C/000860/II/0069 Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, "Update of section 4.8 of the SmPC of all strengths and of section 5.1 of the 600 mg strength SmPC based on the final results (i.e. through 96 weeks) of study PN292 (ONCEMRK), the pivotal Phase 3 study evaluating the safety and efficacy of raltegravir 1200 mg QD (2 x 600 mg tablets) versus raltegravir 400 mg BID, each in combination with emtricitabine/tenofovir disoproxil fumarate in treatment-naïve HIV-1 infected adult subjects. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC." Opinion adopted on 08.02.2018. Request for Supplementary Information adopted on 07.12.2017.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Izba - travoprost - EMEA/H/C/002738/II/0008 Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information in line with Travoprost 40 µg/mL Eye Drops PI, based on the review of clinical trial and post-marketing data along with	Positive Opinion adopted by consensus on 15.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

literature references. The package leaflet section 4 is updated accordingly." Opinion adopted on 15.02.2018. Request for Supplementary Information adopted on 07.12.2017, 05.10.2017.	
Lucentis - ranibizumab - EMEA/H/C/000715/II/0069 Novartis Europharm Limited, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to include information on the diabetic retinopathy score (DRSS) in diabetic macular edema patients (DME) based on pooled data from studies RFB002D2301 (RESTORE), RFB002D2303 (REVEAL) and RFB002D2305 (REFINE)." Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0003 AbbVie Limited, Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC in order to remove the restriction relating to co-administration with omeprazole, based on new analyses of previously submitted data from the Phase 1 study M14-715 (Open-label study to assess the effect of acid reducing agent on the pharmacokinetics, safety and tolerability of ABT-493/ABT-530 in healthy adult subjects) and on pharmacokinetic as well as efficacy results from Phase 2 and 3 clinical studies for the subjects who were coadministered GLE/PIB and PPIs including omeprazole 40 mg daily. The Package Leaflet is updated accordingly. The MAH also took the opportunity to implement the newly approved ATC code J05AP57 for Maviret." Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 14.12.2017.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0073 Pfizer Limited, Rapporteur: Greg Markey, "Update of sections 4.4 and 5.1 of the SmPC to include information obtained from Study MenACWY-TT-084 regarding the immunogenicity, safety, and tolerability of MenACWY-TT in subjects with anatomic or functional asplenia, in line with the outcome of	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

the Article 46/049 procedure." Opinion adopted on 22.02.2018.	
Odefsey - emtricitabine / rilpivirine / tenofovir alafenamide - EMEA/H/C/004156/II/0027/G Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, "Update of sections 4.8 and 5.1 of the SmPC to provide the 96 weeks clinical study reports for two Odefsey switch studies (GS-US-366-1216 and GS-US-366-1160), listed as category 3 studies in the Risk Management Plan, in fulfilment of post-authorisation measures (PAM) MEA 1.1 and 2.1 respectively. Study GS-US-366-1216: A Phase 3b, Randomized, Double-Blind Switch Study to Evaluate the Safety and Efficacy of Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) Fixed Dose Combination (FDC) in HIV-1 Positive Subjects who are Virologically Suppressed on Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate (FTC/RPV/TDF). Study GS-US-366-1160: A Phase 3b, Randomized, Double-Blind Study to Evaluate Switching from a Regimen Consisting of Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate (EFV/FTC/TDF) Fixed Dose Combination (FDC) to Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) FDC in Virologically-Suppressed, HIV-1 Infected Subjects. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor administrative amendments in the Product Information and minor linguistic amendments to the DE, NO and SV languages." Opinion adopted on 08.02.2018.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0108 Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth, "Update of sections 4.2, 4.4. and 5.1 (Pradaxa 110 and 150 mg) for the SPAF - DVT/PE indication are proposed based on the results from study	Request for supplementary information adopted with a specific timetable.

1160.186 recomending that patients with non-valvular atrial fibrillation who undergo a PCI with stenting can be treated with PRADAXA® in combination with antiplatelets after haemostasis is achieved. The prescriber guide is also being updated. Study 1160.186 is `A prospective Randomised, open label, blinded endpoint (PROBE) study to Evaluate DUAL antithrombotic therapy with dabigatran etexilate (110 mg and 150 mg b.i.d.) plus clopidogrel or ticagrelor vs. triple therapy strategy with warfarin (INR 2.0-3.0) plus clopidogrel or ticagrelor and aspirin in patients with non-valvular atrial fibrillation that have undergone a percutaneous coronary intervention (PCI) with stenting (RE-DUAL PCI)'. In addition, the MAH took the opportunity to correct in section 4.3 a contraindication that refers to concomitant treatment with heparin, based on the data assessed in the context of variation II/103 to reflect the fact that heparin is administered during ablation procedure at the same time as dabigatran." Request for Supplementary Information adopted on 22.02.2018.	
Revlimid - lenalidomide - EMEA/H/C/000717/II/0097, Orphan Celgene Europe Limited, Rapporteur: Alexandre Moreau, "Update of the SmPC section 4.8. to include solid organ transplant rejection as an adverse reaction (ADR) consistent with the Revlimid Company Core Data Sheet (CCDS). This update is based on a Safety Topic Review (STR) to evaluate reports of solid organ transplant rejection after identifying a case report in a literature article as part of routine safety surveillance. The Package leaflet has been updated accordingly. The MAH also took the opportunity to further align the section 4.8 with the CCDS by updating: - table 2 of section 4.8 of the SmPC to identify the ADR terms reported as serious in the Revlimid Relapse/Refractory and/or Transplant Not Eligible MM (TNE MM) clinical trials (MM-009, MM-010, MM-015 and MM-020). - tables in section 4.8 of the SmPC to annotate for ADR terms for which fatal events have been reported."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 15.02.2018.	
Simponi - golimumab - EMEA/H/C/000992/II/0079 Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.1 of the SmPC in order to update the information on maintenance regimen for patients weighing <80 kg based on analyses of PK, efficacy and safety from the pivotal C0524T18 study. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
Sirturo - bedaquiline - EMEA/H/C/002614/II/0026, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, "Submission of the final report from study TMC207TBC3001 listed as a category 3 study in the RMP. This is an interventional, open-label, non-comparative, uncontrolled study without formal efficacy objectives and associated statistical analyses to provide early access to BDQ for subjects with pulmonary infection due to pre-XDR or XDR strains of M. tuberculosis." Opinion adopted on 08.02.2018.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
SonoVue - sulphur hexafluoride - EMEA/H/C/000303/II/0037/G Bracco International B.V., Rapporteur: Alexandre Moreau, "Grouped variation application in order to align with Company Core Data Sheet (CCDS): - Update of section 4.4 of the SmPC in order to reword warning on hypersensitivity reactions. - Update of section 4.4 of the SmPC in order to reword warning for patients with unstable cardiopulmonary status - Update of section 4.4 of the SmPC in order to delete warning for patients on mechanical ventilation or with unstable neurological diseases - Update of section 4.4 of the SmPC in order to delete warning for patients with clinically significant pulmonary disease, including severe chronic obstructive pulmonary disease - Update of section 4.8 of the SmPC in order to revise table with Adverse Drug Reactions - The Package Leaflet is updated accordingly.	Request for supplementary information adopted with a specific timetable.

In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes/corrections in sections 4.8 and 4.9 of the SmPC." Request for Supplementary Information adopted on 22.02.2018.	
Spinraza - nusinersen - EMEA/H/C/004312/II/0004, Orphan Biogen Idec Ltd, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Qun-Ying Yue, "Update of section 4.8 of the SmPC to include new safety information related to hydrocephalus. The PIL and the RMP (new version 7.0) are proposed to be updated accordingly. In addition, the MAH took the opportunity to correct some typographical errors in section 5.1 of the SmPC" Request for Supplementary Information adopted on 08.02.2018.	Request for Supplementary Information adopted with a specific timetable.
Stelara - ustekinumab - EMEA/H/C/000958/II/0060 Janssen-Cilag International NV, Rapporteur: Greg Markey, "Update of sections 4.8 and 5.1 of the SmPC to update the efficacy data following completion of extension of study IM-UNITI - A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Safety and Efficacy of Ustekinumab Maintenance Therapy in Subjects with Moderately to Severely Active Crohns Disease. In addition, the marketing authorisation holder took the opportunity to introduce editorial changes in the SmPC and PL." Opinion adopted on 08.02.2018.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Sutent - sunitinib - EMEA/H/C/000687/II/0068 Pfizer Limited, Rapporteur: Daniela Melchiorri, "Update of section 4.8 of the SmPC in order to include available long-term safety data pooled from 9 MAH sponsored sunitinib clinical studies in patients with metastatic renal cell carcinoma (MRCC) as reported in a recently published literature article. Further, SmPC sections 4.4 and 4.8 have been reworded to improve readability. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and Package Leaflet and to add the unique barcode identifier in the Labelling."	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 18.01.2018.	
Sycrest - asenapine - EMEA/H/C/001177/II/0030 N.V. Organon, Rapporteur: Greg Markey, "Update of sections 4.4 and 4.8 of the SmPC to add safety information regarding falls as a result of postmarketing reports and published literature review. The package leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Denmark, Norway, Slovenia and Slovakia in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.0." Opinion adopted on 08.02.2018.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tarceva - erlotinib - EMEA/H/C/000618/II/0052 Roche Registration Limited, Rapporteur: Sinan B. Sarac, "Update of section 4.4 of the SmPC in order to include recommendations on Epidermal Growth Factor Receptor (EGFR) mutation status testing, to be in line with current technical and scientific progress. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes and to bring the PI in line with the latest QRD template version 10. Moreover, the MAH took the opportunity to make minor correction of section 4.2 of the SmPC. Furthermore, the Annex II has been corrected, as requested by the EMA, to include Educational Material as an additional risk minimisation measure, which has been already in place in the RMP." Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 20.07.2017.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0041 Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 and 4.8 of the SmPC in order to add anaphylactic reaction as a warning and as an adverse reaction with unknown frequency, based on post-marketing experience. The Package Leaflet is updated accordingly. In addition, the Biogen Idec Ltd took the	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

