26 May 2017
EMA/317902/2017 Corr.*
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Minutes of the meeting on 18-21 April 2017

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

Health and safety information

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

Disclaimers

Some of the information contained in this agenda 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 agenda 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 agenda 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).

* Correction in section 3.2.10

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

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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) April 2017 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 18-21 April 2017.

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

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

1.2. Adoption of agenda

CHMP agenda for 18-21 April 2017.

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 20-23 March 2017.

The CHMP adopted the CHMP minutes for 20-23 March 2017.

The Minutes of the April 2017 CHMP ORGAM meeting held on 10 April 2017, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. - anamorelin - EMEA/H/C/003847

treatment of anorexia, cachexia or unintended weight loss in adult patients with non-small cell lung cancer (NSCLC)

Scope: Oral explanation

Action: Oral explanation to be held on 19 April 2017 at time 11:00

List of Outstanding Issues adopted on 23.02.2017, 10.11.2016. List of Questions adopted on 25.02.2016.

Participation of patients' representatives.

Oral explanation was held on 19 April 2017 at time 11:00. During the oral explanation the company presented the clinical relevance of lean body mass and improvement in body composition parameters.

2.1.2. Cuprior - trientine tetrahydrochloride - Orphan - EMEA/H/C/004005

GMP-Orphan SA; treatment of Wilson's disease

Scope: Oral explanation

Action: Oral explanation to be held on 19 April 2017 at time 16:00

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

List of Outstanding Issues adopted on 23.02.2017, 13.10.2016. List of Questions adopted on 28.04.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues. After discussion the CHMP agreed that no oral explanation was required at this time.

See also 3.1.3.

2.1.3. - masitinib - Orphan - EMEA/H/C/004159

AB Science; treatment of mastocytosis

Scope: Oral explanation

Action: Oral explanation to be held on 20 April 2017 at time 09:00

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 15.09.2016.

An oral explanation was held on 20 April 2017 at 09:00. The applicant outlined the high unmet medical need of the product and provided some explanation and justification on the outstanding issues including on the conduct of the clinical trials.

2.1.4. - vosaroxin - Orphan - EMEA/H/C/004118

treatment acute myeloid leukaemia

Scope: Oral explanation, report from SAG meeting held 5 April 2017

Action: Oral explanation to be held on 19 April 2017 at time 09.00

List of Outstanding Issues adopted on 15.12.2016. List of Questions adopted on 28.04.2016.

The members noted the report from the SAG meeting held on 5 April 2017. The experts expressed different views on the proposed subgroup of patients ⩾ 60 years of age, although the majority considered the proposed subgroup as not appropriate. On the question relating to the clinical benefit of the observed improvement of overall survival the experts also expressed split views. Whereas some experts saw a clinical benefit, others considered the available data not sufficient to come to a conclusion. Given the limited data no clear answer could be given on the biological plausibility for an effect depending on age or other patient characteristics at baseline. Most experts also could not see a convincing association of a higher complete remission rate with an increase of successful haematopoietic stem cell transplantation. The SAG could not conclude on the existence of a real difference in efficacy in older patients with late-relapse v. older patients without late-relapse, but highlighted their concern on the safety in relation with infections. Although some experts considered the safety acceptable, most experts were of a different view especially in light of no established benefits.

An oral explanation was held on 19 April 2017 at 09.00.The applicant focused on the clinical safety and efficacy data and the proposed target patient population.

2.1.5. - padeliporfin - EMEA/H/C/004182

treatment of prostate cancer

Scope: Oral explanation, report from SAG held on 4 April 2017

Action: Oral explanation to be held on 20 April 2017 at time 14:00

List of Outstanding Issues adopted on 15.12.2016. List of Questions adopted on 26.05.2016.

An oral explanation was held on 20 April 2017 at time 14:00

See 3.2.10 List of outstanding issues

2.1.6. - human IgG1 monoclonal antibody specific for human interleukin-1 alpha - EMEA/H/C/004388

treatment of metastatic colorectal cancer

Scope: Oral explanation

Action: Oral explanation to be held on 20 April 2017 at time 11:00

List of Outstanding Issues adopted on 15.12.2016. List of Questions adopted on 21.07.2016.

An oral explanation was held on 20 April 2017 at time 11:00. During the oral explanation, the Company presented the mechanism of action and unmet medical need for colorectal cancer.

The CHMP adopted the BWP report.