opportunity to bring the PI in line with the latest QRD template version 10." Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 09.11.2017, 14.09.2017.	
Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0050 Biogen Idec Ltd, Rapporteur: Martina Weise, "Submission of the final report from an exploratory pharmacogenomics study. This is an exploratory, retrospective pharmacogenomics analysis to investigate the genomic risk factors for the development of severe and prolonged lymphopenia in patients with multiple sclerosis on treatment with Tecfidera." Opinion adopted on 22.02.2018.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Torisel - temsirolimus - EMEA/H/C/000799/II/0069, Orphan Pfizer Limited, Rapporteur: Harald Enzmann, "Update of sections 4.2 and 4.3 of the SmPC in relation to hepatic impairment for patients with mantle cell lymphoma (MCL), as requested to be clarified during the renewal procedure (EMEA/H/C/000799/R/0065). In addition, the MAH took the opportunity to make minor editorial changes in the Package Leaflet." Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 14.12.2017.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Translarna - ataluren - EMEA/H/C/002720/II/0039, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4, and 5.2 of the SmPC to amend posology recommendations, delete a warning and include pharmacokinetic information about patients with hepatic impairment, respectively, based on final results from study PTC124-GD-033-HV (Study 033) listed as a category 3 study in the RMP (MEA009); the Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0 and to implement some editorial changes." Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 14.12.2017.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0047 ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, "Update of sections 4.5 and 5.2 of the SmPC based on new in vitro studies conducted for abacavir (ABC) and lamivudine (3TC). In addition, the MAH took the opportunity to implement minor corrections in section 5.1 of the SmPC and minor editorial changes in the SmPC." Request for Supplementary Information adopted on 01.02.2018, 09.11.2017.	Request for Supplementary Information adopted with a specific timetable.
Trulicity - dulaglutide - EMEA/H/C/002825/II/0025 Eli Lilly Nederland B.V., Rapporteur: Greg Markey, "Update of sections 4.2 and 5.1 of the SmPC to reflect the use of dulaglutide in Type 2 Diabetes Mellitus patients as add-on to sodium-glucose co-transporter 2 inhibitors (SGLT2i) therapy following completion of a study that investigated the effect of once weekly dulaglutide 1.5 mg or 0.75 mg added to SGLT2is, with or without concomitant use of metformin, on glycemic control and safety over a 24-weeks in patients with inadequately controlled T2DM (Study H9X-MC-GBGE (GBGE)). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
Wakix - pitolisant - EMEA/H/C/002616/II/0011, Orphan BIOPROJET PHARMA, Rapporteur: Joseph Emmerich, "Update of section 5.2 of the SmPC in order to include investigations outcomes regarding the new identified metabolites, as requested in variation EMEA/H/C/002616/II/0004/G." Opinion adopted on 22.02.2018.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xeloda - capecitabine - EMEA/H/C/000316/II/0074 Roche Registration Limited, Rapporteur: Harald Enzmann, "Update of section 4.4 of the SmPC with regards to DPD deficiency genotyping, following a request from the PRAC after assessment of LEG-33.1." Request for Supplementary Information adopted on 01.02.2018.	Request for Supplementary Information adopted with a specific timetable.

Zaltrap - aflibercept - EMEA/H/C/002532/II/0044 sanofi-aventis groupe, Rapporteur: Filip Josephson, “Submission of the final report from study EFC11338 / AFLAME, “A Multinational, Randomized, Double-Blind Study of Aflibercept Versus Placebo with Irinotecan/5-FU Combination (FOLFIRI) in Patients with Metastatic Colorectal Cancer (MCRC) After Failure of an Oxaliplatin Based Regimen"” Opinion adopted on 01.02.2018.	Positive Opinion adopted by consensus on 01.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1267 **Docetaxel Winthrop- EMEA/H/C/000808/WS1267/0054** **Taxotere- EMEA/H/C/000073/WS1267/0129** Aventis Pharma S.A., Lead Rapporteur: Alexandre Moreau, “Update of sections 4.4 and 4.8 of the SmPC in order to add a warning of enterocolitis in patients with neutropenia and to update the safety information on enterocolitis to reflect fatal outcomes based on the review of the MAH global pharmacovigilance data base, worldwide scientific literature and main pharmacovigilance textbooks. Update of section 4.7.of the SmPC in order to update the information related to the risk of potential effects of alcohol and the side effects of this medicinal product on the ability to drive and use machines, in line with the outcome of EMEA/H/C/PSUSA/00001152/201611. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.” Opinion adopted on 01.02.2018. Request for Supplementary Information adopted on 09.11.2017.	Positive Opinion adopted by consensus on 01.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1273/G **Effentora- EMEA/H/C/000833/WS1273/0047/G** Teva B.V., Lead Rapporteur: Martina Weise, “Update of sections 4.2 and 4.4 of the SmPC in order to add a warning on Hyperalgesia following an internal cumulative review. The Package Leaflet is updated accordingly. Update of sections 4.4 and 4.45 of the SmPC in order to add a warning on the interaction of	Request for Supplementary Information adopted with a specific timetable.

fentanyl with benzodiazepines or other CNS depressants including alcohol following an internal cumulative review. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce editorial and format changes in the SmPC and PL." Request for Supplementary Information adopted on 01.02.2018.	
WS1289 **Komboglyze-** **EMEA/H/C/002059/WS1289/0039** **Onglyza-** **EMEA/H/C/001039/WS1289/0045** AstraZeneca AB, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to reflect the new saxagliptin renal cut-off value based on post hoc analysis of pooled data from 9 saxagliptin clinical trials. In addition, the Worksharing applicant proposed to combine SmPCs of different strengths, for both Onglyza and Komboglyze. Furthermore, the Worksharing applicant took the opportunity to include required information on two excipients, sodium and lactose, in sections 2 and 4.4 of the SmPC for Onglyza. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
WS1298 **Enurev Breezhaler-** **EMEA/H/C/002691/WS1298/0024** **Seebri Breezhaler-** **EMEA/H/C/002430/WS1298/0024** **Tovanor Breezhaler-** **EMEA/H/C/002690/WS1298/0027** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, "Submission of the final study report of the Post-Authorisation Efficacy Study (PAES) to compare the efficacy, safety and tolerability of glycopyrronium given at a dose of 44 µg QD and 22 µg BID in patients with stable COPD and moderate to severe airflow obstruction." Request for Supplementary Information adopted on 15.02.2018.	Request for supplementary information adopted with a specific timetable.
WS1300/G **Prezista-**	Positive Opinion adopted by consensus on 15.02.2018. The Icelandic and Norwegian CHMP

EMEA/H/C/000707/WS1300/0091/G **Rezolsta-** **EMEA/H/C/002819/WS1300/0022/G** **Symtuza-** **EMEA/H/C/004391/WS1300/0004/G** Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the Prezista, Rezolsta and Symtuza SmPC to reflect the drug-drug interaction results of the pharmacology studies GS-US-216-1008 (DDI between DRV+COBI and HMG CoA reductase inhibitors rosuvastatin and/or atorvastatin) and GS-US-216-4032 (DDI between DRV+COBI and the hormonal contraceptive medication drospirenone/ethinyl estradiol). Update of section 4.9 of the Prezista, Rezolsta and Symtuza SmPC to remove the recommendations regarding emesis and administration of activated charcoal in case of overdose. In addition, the Worksharing applicant (WSA) took the opportunity to harmonize between Prezista, Rezolsta and Symtuza the DDI information with emtricibine/tenofovir alafenamide, clonazepam, isavuconazole, lomitapide, fentanyl, oxycodone, tramadol and lorazepam. The MAH also took the opportunity to align the in-use shelf-life in label and PL with the SmPC. The PL is updated accordingly and the local representatives detail are updated." Opinion adopted on 15.02.2018.	Members were in agreement with the CHMP recommendation.
WS1310 **Descovy-** **EMEA/H/C/004094/WS1310/0026** **Genvoya-** **EMEA/H/C/004042/WS1310/0040** **Odefsey-** **EMEA/H/C/004156/WS1310/0026** **Vemlidy-** **EMEA/H/C/004169/WS1310/0008** Gilead Sciences International Limited, Lead Rapporteur: Robert James Hemmings, "Update of section 4.5 of the Descovy, Genvoya, Odefsey and Vemlidy SmPCs in order to include some information on the drug-drug interaction with sofosbuvir/velpatasvir/voxilaprevir fixed dose combination based on the results of study GS-	Request for Supplementary Information adopted with a specific timetable.

US0367-1657, listed as a category 3 in the Vemlidy RMP, in order to fulfil MEA 006 for Vemlidy. Study GS-US0367 is a phase I multiple dose study to evaluate the drug-drug interaction potential between sofosbuvir/velpatasvir/voxilaprevir fixed dose combination and HIV anti-retrovirals in healthy subjects. In addition, the Worksharing applicant (WSA) took the opportunity to make some small corrections to section 4.5 of the SmPC for Descovy, Genvoya, Odefsey and Vemlidy and to make corrections to the DE, ES, HU, IS, IT, LV, NO, PT, SL and SV translations for Vemlidy." Request for Supplementary Information adopted on 01.02.2018.	
WS1316 **Glyxambi-EMEA/H/C/003833/WS1316/0011** **Jardiance-EMEA/H/C/002677/WS1316/0037** **Synjardy-EMEA/H/C/003770/WS1316/0032** Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC for Jardiance, Synjardy and Glyxambi in order to add clinically relevant information on hear failure and microvascular endpoints based on the results from trial 1245.25 (EMPA-REG OUTCOME study). The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to update section 4.4 of the SmPC to align the statement regarding diabetic ketoacidosis for all SGLT-2 Inhibitors." Request for Supplementary Information adopted on 22.02.2018.	See agenda 9.1
WS1322 **Genvoya-EMEA/H/C/004042/WS1322/0042** **Stribild-EMEA/H/C/002574/WS1322/0090** **Tybost-EMEA/H/C/002572/WS1322/0042** Gilead Sciences International Limited, Lead Rapporteur: Robert James Hemmings, "Update of Section 4.5 of the SmPC for Genvoya, Tybost and Stribild based on data on Drug-drug Interaction between cobicistat containing products and Direct Oral Anticoagulants (DOACs).	Request for supplementary information adopted with a specific timetable.

The Patient Leaflet (PIL) has been updated for all three products as a consequence. The Worksharing MAH has taken this opportunity to introduce some minor administrative amendments throughout the product information for all three products respectively, as needed (i.e., correction of abbreviations, correction of formatting errors and correction of spelling mistakes). Minor administrative update is also made to Annex III for all three products. The MAH has also taken this opportunity to implement some minor linguistic amendments (MLAs) to the translations of the respective product information annexes: - Genvoya: CS, DA, DE, FI, HR, HU, IS, NO, PT and RO languages - Tybost: DA, ES and HU languages - Stribild: DA, DE, ES, FI, FR, IS, LV, MT, NO and RO languages" Request for Supplementary Information adopted on 22.02.2018.	
WS1330 **Bretaris Genuair-** **EMEA/H/C/002706/WS1330/0036** **Brimica Genuair-** **EMEA/H/C/003969/WS1330/0019** **Duaklir Genuair-** **EMEA/H/C/003745/WS1330/0019** **Eklira Genuair-** **EMEA/H/C/002211/WS1330/0036** AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, "Update of sections 4.2 and 6.6 of the SmPC in order to optimize the Instructions for Use (IFU) for the products evaluated in a human factors study. The Package Leaflet is updated accordingly. In addition, the applicant has taken the opportunity to make some minor editorial corrections in the labelling section (Annex III A) of the Product Information for Duaklir Genuair and Brimica Genuair." Opinion adopted on 22.02.2018.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1332 **Renvela-** **EMEA/H/C/000993/WS1332/0041** **Sevelamer carbonate Zentiva-** **EMEA/H/C/003971/WS1332/0013**	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Genzyme Europe BV, Lead Rapporteur: Bart Van der Schueren, “Update of sections 4.2 and 6.6 of the SmPC in order to include the use of food and beverage as an alternative to water for administration of sevelamer carbonate powder for oral suspension. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to revise the Annex A.” Opinion adopted on 22.02.2018.	

B.5.3. CHMP-PRAC assessed procedures

Alecensa - alectinib - EMEA/H/C/004164/II/0010 Roche Registration Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, “Update of sections 4.2 and 5.2 of the SmPC in order to update information on effect of hepatic impairment on PK of alectinib based on final results from study NP29783. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest EC guidance regarding warning statements on sodium.” Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
Amyvid - florbetapir (18F) - EMEA/H/C/002422/II/0029 Eli Lilly Nederland B.V., Rapporteur: Harald Enzmann, PRAC Rapporteur: Valerie Strassmann, “Submission of the final report from study I6E-MC-AVBF listed as a category 3 study in the RMP. This is a non-interventional category 3 PASS: European Drug Usage Survey for Amyvid to assess the usage pattern of Amyvid in the EU. Section 4.4 of SmPC has been reformatted as result of this study. The RMP version 3.1 has also been submitted.” Request for Supplementary Information adopted on 08.02.2018.	Request for supplementary information adopted with a specific timetable.
Atripla - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/000797/II/0127/G Bristol-Myers Squibb and Gilead Sciences Ltd., Rapporteur: Martina Weise, PRAC Rapporteur:	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Martin Huber, “Update of sections 4.3, 4.4, 4.5 and 5.1 of the Atripla SmPC to include the results of the final study report for Study AI266959,; this is an interventional study to determine the concentration-electrocardiographic effects of efavirenz in healthy subjects enriched for Cyp2b6 Polymorphism, to fulfill the legally binding measure (LEG) requested by the PRAC following to the conclusion of the PSUR (EMA/PRAC/679906/2016) for Sustiva. Update of sections 4.4 and 4.8 of the Atripla SmPC to add catatonia as a Psychiatric symptom following an assessment of catatonia cases reported in the literature and via the United States (US) Food and Drug Administration Adverse Event Reporting System (FAERS). Submission of an updated RMP v.17 to remove malignant neoplasms as a potential risk, in line with GVP Module V, and approved by PRAC following the conclusion of the latest annual report on malignancy events (MEA 039.6). The MAH took the opportunity to implement minor editorial changes in the Product Information and minor linguistic amendments to the following languages: DA, DE, ES, FI, FR, HR, HU, IS, MT, NO, PT and SV” Opinion adopted on 08.02.2018.	
Cerdelga - eliglustat - EMEA/H/C/003724/II/0015/G, Orphan Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Dolores Montero Corominas, “Update of sections 4.2., 4.3., 4.4, 4.5. and 5.2. of the SmPC based on the final data from studies POP13777 “Pharmacokinetics of Oral Single-Dose eliglustat in Subjects with Hepatic Impairment” (MEA003.3) and POP13778 “Pharmacokinetics of Oral Single-Dose eliglustat in Subjects with Renal Impairment” (MEA004.3). Annex II D - Conditions Or Restrictions With Regard To The Safe And Effective Use Of The Medicinal Product of the Product Information, additional risk minimisation measures has likewise been amended. The Package Leaflet is updated accordingly. The RMP version 5.0 has also been submitted.” Request for Supplementary Information adopted on 22.02.2018, 14.12.2017.	See agenda 9.1

Defitelio - defibrotide - EMEA/H/C/002393/II/0026, Orphan Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, "Update of sections 4.8 and 5.1 of the SmPC in order to update the frequencies of adverse reactions included in the tabulated list of adverse reactions and to update the clinical efficacy and safety information based on the results from study 2006-05 listed as category 3 in the RMP. This is a phase 3, open-label expanded access study designed to provide access to defibrotide as an investigational new drug to patients with severe hepatic veno-occlusive disease. The final study report is being submitted together with the revised risk management plan (version 3.0). The package leaflet is also being updated accordingly. In addition, the MAH took the opportunity to bring the SmPC in line with the latest QRD template (version 10), to update the list of local representatives in the package leaflet and to correct a translation error in the Polish, Finnish, Danish and Latvian languages." Request for Supplementary Information adopted on 08.02.2018, 30.11.2017, 28.09.2017.	Request for Supplementary Information adopted with a specific timetable.
Defitelio - defibrotide - EMEA/H/C/002393/II/0027, Orphan Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, "Submission of an updated RMP version 4.0 in order to re-classify the imposed non-interventional PASS listed as a category 2 study in the RMP (specific obligation) to a study listed as a category 3 in the RMP (required additional pharmacovigilance activities). This study is an observational registry (DF-VOD2013-03-REG) which aims to record safety and outcome data in patients diagnosed with severe VOD following HSCT treated or not with defitelio. The Annex II of the product information is updated accordingly." Request for Supplementary Information adopted on 22.02.2018, 09.11.2017.	Request for supplementary information adopted with a specific timetable.
Fotivda - tivozanib - EMEA/H/C/004131/II/0002 EUSA Pharma (UK) Limited, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Jolanta Gulbinovic, "Update of the section 5.2 of the SmPC with additional information on transporter proteins	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