2.1.7. - patiromer sorbitex calcium - EMEA/H/C/004180

treatment of hyperkalaemia

Scope: Possible oral explanation to be held on 20 April 2017 at time 18:00

Action: For adoption

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 15.09.2016.

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

See 3.2.11 List of outstanding issues

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Besponsa - inotuzumab ozogamicin - Orphan - EMEA/H/C/004119

Pfizer Limited; treatment B-cell precursor acute lymphoblastic leukaemia (ALL)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 15.09.2016.

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 inotuzumab 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 11 April 2017.

The summary of opinion was circulated for information.

The CHMP adopted the similarity Assessment Report for Inotuzumab ozogamicin.

The CHMP adopted the BWP report.

3.1.2. Brineura - cerliponase alfa - Orphan - EMEA/H/C/004065

Accelerated assessment

BioMarin International Limited; treatment of neuronal ceroid lipofuscinosis type 2

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 21.02.2017. List of Questions adopted on 13.12.2016.

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

The Committee adopted a positive opinion recommending the granting of a marketing authorisation under exceptional circumstances by majority (29 positive out of 30 votes) together with the CHMP assessment report and translation timetable.

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

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

The divergent position (Johann Lodewijk Hillege) was appended to the opinion.

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

The CHMP noted the letter of recommendations dated 21 April 2017.

The summary of opinion was circulated for information.

The CHMP adopted the BWP report.

3.1.3. Cuprior - trientine tetrahydrochloride - Orphan - EMEA/H/C/004005

GMP-Orphan SA; treatment of Wilson's disease

Scope: Oral explanation

Action: Oral explanation to be held on 19 April 2017 at time 16:00

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

List of Outstanding Issues adopted on 23.02.2017, 13.10.2016. List of Questions adopted on 28.04.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues. After discussion, the CHMP agreed that no oral explanation was required at this time, because the outstanding issues were considered solved.

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

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

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

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

The summary of opinion was circulated for information.

3.1.4. Erelzi - etanercept - EMEA/H/C/004192

Sandoz GmbH; treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis, plaque psoriasis and paediatric plaque psoriasis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 01.04.2016.

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

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

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

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

The CHMP noted the letter of recommendation dated 12 April 2017.

The summary of opinion was circulated for information.

The CHMP adopted the BWP report.

3.1.5. Febuxostat Mylan - febuxostat - EMEA/H/C/004374

Mylan S.A.S; treatment of hyperuricaemia

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 15.09.2016.

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

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

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

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

The summary of opinion was circulated for information.

3.1.6. Kevzara - sarilumab - EMEA/H/C/004254

sanofi-aventis groupe; treatment of active rheumatoid arthritis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 10.11.2016.

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 sarilumab 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 12 April 2017.

The summary of opinion was circulated for information.

The CHMP adopted the BWP report.

3.1.7. Rixathon - rituximab - EMEA/H/C/003903

Sandoz GmbH; treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL), Rheumatoid arthritis and Granulomatosis with polyangiitis and microscopic polyangiitis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 15.09.2016.

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

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

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

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

The CHMP noted the letter of recommendations dated 19 April 2017.

The summary of opinion was circulated for information.

3.1.8. Riximyo - rituximab - EMEA/H/C/004729

Sandoz GmbH; treatment of Non-Hodgkin's lymphoma (NHL), Rheumatoid arthritis and Granulomatosis with polyangiitis and microscopic polyangiitis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 23.02.2017.

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

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

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

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

The CHMP noted the letter of recommendations dated 19 April 2017.

The summary of opinion was circulated for information.

3.1.9. Skilarence - dimethyl fumarate - EMEA/H/C/002157

Almirall S.A; treatment of moderate to severe plaque psoriasis in adults in need of systemic drug therapy

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 28.04.2016.

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

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

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

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

The CHMP noted the letter of recommendations dated 21 April 2017.

The summary of opinion was circulated for information.

3.1.10. Spinraza - nusinersen - Orphan - EMEA/H/C/004312

Accelerated assessment

Biogen Idec Ltd; for the treatment of Spinal Muscular Atrophy (SMA).

Scope: Opinion

Action: For adoption

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

Oral explanation held on 22.03.2017. List of Outstanding Issues adopted on 23.03.2017. List of Questions adopted on 24.01.2017.

The CHMP discussed the proposed post-authorisation measures and the final wording of the indication.

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 nusinersen is a new active substance, as claimed by the applicant.