based on the results of an in vitro interaction transporter study. The updated RMP version 2.0 was also submitted." Opinion adopted on 08.02.2018.	
Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/II/0064 Gilead Sciences International Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of section 4.2, 4.4,4.8, 5.1 and 5.2 of the SmPC in order to update the safety and efficacy information based on interim results from study GS-US-334-0154 listed as a category 3 study in the RMP; this is a study to evaluate the safety, efficacy and pharmacokinetics of treatment with Ledipasvir/Sofosbuvir Fixed-Dose Combination for 12 weeks in Genotype 1 or 4 HCV-Infected Subjects with Renal Insufficiency; the Package Leaflet is updated accordingly. The RMP version 3.2 has also been submitted." Request for Supplementary Information adopted on 22.02.2018.	Request for supplementary information adopted with a specific timetable.
Imraldi - adalimumab - EMEA/H/C/004279/II/0002/G Samsung Bioepis UK Limited (SBUK), Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga Opinion adopted on 08.02.2018. Request for Supplementary Information adopted on 30.11.2017.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0037/G Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus, "Update of section 4.4 of the SmPC to add information regarding the risks of encephalitis, sarcoidosis and graft versus host disease (GVHD), including the occurrence of fatal GVDH events that have been reported with pembrolizumab in patients with a history of allogeneic Haematopoietic Stem Cell Transplantation (HSCT), and update of section 4.8 of the SmPC to add encephalitis as a 'rare' new ADR. Further, section 4.2 of the SmPC has been updated to include the recommendation to permanently discontinue pembrolizumab at the first occurrence of Grade 3 or 4 encephalitis and Grade 3 or 4 Guillain-Barré syndrome (GBS). The Package Leaflet has been updated	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

accordingly as well as the Annex II; the information regarding educational material in the section 'additional risk minimisation measures'. In addition, the MAH took the opportunity to implement minor changes in the SmPC section 5.1 and editorial changes in the SmPC and Package Leaflet. An updated RMP version 14.0 was agreed during the procedure." Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 14.12.2017.	
Neulasta - pegfilgrastim - EMEA/H/C/000420/II/0093/G Amgen Europe B.V., Rapporteur: Robert James Hemmings, PRAC Rapporteur: Patrick Batty Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 14.12.2017, 14.09.2017, 22.06.2017.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Opdivo - nivolumab - EMEA/H/C/003985/II/0036/G Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, "C.I.4 (Type II) - Update of sections 4.2, 5.1, 5.2 and 6.6 of the SmPC in order to introduce new dosing regimens and schedule. C.I.4 (Type II) - Update of sections 4.2, 5.1, 5.2 and 6.6 of the SmPC in order to introduce change the infusion time from 60 minutes to 30 minutes These changes are based on interim results from study CA209153; this is a phase IIIb/IV safety trial of nivolumab in subjects with advanced or metastatic non-small cell Lung cancer who have progressed during or after receiving at least one prior systemic regimen; The Package Leaflet is updated accordingly. The RMP version 10.0 has also been submitted." Request for Supplementary Information adopted on 22.02.2018, 14.09.2017.	See agenda 9.1
RoActemra - tocilizumab - EMEA/H/C/000955/II/0074/G Roche Registration Limited, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski Opinion adopted on 22.02.2018. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 11.01.2018.	
Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391/II/0003/G Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams, "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to reflect the week-48 results from 2 studies (TMC114FD2HTX3001 and TMC114IFD3013) listed as category 3 studies in the RMP; these are phase 3 studies to evaluate the efficacy and safety of D/C/F/TAF once daily fixed-dose combination regimen versus a regimen consisting of DRV/COBI FDC co-administered with FTC/TDF FDC in ARV treatment-naïve HIV-1 infected subjects (study TMC114FD2HTX3001) and to evaluate switching to a D/C/F/TAF once-daily single-tablet regimen versus continuing the current regimen consisting of a boosted protease inhibitor combined with FTC/TDF in virologically-suppressed, HIV-1 infected subjects (study TMC114IFD3013). The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to make minor editorial revision in the product information." Request for Supplementary Information adopted on 08.02.2018.	Request for Supplementary Information adopted with a specific timetable.
Tamiflu - oseltamivir - EMEA/H/C/000402/II/0128 Roche Registration Limited, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of section 4.6 of the SmPC in order to reflect the final study results from non-interventional safety study BV29684, which assessed the safety of oseltamivir exposure in pregnant women, and was listed as a category 3 study in the RMP (MEA099). The RMP version 15.0 has also been updated to reflect the study results." Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 09.11.2017, 20.07.2017.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0002/G Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Sanches de Castro Lopes Silva, “Grouped variations consisting of: 1) update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add myocarditis as a new adverse reaction based on the results of a cumulative review of cases of suspected myocarditis. As a consequence, the information regarding the posology and special warnings have been updated. Annex II, the Package Leaflet and the RMP (version 2.0) have been updated accordingly; 2) update of the RMP to add haemolytic anaemia as a new important identified potential risk” Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 14.12.2017.	
Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0036/G Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, “Update of sections 4.4 and 4.5 of the SmPC concerning the adverse reaction “flushing” based on submission of the final study reports for study 109HV321 and study 109MS406. Study 109HV321 is a randomized, double-blind, phase 3b study to evaluate the safety and tolerability of BG00012 when administered as 240 mg twice daily dose regimen with and without aspirin compared to placebo or following a slow titration (Category 3). Study 109MS406 (ASSURE) is a phase 4, randomized, double-blind study with a safety extension period to evaluate the effect of aspirin on flushing events in subjects with relapsing-remitting multiple sclerosis treated with dimethyl fumarate delayed-release capsules (Category 4).” Opinion adopted on 08.02.2018. Request for Supplementary Information adopted on 28.09.2017, 05.05.2017.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0037 Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, “Update of section 4.5 of the SmPC to update the information of concomitant administration of non-live vaccines based on the clinical study report for study 109MS307; this is a category 3, open-label study aimed to assess the immune response to vaccination in Tecfidera-treated patients versus Interferon-treated patients with relapsing forms of multiple sclerosis. The	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

package leaflet is updated accordingly. The RMP version 10.0 has also been approved." Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 12.10.2017, 05.05.2017.	
Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0002/G, Orphan Ipsen Pharma, Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski, "Submission of the final report from studies LX301 (pivotal phase III study) and LX303 (supportive phase III study) two randomised, multicentre, double-blind, placebo-controlled studies listed as category 3 studies in the RMP. The objective of study LX301 is to evaluate the efficacy and safety of telotristat etriprate in patients with carcinoid syndrome not adequately controlled by Somatostatin Analog (SSA) therapy; while the objective of study LX303 is to evaluate the safety and efficacy of telotristat etiprate in patients with carcinoid syndrome. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to provide updated safety data from the long-term extension study LX302; a phase 3, multicentre, open-label study to further evaluate the safety and tolerability of telotristat. The RMP (version 3.0) was updated to reflect those safety data. The requested group of variations proposed amendments to the Risk Management Plan (RMP)." Opinion adopted on 08.02.2018.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1292 Evotaz-EMEA/H/C/003904/WS1292/0019 Reyataz-EMEA/H/C/000494/WS1292/0114 Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Joseph Emmerich, Lead PRAC Rapporteur: Caroline Laborde, "Update of section 4.3 and 4.5 of the SmPC in order to add a contraindication with lurasidone to reflect this interaction based on literature data. The Package Leaflet is updated accordingly. The RMP of Reyataz/Evotaz versions 14.1 and 6.1 respectively have been submitted." Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 14.12.2017.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.4. PRAC assessed procedures

PRAC Led **Eperzan - albiglutide -** **EMEA/H/C/002735/II/0029/G** GlaxoSmithKline Trading Services Limited, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "II: C.I.11.b - Update of the RMP to amend Study 201805 (category 3 study): "Observational Study of the Risk of Common Malignant Neoplasms and Malignant Neoplasms of Special Interest (Thyroid and Pancreatic Cancer) in Subjects Prescribed Albiglutide Compared to Those Prescribed Other Antidiabetic Agents", in order to use a different database to study the risk of neoplasms in association with albiglutide exposure II: C.I.11.b – Update of the RMP to add a new category 3 study as an additional pharmacovigilance activity – Study 207351: "Observational Study to Assess Maternal and Fetal Outcomes following exposure to Albiglutide during Pregnancy"" Opinion adopted on 22.02.2018. Request for Supplementary Information adopted on 09.11.2017, 22.06.2017, 26.01.2017.	Positive Opinion adopted by consensus on 22.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Eylea - aflibercept -** **EMEA/H/C/002392/II/0039** Bayer AG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report from the post authorisation safety study 16526, listed as a category 3 study in the RMP. This is an observational study to evaluate the physician and patient knowledge of safety and safe use information for Aflibercept in Europe as stated in the EU Educational Material of Eylea." Request for Supplementary Information adopted on 08.02.2018, 30.11.2017.	Request for Supplementary Information adopted with a specific timetable.
PRAC Led **Inflectra - infliximab -** **EMEA/H/C/002778/II/0054** Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Submission of the final study report of the Post-Marketing Surveillance of Inflectra 100 mg (Infliximab) to Evaluate Its	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Safety and Efficacy in Korea. The study intended to identify any unexpected adverse event and serious adverse event and frequency and pattern of occurrence of adverse events under the condition of general clinical practice and determine any factor that may affect the safety and efficacy." Opinion adopted on 08.02.2018. Request for Supplementary Information adopted on 28.09.2017.	
PRAC Led **Remsima - infliximab - EMEA/H/C/002576/II/0045** Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Submission of the final study report of the Post-Marketing Surveillance of REMSIMA 100 mg (Infliximab) to Evaluate Its Safety and Efficacy in Korea. The study intended to identify any unexpected adverse event and serious adverse event and frequency and pattern of occurrence of adverse events under the condition of general clinical practice and determine any factor that may affect the safety and efficacy." Opinion adopted on 08.02.2018. Request for Supplementary Information adopted on 28.09.2017.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0045** Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from study 109MS419 listed as a category 3 study in the RMP. This is a retrospective, multicentre, observational study aimed to assess the effect of tecfidera delayed-release capsules on lymphocyte subsets in patients with relapsing forms of multiple sclerosis." Opinion adopted on 08.02.2018. Request for Supplementary Information adopted on 28.09.2017.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0049** Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

liaison: Martina Weise, “Submission of the final report from study 109MS409 listed as a category 3 study in the RMP. This is an observation study aimed to estimate the proportion of dimethyl fumarate use that is prescribed “on-label” versus “off-label” in Germany.” Opinion adopted on 08.02.2018.	
PRAC Led **WS1264** **Ariclaim-** **EMEA/H/C/000552/WS1264/0068** **Cymbalta-** **EMEA/H/C/000572/WS1264/0072** **Duloxetine Lilly-** **EMEA/H/C/004000/WS1264/0008** **Xeristar-** **EMEA/H/C/000573/WS1264/0075** **Yentreve-** **EMEA/H/C/000545/WS1264/0058** Eli Lilly Nederland B.V., Duplicate, Duplicate of Yentreve, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto Yerro, “Submission of the final report from study F1J-MC-B056 listed as a category 3 study in the RMP. This is a non-interventional non-imposed study aimed to investigate the association between duloxetine exposure and suicide-related behaviours and ideation in women with stress urinary inconsistence (SUI). The RMP version 12.4 has also been updated to reflect the study results.” Opinion adopted on 08.02.2018. Request for Supplementary Information adopted on 30.11.2017.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1299** **Enurev Breezhaler-** **EMEA/H/C/002691/WS1299/0025** **Seebri Breezhaler-** **EMEA/H/C/002430/WS1299/0025** **Tovanor Breezhaler-** **EMEA/H/C/002690/WS1299/0028** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, Lead PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, “Submission of the final study report of the Category 1 Post-Authorisation Safety Study (PASS) on cardio and cerebrovascular outcomes	Request for Supplementary Information adopted with a specific timetable.

(Multinational, multidatabase cohort study to assess adverse cardiovascular and cerebrovascular outcomes and mortality in association with inhaled NVA237 in Europe / CNVA237A2402T) with subsequent update of Annex II. Consequently the deletion from the list of additional monitoring led to the update of Annex I and IIIB. The MAH also took this oppotunity to update the local representatives. The RMP version 8 was submitted." Request for Supplementary Information adopted on 08.02.2018.	
PRAC Led **WS1340** **Ultibro Breezhaler-** **EMEA/H/C/002679/WS1340/0022** **Ulunar Breezhaler-** **EMEA/H/C/003875/WS1340/0022** **Xoterna Breezhaler-** **EMEA/H/C/003755/WS1340/0025** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, Lead PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final report of the multinational, multi-database drug utilization study of indacaterol/glycopyrronium bromide (QVA149) in Europe (CQVA149A2401) with the objective to estimate the use of QVA149 off-label and in the subpopulations with missing information mentioned in the risk management plan (RMP)." Request for Supplementary Information adopted on 08.02.2018.	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

WS1284 **Kalydeco-** **EMEA/H/C/002494/WS1284/0068** **Orkambi-** **EMEA/H/C/003954/WS1284/0029** Vertex Pharmaceuticals (Europe) Ltd., Lead	Positive Opinion adopted by consensus on 15.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Rapporteur: Concepcion Prieto Yerro Opinion adopted on 15.02.2018.	
WS1297 **Infanrix hexa-** **EMEA/H/C/000296/WS1297/0236** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 08.02.2018.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1309 **HyQvia-EMEA/H/C/002491/WS1309/0039** **Kiovig-EMEA/H/C/000628/WS1309/0081** Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus, Opinion adopted on 08.02.2018.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1318 **Mirapexin-** **EMEA/H/C/000134/WS1318/0086** **Sifrol-EMEA/H/C/000133/WS1318/0077** Boehringer Ingelheim International GmbH, Lead Rapporteur: Mark Ainsworth, “To update the Product Information in relation to the signal "dystonia" for a cumulative review of the literature and postmarketing data concerning pramipexole following PRAC assessment (EPITT No. 18866) on 06 April 2017. In addition, the MAH introduced minor linguistic amendments to the German, Danish, Italian, Finnish, Hungarian, Spanish, Romanian, Icelandic, Norwegian, Latvian, Estonian and Swedish translations of the Annexes for Sifrol® and Mirapexin®.” Opinion adopted on 08.02.2018.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1323 **Aflunov-** **EMEA/H/C/002094/WS1323/0041** **Foclivia-** **EMEA/H/C/001208/WS1323/0035** Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Opinion adopted on 01.02.2018.	Positive Opinion adopted by consensus on 01.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1327 **Corbilta-** **EMEA/H/C/002785/WS1327/0014** **Levodopa/Carbidopa/Entacapone Orion-** **EMEA/H/C/002441/WS1327/0024** **Stalevo-EMEA/H/C/000511/WS1327/0084** Orion Corporation, Lead Rapporteur: Outi Mäki-	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Ikola, “Update of the Annexes to QRD product information template versions 10 and 9.1 including the combined SmPCs for different tablet strengths. Additionally, minor linguistic amendments were performed. Furthermore the contact information details of local representatives for BG and RO for Stalevo and for CZ, DK and ES for Corbilta were updated. Finally, the labeling text was updated according to the approved mock-up review processes.” Opinion adopted on 08.02.2018.	
WS1328/G **Epclusa-** **EMEA/H/C/004210/WS1328/0021/G** **Harvoni-** **EMEA/H/C/003850/WS1328/0063/G** **Sovaldi-** **EMEA/H/C/002798/WS1328/0047/G** **Vosevi-** **EMEA/H/C/004350/WS1328/0008/G** Gilead Sciences International Limited, Lead Rapporteur: Filip Josephson Opinion adopted on 08.02.2018.	Positive Opinion adopted by consensus on 08.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1331 **Ariclaim-** **EMEA/H/C/000552/WS1331/0070** **Cymbalta-** **EMEA/H/C/000572/WS1331/0074** **Duloxetine Lilly-** **EMEA/H/C/004000/WS1331/0010** **Xeristar-** **EMEA/H/C/000573/WS1331/0077** Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim, Yentreve, Lead Rapporteur: Concepcion Prieto Yerro Opinion adopted on 01.02.2018.	Positive Opinion adopted by consensus on 01.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1334/G **Combivir-** **EMEA/H/C/000190/WS1334/0091/G** **Epivir-** **EMEA/H/C/000107/WS1334/0105/G** **Kivexa-** **EMEA/H/C/000581/WS1334/0074/G** **Trizivir-** **EMEA/H/C/000338/WS1334/0106/G** ViiV Healthcare UK Limited, Lead Rapporteur: Joseph Emmerich Opinion adopted on 15.02.2018.	Positive Opinion adopted by consensus on 15.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Hexacima- **EMEA/H/C/002702/WS1286/0075** **Hexaxim-** **EMEA/H/W/002495/WS1286/0080** **Hexyon-** **EMEA/H/C/002796/WS1286/0079** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 01.02.2018.	Positive Opinion adopted by consensus on 01.02.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hexacima- **EMEA/H/C/002702/WS1304/0076** **Hexaxim-** **EMEA/H/W/002495/WS1304/0081** **Hexyon-** **EMEA/H/C/002796/WS1304/0080** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 15.02.2018.	Request for supplementary information adopted with a specific timetable.

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

Maci - matrix applied characterised autologous cultured chondrocytes - EMEA/H/C/002522/II/0014/G, ATMP Vericel Denmark ApS, Rapporteur: Christiane Niederlaender Request for Supplementary Information adopted on 08.12.2017. Withdrawal request submitted on 19.02.2018.	The MAH withdrew the procedure on 19.02.2018.

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

Invokana - canagliflozin - EMEA/H/C/002649/II/0034 MAH: Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Valerie Strassmann, , "Update of sections 4.1, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information on cardiovascular events following final results from CANVAS Program (DIA3008 and DIA4003); the Package Leaflet is updated accordingly. Study DIA3008 is phase 3 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of JNJ-28431754 on Cardiovascular Outcomes in Adult Subjects With Type 2 Diabetes Mellitus Study DIA4004 is phase 4 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of Canagliflozin on Renal Endpoints in Adult Subjects With Type 2	Request for supplementary information adopted with a specific timetable.

Diabetes Mellitus The RMP version 7.2 has also been submitted." Request for Supplementary Information adopted on 25.01.2018.	
Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0034 MAH: Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.1, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information on cardiovascular events following final results from CANVAS Program (DIA3008 and DIA4003); the Package Leaflet is updated accordingly. Study DIA3008 is phase 3 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of JNJ-28431754 on Cardiovascular Outcomes in Adult Subjects With Type 2 Diabetes Mellitus Study DIA4004 is phase 4 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of Canagliflozin on Renal Endpoints in Adult Subjects With Type 2 Diabetes Mellitus The RMP version 7.2 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet andto bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 25.01.2018.	Request for Supplementary Information adopted with a specific timetable.