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

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

The CHMP noted the letter of recommendations dated 19 April 2017.

The summary of opinion was circulated for information.

3.1.11. Ucedane - carglumic acid - EMEA/H/C/004019

Lucane Pharma; treatment of hyperammonaemia

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 15.09.2016.

The members discussed the difference of available tablet strengths compared to the originator product, taking into account the possibility to break the tablet at the score lines. It was agreed that a quartering of the tablet without the appropriate score lines was not acceptable (e.g. using a knife or tablet splitter) and therefore the 50 mg dose will not be included in the SmPC for Ucedane.

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

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

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

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

The summary of opinion was circulated for information.

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

3.2.1. - insulin lispro - EMEA/H/C/004303

treatment of diabetes mellitus

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 26.01.2017.

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.

The CHMP adopted the BWP report.

3.2.2. - rurioctocog alfa pegol - EMEA/H/C/004195

treatment of haemophilia A

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 15.12.2016. List of Questions adopted on 21.07.2016.

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

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

The CHMP adopted the BWP report.

3.2.3. - adalimumab - EMEA/H/C/004279

treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 10.11.2016.

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

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

The CHMP adopted the BWP report.

3.2.4. - ribociclib - EMEA/H/C/004213

treatment of breast cancer

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 26.01.2017.

The Committee was reminded of the status of this application and its remaining outstanding issues. The CHMP noted the answers from Oncology Working Party related to extrapolation in HR positive breast cancer.

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

3.2.5. - brodalumab - EMEA/H/C/003959

moderate to severe plaque psoriasis

Scope: Day 180 list of outstanding issue

Action: For adoption

Oral explanation held on 24.01.2017. List of Outstanding Issues adopted on 26.01.2017, 10.11.2016, 15.09.2016. List of Questions adopted on 01.04.2016.

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

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

3.2.6. - cladribine - EMEA/H/C/004230

treatment of highly active relapsing-remitting multiple sclerosis (MS)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 10.11.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues. The CHMP noted the discussions held in April PRAC meeting.

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

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

3.2.7. - cenegermin - Orphan - EMEA/H/C/004209

Accelerated assessment

Dompe farmaceutici s.p.a.; treatment of neurotrophic keratitis

Scope: Day 120 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.02.2017.

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.

The CHMP adopted the BWP report.

The CHMP agreed to keep the product on the accelerated assessment timetable.

3.2.8. - midostaurin - Orphan - EMEA/H/C/004095

Novartis Europharm Ltd; treatment of mastocytosis and treatment of acute myeloid leukaemia

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 15.12.2016.

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

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

3.2.9. - atezolizumab - EMEA/H/C/004143

treatment of locally advanced or metastatic urothelial carcinoma, treatment of non-small cell lung carcinoma (NSCLC)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 15.09.2016.

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

issues.

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

The CHMP adopted the BWP report.

3.2.10. - padeliporfin - EMEA/H/C/004182

treatment of prostate cancer

Scope: Oral explanation, report from SAG held on 4 April 2017

Action: Oral explanation to be held on 20 April 2017 at time 14:00

List of Outstanding Issues adopted on 15.12.2016. List of Questions adopted on 26.05.2016.

The CHMP noted the report from the SAG. According to the SAG report, direct comparisons between active surveillance, radical therapy or padeliporfin are not available and it is difficult to speculate on the merit of different strategies in terms of long terms outcomes. The SAG had divergent views about the overall benefits and risks of padeliporfin. For a majority of SAG members, the risk of a detriment in long-term outcome was considered unknown in this low risk population, and this was considered a concern given the availability of alternative management options and treatments, despite the high rate of early and longstanding adverse effects associated with radical treatment. However, some SAG members disagreed, and considered that padeliporfin could be a useful procedure for higher risk patients (in this low risk group) who prefer deferring radical therapy and potentially avoiding it altogether. According to this view, the risk of detriment long term was considered acceptable.

An oral explanation was held on 20 April 2017 at 14:00. In the oral explanation, the applicant provided some clarifications on the clinical programme set-up and outcomes as well as the studied patient population on the proposed indication.

The Committee agreed to a draft 2nd list of outstanding issues with a specific timetable.

Post-meeting note: The final 2nd list of outstanding issues was adopted via written procedure on 28 April 2017.

3.2.11. - patiromer sorbitex calcium - EMEA/H/C/004180

treatment of hyperkalaemia

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 15.09.2016.

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

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.

3.2.12. - telotristat ethyl - Orphan - EMEA/H/C/003937

Ipsen Pharma; treatment of carcinoid syndrome

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 10.11.2016.

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

The Committee adopted a list of outstanding issues

The CHMP agreed to the request by the applicant for clock stop to respond to the 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. - glecaprevir / pibrentasvir - EMEA/H/C/004430

Accelerated assessment, indicated for the treatment of chronic hepatitis C virus (HCV) infection in adults

Scope: Day 90 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.

The CHMP agreed to keep the product on the accelerated assessment timetable.

3.3.2. - hydrocortisone - PUMA - EMEA/H/C/004416

treatment of adrenal insufficiency

Scope: Day 120 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.

The CHMP adopted the similarity Assessment Report.

3.3.3. - anagrelide - EMEA/H/C/004585

reduction of elevated platelet counts in at risk essential thrombocythaemia patients

Scope: Day 120 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. - benralizumab - EMEA/H/C/004433

treatment of severe asthma with an eosinophilic phenotype

Scope: Day 120 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.

The CHMP adopted the BWP report.

3.3.5. - betrixaban - EMEA/H/C/004309

treatment of prophylaxis of venous thromboembolism (VTE)

Scope: Day 120 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.

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

3.3.6. - burosumab - Orphan - EMEA/H/C/004275

Kyowa Kirin Limited; treatment of X-linked hypophosphataemia (XLH)

Scope: Day 120 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.

The CHMP adopted the BWP report.

The CHMP agreed to consult an ad-hoc expert group.

3.3.7. - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781

treatment of adult patients with chronic obstructive pulmonary disease (COPD)

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.8. - eteplirsen - Orphan - EMEA/H/C/004355

AVI Biopharma International Ltd; treatment of Duchenne muscular dystrophy

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.9. - fulvestrant - EMEA/H/C/004649

treatment of breast cancer

Scope: Day 120 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.

3.3.10. - guselkumab - EMEA/H/C/004271

treatment of plaque psoriasis

Scope: Day 120 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.

The CHMP adopted the BWP report.

3.3.11. - bevacizumab - EMEA/H/C/004360

treatment of metastatic breast cancer, unresectable advanced, metastatic or recurrent non-small cell lung cancer, unresectable advanced metastatic or recurrent non-squamous non-small cell lung cancer, advanced and/or metastatic renal cell cancer, advanced epithelial

ovarian, fallopian tube, or primary peritoneal cancer, platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer

Scope: Day 120 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.

The CHMP adopted the assessment report on similarity

The CHMP adopted the BWP report.

3.3.12. - bevacizumab - EMEA/H/C/004728

treatment of metastatic breast cancer, unresectable advanced, metastatic or recurrent non-small cell lung cancer, unresectable advanced metastatic or recurrent non-squamous non-small cell lung cancer, advanced and/or metastatic renal cell cancer, advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer, platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer

Scope: Day 120 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.

The CHMP adopted the similarity Assessment Report

3.3.13. - 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: Day 120 list of questions, request by the applicant for extension of clock stop to respond to the day 120 list of questions adopted

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.

The CHMP adopted the similarity Assessment Report

The CHMP agreed to the request by the applicant for extension to the clock stop to respond to the day 120 list of questions adopted.

The CHMP adopted the BWP report.

3.3.14. - semaglutide - EMEA/H/C/004174

to improve glycaemic control in adults with type 2 diabetes and to prevent cardiovascular events

Scope: Day 120 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.

The CHMP adopted the BWP report.

3.3.15. - ritonavir - EMEA/H/C/004549

treatment of HIV-1

Scope: Day 120 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.

3.3.16. - rotigotine - EMEA/H/C/004286

treatment of idiopathic Restless Legs Syndrome and Parkinson's disease

Scope: Day 120 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.

3.3.17. - Herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336

prevention of herpes zoster (HZ) and HZ-related complications

Scope: Day 120 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.

The CHMP adopted the BWP report.

3.3.18. - sofosbuvir / velpatasvir / voxilaprevir - EMEA/H/C/004350

Accelerated assessment

Treatment of chronic hepatitis C virus in adults (HCV) infection in adults

Scope: Day 90 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.

The CHMP agreed to keep the product on the accelerated assessment timetable.

3.3.19. - tacrolimus - EMEA/H/C/004435

prophylaxis of transplant rejection and treatment of allograft rejection

Scope: Day 120 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.