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

fremanezumab - EMEA/H/C/004833
, prevention of episodic and chronic migraine

cannabidiol - EMEA/H/C/004675, Orphan
GW Research Ltd, Adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS)

asparaginase - EMEA/H/C/004736, Orphan
ERYTECH Pharma S.A., treatment of acute lymphoblastic leukaemia

lorlatinib - EMEA/H/C/004646, treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC)

lusutrombopag - EMEA/H/C/004720,
treatment of thrombocytopenia

treosulfan - EMEA/H/C/004751, Orphan,
medac Gesellschaft fur klinische
Spezialpraparate mbH, conditioning treatment
prior to allogeneic haematopoietic stem cell
transplantation (alloHSCT)
transplantation (alloHSCT)

canakinumab - canakinumab -
EMEA/H/C/004754, prevention of major
cardiovascular events

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

Elocta - efmoroctocog alfa -
EMEA/H/C/003964/X/0021
Swedish Orphan Biovitrum AB (publ),
Rapporteur: Jan Mueller-Berghaus, “Extension
application to introduce new strength of 4000
IU, 5000 IU and 6000 IU primarily enabling
phophylactic dosing in adult patients.”

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

axicabtagene ciloleucel -
EMEA/H/C/004480, Orphan, ATMP
Kite Pharma EU B.V., treatment of diffuse large
B-cell lymphoma (DLBCL), primary mediastinal
B-cell lymphoma (PMBCL) and transformed
follicular lymphoma (TFL)
List of Questions adopted on 08.12.2017.

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

afamelanotide -
EMEA/H/C/002548/S/0019, Orphan
Clinuvel (UK)

anagrelide - EMEA/H/C/000480/S/0081

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

Corbilta - levodopa / carbidopa /
entacapone - EMEA/H/C/002785/R/0015
Orion Corporation, Rapporteur: Outi Mäki-Ikola,
Co-Rapporteur: Bruno Sepodes, PRAC
Rapporteur: Kirsti Villikka

Defitelio - defibrotide -
EMEA/H/C/002393/R/0032, Orphan

Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams

Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/R/0054
Omrix Biopharmaceuticals N. V., Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Brigitte Keller-Stanislawski

Xofigo - radium-223 - EMEA/H/C/002653/R/0030
Bayer AG, Rapporteur: Harald Enzmann, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Patrick Batty

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

Dexdor - dexmedetomidine - EMEA/H/C/002268/II/0026
Orion Corporation, Rapporteur: Greg Markey, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams, “Extension of Indication to include "For sedation of non-intubated adult patients prior to and/or during diagnostic or surgical procedures requiring sedation, i.e. procedural/awake sedation" for Dexdor;
as a consequence, section 4.1, 4.2, 4.4, 4.6, 4.7, 4.8 and 5.1 of the SmPC. The Package Leaflet is updated in accordance.
RMP version 7 has been submitted”

Jinarc - tolvaptan - EMEA/H/C/002788/II/0009
Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Julie Williams, “Extension of Indications based on the results of a completed Post Authorisation Efficacy Study (PAES, Trial 156-13-210) as mandated by Annex II of the Product Information with tolvaptan (ANX 006). Trial 156-13-210 is a Phase 3b, Multi-centre, Randomized-withdrawal, Placebo-controlled, Double-blind, Parallel-group Trial to Compare the Efficacy and Safety of Tolvaptan (45 to 120 mg/day, Split-dose) in Subjects with Chronic Kidney Disease between

Late Stage 2 to Early Stage 4 Due to Autosomal Dominant Polycystic Kidney Disease.

Updates to SmPC Sections 4.1, 4.8 (to add 'abdominal pain' to the table of adverse events and present the data in line with QRD recommendations) and 5.1 are being proposed. The Package Leaflet is updated in accordance. Minor additional editorial changes to the PI were also carried out.

Version 13.2 of the RMP was submitted, updated to reflect the study results."

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0042

Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus, "Extension of Indication to include treatment as monotherapy of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) on or after platinum-containing chemotherapy based on the results from KEYNOTE-040 (KN040) with supportive data from two additional single arm studies (KEYNOTE-012/ KEYNOTE-055). KN040 is a randomized, multi-center, pivotal phase III study investigating KEYTRUDA as a monotherapy versus standard treatment (methotrexate, docetaxel or cetuximab) in 495 patients with recurrent or metastatic HNSCC who have previously progressed on prior platinum. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to include in SmPC section 5.2 the description of pembrolizumab PK results on time-dependent change in clearance using a time-dependent pharmacokinetic (TDPK) model structure rather than the static PK model structure.
An updated RMP version 15.1 was provided as part of the application."

Qtern - saxagliptin / dapagliflozin - EMEA/H/C/004057/II/0013

AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, "Extension of Indication to include new indication to improve glycaemic control when metformin, with or without sulphonylurea, does not provide adequate glycaemic control, and where any additional oral monotherapy is

unlikely to bring patients to target, for Qtern; as a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated.
In addition, the MAH took the opportunity to introduce minor editorial changes to sections 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC, to Package Leaflet, to Annex II and Annex A."

Venclyxto - venetoclax - EMEA/H/C/004106/II/0008, Orphan
AbbVie Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, "Extension of Indication to include Venclyxto in combination with rituximab for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy.
As a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated.
The Package Leaflet is updated in accordance.
This submission also fulfils the Annex II condition to submit the results of the MURANO study comparing venetoclax plus rituximab to bendamustine plus rituximab in patients with relapsed/refractory CLL.
In addition, RMP version 3.0 is submitted."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Dupixent - dupilumab - EMEA/H/C/004390/II/0003/G
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

Eptifibatide Accord - eptifibatide - EMEA/H/C/004104/II/0003
Accord Healthcare Ltd, Generic, Generic of Integrilin, Rapporteur: Jayne Crowe

Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0093/G
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0028
GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus

Naglazyme - galsulfase - EMEA/H/C/000640/II/0070

BioMarin Europe Ltd, Rapporteur: Greg Markey

NexoBrid - concentrate of proteolytic enzymes enriched in bromelain - EMEA/H/C/002246/II/0035, Orphan
MediWound Germany GmbH, Rapporteur: Harald Enzmann

Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0163
Pfizer Limited, Rapporteur: Kristina Dunder

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

Abraxane - paclitaxel - EMEA/H/C/000778/II/0087
Celgene Europe Limited, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.8 of the SmPC in order to include the warning tumour lysis syndrome following a safety cumulative review of this signal. In addition, the marketing authorisation holder took the opportunity to update the wording on section 4.6 to introduce additional recommendation to perform a pregnancy test prior treatment with paclitaxel. The package leaflet has been updated accordingly."

Celsentri - maraviroc - EMEA/H/C/000811/II/0054/G
ViiV Healthcare UK Limited, Rapporteur: Filip Josephson, "Update of sections 4.5, 5.1 and 5.2 of the SmPC in order to update the in vitro data regarding drug metabolising enzymes and drug transporters from several completed in vitro studies and to support the addition of pharmacogenomic information based on final results from study (A4001110), respectively. The Package Leaflet is updated accordingly. Additionally, minor changes are introduced in other sections of the SmPC."

Daklinza - daclatasvir - EMEA/H/C/003768/II/0028
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, "Submission of the final report from study AI444379. This is an interventional open-label phase 3 study evaluating daclatasvir and sofobuvir with ribavirin in cirrhotic subjects with genotype 3 chronic hepatitis C infection to

demonstrate the sustained virologic response at follow-up Week 12 (SVR12) rate, defined as hepatitis C virus (HCV) ribonucleic acid (RNA) < lower limit of quantification (LLOQ) target detected (TD) or target not detected (TND) at follow-up Week 12 in subjects treated with 24 weeks of daclatasvir (DCV) + sofosbuvir (SOF) + ribavirin (RBV) therapy was greater than the historical threshold sustained virologic response (SVR) rate."

Isentress - raltegravir - EMEA/H/C/000860/II/0073

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

Jinarc - tolvaptan - EMEA/H/C/002788/II/0010

Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, "Submission of the final report from a completed PK study (156-14-216, a Phase 1, Single centre, Open-label, drug interaction trial to Investigate the Effect of Oral Flucomazole, a Moderate CYP3A4 Inhibitor, on Tolvaptan Pharmcokinetic in Healthy Adult Subjects - MEA 003)."

Praluent - alirocumab - EMEA/H/C/003882/II/0036

sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the clinical study report of study LTS13463 (Open-Label Extension Study of EFC12492, R727-CL-1112, EFC12732, & LTS11717 Studies to Assess the Long-Term Safety and Efficacy of Alirocumab in Patients with Heterozygous Familial Hypercholesterolemia) as per MEA010."

Taltz - ixekizumab - EMEA/H/C/003943/II/0016

Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, "Update section 5.1 of the SmPC to include the results of study RHBS (a Phase 3b, multicenter, randomised, double blind, double dummy, active comparator, and parallel group study of the efficacy and safety of ixekizumab versus ustekinumab for the treatment of

moderate to severe psoriasis). The MAH took the opportunity to introduce minor typographical amendments in the product information."

Xalkori - crizotinib - EMEA/H/C/002489/II/0054

Pfizer Limited, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the SmPC to reflect the final analysis of overall survival (OS), a secondary endpoint, in Study A8081014, a randomized phase 3 trial comparing oral crizotinib to first line chemotherapy in patients with ALK-positive advanced non-squamous non-small cell lung cancer (NSCLC)."

Xeljanz - tofacitinib - EMEA/H/C/004214/II/0008

Pfizer Limited, Rapporteur: Robert James Hemmings, "Submission of the final CSR for study A3921187 described in Part IV of the RMP. Study A3921187 is a phase 3b/4 randomized double-blind study of 5 mg of Tofacitinib with and without methotrexate in comparison to adalimumab with methotrexate in subjects with moderately to severely active rheumatoid arthritis."

Xeljanz - tofacitinib - EMEA/H/C/004214/II/0010

Pfizer Limited, Rapporteur: Robert James Hemmings, "To update sections 4.4 and 4.8 of the SmPC and PIL to add a warning on Hypersensitivity in post-marketing experience and to add drug hypersensitivity, angioedema, and urticaria as ADRs with frequency not known, following a PRAC signal recommendation.
The Package Leaflet is updated accordingly."

Xeljanz - tofacitinib - EMEA/H/C/004214/II/0011

Pfizer Limited, Rapporteur: Robert James Hemmings, "To update section 4.4 of the SmPC to indicate that post-marketing cases of HB reactivation have been reported following routine pharmacovigilance review."

Xydalba - dalbavancin - EMEA/H/C/002840/II/0021

Allergan Pharmaceuticals International Ltd, Rapporteur: Filip Josephson, "Update to sections 4.4 and 4.8 of the product information in order

to include back-pain as a symptom of infusion-related reactions in alignment with the last version Company Core Data Sheet (CCDS).

In addition, the MAH took the opportunity to add a precautionary statement to Section 6.6 to include flushing of the intravenous lines before and after dalbavancin infusion, to bring the PI in line with the latest QRD template version 10 and to update the local representatives in the PL"

Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0009

Pfizer Ireland Pharmaceuticals, Rapporteur: Robert James Hemmings, "Update of sections 4.2 and 4.8 of the SmPC in order to reflect the availability of final CSR for the paediatric study C3591004 (D4280C00015). Study D4280C00015 is a single blind, randomised, multi-centre, active controlled, trial to evaluate safety, tolerability, pharmacokinetics and efficacy of ceftazidime and avibactam when given in combination with metronidazole, compared with meropenem, in children from 3 months to less than 18 years of age with complicated intra-abdominal infections (cIAIs). In addition, the MAH has updated the sodium statements in the SmPC (section 4.4) and Package Leaflet to align with the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'.
The legal status 'medicinal product subject to medical prescription' is proposed to be removed from Annex IIIA, as per the QRD template Moreover, the MAH is introducing a correction in the Polish annexes (from ZAVICEFTA 2 g + 0.5g to ZAVICEFTA 2 g/0.5g)."

WS1348
Exviera-EMEA/H/C/003837/WS1348/0035
Viekirax-
EMEA/H/C/003839/WS1348/0042

AbbVie Limited, Lead Rapporteur: Filip Josephson, "Submission of the final report from study (M14-227) listed as a category 3 study in the RMP. This is a Phase 3b study designed to evaluate the safety and efficacy of ombitasvir/paritaprevir/ritonavir and dasabuvir in HCV infected patients with Child-Pugh B decompensated cirrhosis."

WS1356/G
Humalog-
EMEA/H/C/000088/WS1356/0163/G
Liprolog-
EMEA/H/C/000393/WS1356/0125/G
Eli Lilly Nederland B.V., Lead Rapporteur: Robert James Hemmings, "C.I.4: Update of sections 4.2 and 6.6 of the SmPC of Humalog/Liprolog in cartridges following the signal PRAC recommendation (EPITT 18893); the Package Leaflet and Labelling are updated.

B.II.e.5.b: To delete the BASAL presentations: EU/1/96/007/010, 029, 037 and 038 for Humalog Basal and EU/1/01/195/022, 023, 026 and 027 for Liprolog Basal.

In addition, the Worksharing applicant (WSA) took the opportunity to combine all SmPCs resulting in four SmPCs: 100 units/ml presentations, Mix 25 100 units/ml presentations, Mix50 100 units/ml presentations and 200 units/ml presentations. The MAH also brought the product information in line with the latest QRD template version 10, 02/2016. Minor editorial changes have been included."

B.6.10. CHMP-PRAC assessed procedures

Advate - octocog alfa -
EMEA/H/C/000520/II/0091
Baxter AG, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 4.2 of the SmPC in order to remove a statement that the use of 2 ml presentations has not been documented for paediatric subjects below 2 years of age. This update follows final results from study 061101 listed as a category 3 study in the RMP; this was a prospective, non-interventional, post-marketing surveillance study that assessed the safety and efficacy of Advate reconstituted in 2 ml of sterile water for injection during routine clinical practice in the EU.
The Package Leaflet is updated accordingly. The RMP version 15.1 has also been submitted."

Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) -
EMEA/H/C/001104/II/0161
Pfizer Limited, Rapporteur: Kristina Dunder,

PRAC Rapporteur: Qun-Ying Yue, “Submission of the final study report from study B1851041, a phase 4 post marketing study to determine ' National trends in Ambulatory Care Visits for Otitis Media in Children Under the Age of Five in the United States.' Consequently, the RMP version 12 has been updated.”

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0129

CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Update of section 4.3 of the SmPC to remove the hyperprolineamia contraindication. The package leaflet and RMP (version 6.0) are updated accordingly.”

Revlimid - lenalidomide - EMEA/H/C/000717/II/0098, Orphan

Celgene Europe Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, “Update of the Annex II key elements of the risk minimisation programme with information on prescription duration and to revise due dates of the PASS CC-5013-MDS-10 and 12. The section 4.4 of the SmPC has been updated accordingly. Furthermore, the RMP version 35 has been revised in line with the updated Guideline on Good Pharmacovigilance Practices (GVP) Module V to propose the reclassification and/or renaming of known safety concerns associated with the use of lenalidomide. Consequently, Annex IID has been updated accordingly.”

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0004

Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Update of section 4.8 of the SmPC in order to update the safety information based on the primary results from study IMvigor211 in order to fulfil ANX 002 (the submission of the final CSR being listed as an imposed PAES in Annex II.D). This is a phase III, open-label, multicentre, randomized study to investigate the efficacy and safety of atezolizumab (anti- PD-L1 antibody) compared with chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer after failure with platinum-containing chemotherapy. The Package Leaflet and the RMP (version 3.0, according to GVP module V

revision 2) are updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to implement some editorial changes throughout the Product Information."	
Yervoy - ipilimumab - **EMEA/H/C/002213/II/0054** Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "Update of section 5.1 of the SmPC to update the overall survival data of ipilimumab 3mg/kg monotherapy pooled across studies based on the final results of study CA184332 and CA184338 listed as category 3 studies in the RMP, in order to fulfil MEA 035 and MEA 030.1 respectively. Study CA184332 is a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab as first line therapy in a community practice setting and study CA184438 is a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab as first line therapy. The RMP version 18.4 has also been submitted."	
WS1335 **Rixathon-** **EMEA/H/C/003903/WS1335/0010** **Riximyo-** **EMEA/H/C/004729/WS1335/0010** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Doris Stenver, "Submission of final study reports for studies GP13-302 (a randomized, double-blind, parallel-group safety study with the aim to specifically address a potential safety risk of a switch from treatment with originator rituximab (Mabthera/Rituxan) to treatment with GP2013) and GP13-201 (a 52-week multicenter, randomized, double-blind, parallel-arm, comparative study in patients with active Reumathoid Arthritis (RA) refractory or intolerant to standard DMARDs and one or up to three anti-TNFs therapies). The RMP (version 3.0) has been updated accordingly."	
WS1343 **Relvar Ellipta-** **EMEA/H/C/002673/WS1343/0036** **Revinty Ellipta-** **EMEA/H/C/002745/WS1343/0032**	

Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, “C.I.11.b) Submission of an updated RMP version 9.2 to reflect the addition of information with regards SLS-asthma completion (HZA115150- interventional post-authorisation safety Category 1 study to further investigate the risk of pneumonia-ANX005), to update the important identified risk of pneumonia with regards findings from the study, and to provide a justification for removal of the important potential risk of asthma related intubations and deaths and a justification for removal of missing information related to long term use in asthma (>1 year). Consequently Annex II condition of the product information is updated accordingly.”

B.6.11. PRAC assessed procedures

PRAC Led

Bemfola - follitropin alfa - EMEA/H/C/002615/II/0016

Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Update of the RMP version 2 based on the phase-3 multicentre study conducted to compare the efficacy and safety of two r-hFSH formulations in normal ovulatory women 35 to 42 years of age undergoing in vitro fertilisation (IVF) (CSR FIN3002).”

PRAC Led

Bronchitol - mannitol - EMEA/H/C/001252/II/0031, Orphan

Pharmaxis Pharmaceuticals Limited, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, “Submission of the final report of a survey of healthcare professionals listed as a category 3 study in the RMP. This is a final survey aimed to measure to the effectiveness of the educational materials at 6 months post-launch and 6 months post-redistribution of the revised healthcare professional leaflet. The RMP version 7.0 has also been submitted.”

PRAC Led

Edarbi - azilsartan medoxomil -

EMEA/H/C/002293/II/0021
Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from the drug utilisation study listed as a category 3 study in the RMP. This post-authorisation safety study is a retrospective non-interventional cohort study using a patient level electronic medical records database in Germany aimed to describe the prescription of azilsartan medoxomil in patients with essential hypertension and those prescribed azilsartan medoxomil for other reasons."