3.3.20. - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363

treatment of adult patients with chronic obstructive pulmonary disease (COPD)

Scope: Day 120 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.

3.3.21. - ciclosporin - Orphan - EMEA/H/C/004411

Accelerated assessment

Santen Oy; treatment of severe vernal keratoconjunctivitis (VKC)

Scope: Day 90 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.

The CHMP agreed to keep the product on the accelerated assessment timetable.

3.3.22. - human fibrinogen / human thrombin - EMEA/H/C/004446

treatment of haemostasis

Scope: Day 120 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.

The CHMP adopted the BWP report.

3.3.23. - ngr-htnf - Orphan - EMEA/H/C/004455

MolMed SpA; treatment of advanced malignant pleural mesothelioma

Scope: Day 120 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.

The CHMP adopted the BWP report.

3.4. Update on on-going initial applications for Centralised procedure

3.4.1. - spheroids of human autologous matrix-associated chondrocytes - ATMP - EMEA/H/C/002736

Claimed indication: repair of symptomatic articular cartilage defects of the femoral condyle and the patella of the knee (International Cartilage Repair Society [ICRS] grade III or IV) with defect sizes up to 10 cm^2 in adults

Scope: update on the CAT discussion

Action: For discussion

List of Outstanding Issues adopted on 17.02.2017. List of Questions adopted on 19.04.2013.

The CHMP was updated on discussions at the CAT at their April meeting.

The CHMP agreed to the 2nd list of outstanding issues as adopted at the April 2017 CAT meeting with a specific timetable.

The CHMP adopted the BWP report.

3.4.2. - iloperidone - EMEA/H/C/004149

treatment of schizophrenia

Scope: list of experts for SAG meeting

Action: For adoption

The CHMP adopted the list of experts for the SAG Psychiatry meeting.

3.4.3. - alpha-1-antitrypsin - Orphan - EMEA/H/C/003934

Kamada BioPharma Limited at Fieldfisher LLP; treatment and maintenance therapy of adult patients with congenital deficiency of alpha-1 antitrypsin and lung disease with clinical evidence of emphysema and airway obstruction (FEV1/SVC<70%)

Scope: Request by the applicant for an extension of clock stop to respond to the List of Outstanding Issues adopted on 23 March 2017. The extension was not agreed. The Committee agreed via written procedure on 12 April on a shorter extension to the clock stop with a specific timetable.

Action: For information

List of Outstanding Issues adopted on 23.03.2017. List of Questions adopted on 21.07.2016.

The CHMP noted the agreement to the clock stop extension as adopted via written procedure on 12 April 2017.

3.4.4. - pegfilgrastim - EMEA/H/C/004413

treatment of neutropenia

Scope: Letter from the applicant dated 7 April 2017 requesting an extension of clock stop to respond to Day 120 list of questions adopted on 23.03.2017

Action: For adoption

List of Questions adopted on 23.03.2017.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to Day 120 list of questions adopted on 23.03.2017.

3.4.5. - cariprazine - EMEA/H/C/002770

treatment of schizophrenia

Scope: cancellation of the consultation of expert Healthcare Professionals (ophthalmology)

Action: For information

List of Outstanding issues adopted on 23.02.2017. List of Questions adopted on 21.07.2016.

The CHMP noted that the consultation of expert Healthcare Professionals (ophthalmology) was cancelled.

3.4.6. - enclomifene - EMEA/H/C/004198

treatment of hypogonadotrophic hypogonadism

Scope: Request by the applicant requesting an extension of clock stop to respond to Day 120 list of questions adopted on 26.01.2017.

Action: For adoption

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the Day 120 list of questions adopted on 26 January 2017.

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

No items

3.6. Initial applications in the decision-making phase

3.6.1. Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029

AstraZeneca AB; for the treatment of hyperkalaemia

Scope: update

Action: For discussion

The CHMP was updated and will consider the potential impact of this new information on the adopted CHMP opinion.

3.7. Withdrawals of initial marketing authorisation application

3.7.1. Solithromycin Triskel EU Services - solithromycin - EMEA/H/C/004179

Triskel EU Services Ltd; treatment of bacterial infections

Scope: letter from the applicant dated 27.03.2017 informing about the withdrawal of initial marketing authorisation application

Action: For information

The CHMP noted the withdrawal letter. The CHMP noted the withdrawal question-and-answer document.

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. Celsentri - maraviroc - EMEA/H/C/000811/X/0046/G

ViiV Healthcare UK Limited

Rapporteur: Filip Josephson, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Qun-Ying Yue

Scope: "Extension application to introduce new pharmaceutical form (20mg/ml oral solution) and 2 new strengths of film-coated tablets (25mg and 75mg) to the currently approved presentations for Celsentri, grouped with extension of indication to include paediatric use (2 to 18 years).

As a consequence, sections 4.2 and 4.8 of the SmPC are updated to detail posology in paediatric patients and to update the safety information, respectively.

The Package Leaflet and Labelling are updated in accordance.

Furthermore, the PI is brought in line with the latest QRD template version 10."

Action: For adoption

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 13.10.2016.

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.

4.1.2. Nexium Control - esomeprazole - EMEA/H/C/002618/X/0016

Pfizer Consumer Healthcare Ltd

Rapporteur: Romaldas Mačiulaitis, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Simona Kudeliene

Scope: "Extension application to introduce a new pharmaceutical form (Gastro-resistant capsule, hard)"

Action: For adoption

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 10.11.2016.

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

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

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

4.1.3. Revestive - teduglutide - Orphan - EMEA/H/C/002345/X/0029

Shire Pharmaceuticals Ireland Ltd

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Torbjorn Callreus

Scope: “Extension application to add a new strength of 1.25mg (paediatric formulation).”

Action: For adoption

List of Questions adopted on 10.11.2016.

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

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

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

The CHMP noted the letter of recommendation dated 18 April 2017.

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. Kuvan - sapropterin - Orphan - EMEA/H/C/000943/X/0047

BioMarin International Limited

Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner

Scope: “Extension application to introduce a new pharmaceutical form associated with new strength (100 mg and 500 mg powder for oral solution).”

Action: For adoption

List of Questions adopted on 23.02.2017.

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. Samsca - tolvaptan - EMEA/H/C/000980/X/0024

Otsuka Pharmaceutical Europe Ltd

Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Julie Williams

Scope: "Extension application to add a new strength of 7.5 mg tablets."

Action: For adoption

The Committee discussed the issues identified in this application. It was noted that conclusive efficacy and safety data is needed for the proposed new strength.

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

4.3.2. Signifor - pasireotide - Orphan - EMEA/H/C/002052/X/0030/G

Novartis Europharm Ltd

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

Scope: "Extension application to introduce two new strengths of the 'powder and solvent for suspension for injection pharmaceutical form' (10 mg and 30 mg) grouped with a type II variation (C.I.6.a) to extend the indication to include 'Treatment of adult patients with Cushing's disease for whom surgery is not an option or for whom surgery has failed' to the intramuscular injection formulations."

Action: For adoption

The Committee discussed the issues identified in this application. It was noted that there were questions related to clinical parts of the dossier.

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

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

4.4.1. Tasigna - nilotinib - Orphan - EMEA/H/C/000798/X/0088/G

Novartis Europharm Ltd

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Doris Stenver

Scope: "Extension of Indication to include treatment of paediatric patients with newly diagnosed Philadelphia chromosome-positive chronic myelogenous leukemia in chronic phase (Ph+ CML-CP), or with Ph+ CML-CP resistant or intolerant to prior therapy including imatinib, based on results from two clinical studies in paediatric patients conducted in

accordance with the approved Tasigna Paediatric Investigation Plan (PIP), the Phase I PK study CAMN107A2120 and the Phase II safety and efficacy study CAMN107A2203. An updated RMP version 18.0 was provided as part of the application.
Extension application to add a new strength of 50mg hard capsules.
In addition, the applicant proposes to merge the SmPCs for the 50 mg and 200 mg strengths."

Letter from the applicant dated 30 March 2017 requesting an extension of clock stop to respond to the list of questions adopted on 23.03.2017

Action: For adoption

List of Questions adopted on 23.03.2017.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the list of questions adopted on 23.03.2017.

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. Avastin - bevacizumab - EMEA/H/C/000582/II/0092

Roche Registration Limited

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Doris Stenver

Scope: "Extension of Indication to include the use of Avastin in combination with paclitaxel and carboplatin for the for treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor–targeted agents. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated with efficacy and safety information from study GOG-0213. The Package Leaflet and RMP (v. 27.1) are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 15.12.2016.

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

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

Assessment Report and translation timetable.

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

The summary of opinion was circulated for information.