PRAC Led
Imraldi - adalimumab -
EMEA/H/C/004279/II/0004
Samsung Bioepis UK Limited (SBUK), Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 2.1 in order to indicate changes in the distribution method for the Imraldi Patient Alert Card (PAC)from being included in the Annex IIIa of the Product Information to be provided to patients by healthcare professionals by including the PAC in the physician educational material. The Annex IIIa of the PI is updated accordingly."

PRAC Led
Lucentis - ranibizumab -
EMEA/H/C/000715/II/0070/G
Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "1. Type II- C.I.13: Submission of the final report from study LUMINOUS study (CRFB002A2406), an observational, multicenter study to assess the long term safety and effectiveness of ranibizumab in routine clinical practice, in fulfilment of the post-authorisation measures MEA 036, MEA 048 and MEA 054. Consequentially, the RMP has been updated to reflect these changes.
2. Type II-C.I.11: Submission of an updated RMP version 17.0 (RMP template Rev. 2) according to GVP Module V to include changes not consequential to LUMINOUS study. In addition, the MAH is proposing the removal of the use of educational materials and targeted

follow-up checklists listed in Annex II-D of the Product Information."

PRAC Led

MabThera - rituximab - EMEA/H/C/000165/II/0144

Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Update the RMP to remove the additional risk minimization measure of Educational Outreaches for the important identified risk of Infusion Related Reactions and Acute Infusion Related Reactions (IRR). Therefore, the RMP has been updated accordingly to version 16.0."

PRAC Led

NutropinAq - somatropin - EMEA/H/C/000315/II/0069/G

Ipsen Pharma, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "II: C.I.11: Submission of an updated RMP version 3.0 in order to include formatting in accordance with the new RMP template and to include updates from the post-approval safety study (PASS) International Cooperative Growth Study (iNCGS) Post Marketing Surveillance Program For NutropinAq.
II: C.I.13: Submission of the final report from International Cooperative Growth Study (iNCGS) Post Marketing Surveillance Program For NutropinAq. This study collected long-term safety and effectiveness data on NutropinAq during treatment of paediatric growth disorders for which growth hormone is indicated."

PRAC Led

Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/II/0055

Merck Serono Europe Limited, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "The update Risk Management Plan version 5.1 for Pergoveris to
· Align the RMP template with Good Pharmacovigilance Practice (GVP) Module V, revision 1.
· Add the reference to Pergoveris solution for injection in pre-filled pen (300IU/150IU, 450IU/225IU and 900IU/450IU) following the approval in the European Union (EU) on the 8th of May 2017.

· Revise the epidemiology section based on the recent literature data.
· Revise non-clinical part of the safety specification section with the data available from r-hFSH (recombinant human follicle stimulating hormone), r-hLH (recombinant human luteinizing hormone) and Pergoveris. The clinical trial section has been updated for clinical studies for r-hFSH/r-hLH for Ovulation Induction (OI) and Assisted Reproductive Technologies (ART).
· Update the patient exposure data and other sections based on the cases received up to the data lock point (DLP) of 31 July 2017 i.e. non-study post authorisation exposure section and additional EU requirements for the safety specification section and include other minor changes such as update of the reporting rates."

PRAC Led

Resolor - prucalopride -
EMEA/H/C/001012/II/0042

Shire Pharmaceuticals Ireland Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Submission of the final clinical study report for the post-authorization drug utilization study SHP555-804 in fulfilment of MEA 006.11 A drug utilisation study to examine characteristics of patients prescribed prucalopride (Resolor) and a pharmacoepidemiological study of the occurrence of major cardiovascular events, pregnancy, and pregnancy outcomes in the UK CPRD Database. The RMP (v 14.0) has also been updated to reflect the study results."

PRAC Led

Tasigna - nilotinib -
EMEA/H/C/000798/II/0092, Orphan

Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 21.0 in order to delete the important identified risk 'Myelosuppression', and to upgrade the risk 'Cardiac failure' from an important potential to an important identified risk. In addition, changes in the definition of the identified risks 'Hepatotoxicity' and 'Fluid retention' have been implemented."

PRAC Led

Xeljanz - tofacitinib -
EMEA/H/C/004214/II/0009
Pfizer Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Sabine Straus, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final CSR for study A3921024 listed as a category 3 study in the RMP (MEA 003). Study A3921024 is a long term, open label follow-up study to evaluate the long-term safety of patients on 5 mg BID of XELJANZ with a secondary objective of evaluating sustained efficacy in patients with rheumatoid arthritis."

PRAC Led
Xofigo - radium-223 -
EMEA/H/C/002653/II/0031
Bayer AG, Rapporteur: Harald Enzmann, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Submission of Clinical Study Report for study 17399. This is an observational post-authorisation safety study (PASS) listed as category 4 in the RMP to evaluate the use of radium-223 dichloride in patients in Sweden with a diagnosis of CRPC with bone metastases (mCRPC) and patients in whom radium-223 dichloride may have been potentially used off-label."

PRAC Led
Zavicefta - ceftazidime / avibactam -
EMEA/H/C/004027/II/0008
Pfizer Ireland Pharmaceuticals, PRAC Rapporteur: Jolanta Gulbinovic, PRAC-CHMP liaison: Rugile Pilviniene, "To provide an updated Risk Management Risk (version 2.0) in order to incorporate data from the REPROVE study (already submitted in procedure II-02), align the RMP with the current EU template, and add current post-marketing experience relative to the RMP data lock point (24/8/17). The Phase 3 REPROVE study was a randomized, multicentre, double-blind, double-dummy, parallel group comparative study to determine the efficacy, safety and tolerability of CAZ-AVI (2000 mg ceftazidime and 500 mg avibactam) versus meropenem (1000 mg) in the treatment of NP, including VAP, in hospitalised adults 18 years of age or older."

PRAC Led
WS1355

Prezista-
EMEA/H/C/000707/WS1355/0094
Rezolsta-
EMEA/H/C/002819/WS1355/0024
Janssen-Cilag International NV, Lead PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, “To amend the RMP with an amended due date for the final report for study GS-US-216-0128 from Q1 2022 to Q1 2024.”

PRAC Led
WS1357
Efficib-EMEA/H/C/000896/WS1357/0089
Janumet-
EMEA/H/C/000861/WS1357/0089
Januvia-
EMEA/H/C/000722/WS1357/0063
Ristaben-
EMEA/H/C/001234/WS1357/0055
Ristfor-EMEA/H/C/001235/WS1357/0076
TESAVEL-
EMEA/H/C/000910/WS1357/0063
Velmetia-
EMEA/H/C/000862/WS1357/0092
Xelevia-EMEA/H/C/000762/WS1357/0067
Merck Sharp & Dohme Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP version 10 in order to remove “theoretic carcinogenic potential” form the list of safety concerns, currently classified as “missing information”.”

B.6.12. CHMP-CAT assessed procedures

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS1341/G
Tivicay-
EMEA/H/C/002753/WS1341/0033/G
Triumeq-
EMEA/H/C/002754/WS1341/0052/G
ViiV Healthcare UK Limited, Lead Rapporteur: Filip Josephson

WS1345/G
Ebymect-
EMEA/H/C/004162/WS1345/0030/G
Edistride-
EMEA/H/C/004161/WS1345/0024/G
Forxiga-
EMEA/H/C/002322/WS1345/0043/G
Qtern-
EMEA/H/C/004057/WS1345/0015/G
Xigduo-
EMEA/H/C/002672/WS1345/0041/G
AstraZeneca AB, Lead Rapporteur: Kristina Dunder

WS1358
Amgevita-
EMEA/H/C/004212/WS1358/0004
Solymbic-
EMEA/H/C/004373/WS1358/0004
Amgen Europe B.V., Lead Rapporteur: Kristina Dunder

WS1360
Zutectra-
EMEA/H/C/001089/WS1360/0035
Biotest Pharma GmbH, Lead Rapporteur: Jan Mueller-Berghaus

WS1361
Azilect-EMEA/H/C/000574/WS1361/0079
Rasagiline ratiopharm-
EMEA/H/C/003957/WS1361/0012
Teva B.V., Lead Rapporteur: Bruno Sepodes

WS1367
Abseamed-
EMEA/H/C/000727/WS1367/0069
Binocrit-
EMEA/H/C/000725/WS1367/0069
Epoetin alfa Hexal-
EMEA/H/C/000726/WS1367/0068
Sandoz GmbH, Lead Rapporteur: Alexandre Moreau

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - 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.

Qualification of Biomarkers:

HTA:

G.2. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 19-22 February 2018 CHMP plenary:

Ophtalmology	
Adenovirus associated viral vector serotype 8 containing the human CNGB3 gene (AAV2/8-hCARp.hCNGB3); (SME);ATMP; Treatment of achromatopsia associated with defects in CNGB3	The CHMP granted eligibility to *PRIME at the proof of principle stage* and adopted the critical summary report.
Haematology - Hemostaseology	
(SME); Treatment of Hematopoietic stem cell transplant-associated thrombotic microangiopathy	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Uro-nephrology	
(SME); Treatment of Immunoglobulin A nephropathy	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Psychiatry	
treatment of patients with chronic schizophrenia who are experiencing inadequate benefit on their current antipsychotic therapy	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Endocrinology-Gynaecology-Fertility-Metabolism	
(SME);Treatment of Allan-Herndon-Dudley-Syndrome	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Pneumology-Allergology	
(SME);Treatment of F508del cystic fibrosis	The CHMP denied eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in February 2018 for March 2018 CHMP adoption of outcomes

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