5.1.2. Cubicin - daptomycin - EMEA/H/C/000637/II/0061

Merck Sharp & Dohme Limited

Rapporteur: Greg Markey, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Julie Williams

Scope: "Extension of indication to extend the S. aureus bacteraemia indication to include paediatric patients 1 to 17 years of age; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet and Labelling are updated accordingly.

In addition, the marketing authorisation holder (MAH) took the opportunity to bring the product information in line with the latest QRD template version 10 and to combine the SmPCs for both strengths (350 and 500 mg). The MAH also updated the RMP, from last approved version 9.1 to the current proposed version 10.0."

Action: For adoption

The Committee discussed the issues identified in this application. The Committee noted that the safety and efficacy aspects in the paediatric population need to be answered.

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

5.1.3. Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/II/0039

Gilead Sciences International Ltd

Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension of indication to add treatment of chronic hepatitis C in adolescents aged 12 to < 18 years.
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 and Risk Management Plan (RMP version 2) are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 26.01.2017.

The Committee discussed the issues identified in this application. It was noted that there are questions related to population pharmacokinetic modelling for exposure prediction in adolescents, which will also have implication for future younger age cohorts.

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

5.1.4. Opdivo - nivolumab - EMEA/H/C/003985/II/0019

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of Indication to include the treatment of locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy for Opdivo.
As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the proposed indication, add a warning about the patient populations excluded from the clinical trial, and update the safety information. The Package Leaflet is updated in accordance.
Moreover, the updated RMP version 7.0 has been submitted"

Action: For adoption

Request for Supplementary Information adopted on 23.03.2017, 15.12.2016.

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. Tasigna - nilotinib - Orphan - EMEA/H/C/000798/II/0084/G

Novartis Europharm Ltd

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Doris Stenver

Scope: "Update of sections 4.2, 4.4, 4.6, 4.8, 5.1 and 6.6 of the SmPC based on the results from:
- Study CAMN107I2201 (ENESTfreedom: A Phase II, single-arm study evaluating nilotinib treatment discontinuation (treatment-free remission (TFR)) in newly-diagnosed patients with Philadelphia chromosome-positive chronic myelogenous leukemia in chronic phase (Ph+ CML-CP) who achieved a sustained deep molecular response;
- Study CAMN107A2408 (ENESTop): A Phase II, single-arm study evaluating nilotinib treatment discontinuation (treatment-free remission (TFR)) in patients with Ph+ CML-CP who achieved a sustained deep molecular response on nilotinib treatment after switching from imatinib treatment;
- Study CAMN107A2405 (ENESTcmr): A Phase III open-label, randomised study to evaluate nilotinib or imatinib treatment in patients with Ph+ CML-CP who have not achieved a deep molecular response after previous imatinib therapy.
The Package Leaflet has been updated accordingly. Additional changes to the labelling were implemented in line with the latest QRD template version 10.
An updated RMP, version 20, was agreed during the procedure."

Report from SAG Oncology held 4 April 2017

Action: For adoption

Request for Supplementary Information adopted on 23.02.2017, 13.10.2016.

The CHMP noted the report from SAG. The SAG experts outlined the value of treatment-free remission for the patients and physicians but also highlighted the importance of intensive monitoring of disease activity and re-initiation. The SAG considered the proposed precautionary measures as sufficient and recommended to continue the efforts to optimise treatment duration and follow-up. The generation of further follow-up data was considered required to confirm the longer-term outcomes.

The CHMP agreed that a drug utilisation study was not required at this stage.

The Committee discussed the available data and confirmed that all issues previously identified in this application had been addressed.

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

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

The summary of opinion was circulated for information.

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

5.2.1. Bydureon - exenatide - EMEA/H/C/002020/II/0041

AstraZeneca AB

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

Scope: “Update of section 4.1 of the SmPC in order to align with more recently approved glucose-lowering agents and with “Reflection paper on the wording of indication for medicinal products for treatment of type 2 diabetes” and update of section 5.1 based on the study D5553C00003 (Duration 8 study) which evaluated concomitant add-on treatment with the combination of exenatide once weekly 2 mg and dapagliflozin 10 mg once daily in patients with type 2 diabetes mellitus who have inadequate glycaemic control on metformin. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in the SmPC and Package Leaflet. Furthermore, the updated RMP version 24 has been submitted.”

Letter from the applicant dated 13 April 2017 requesting an extension of clock stop to respond to Request for supplementary information adopted on 23.03.2017

Action: For adoption

Request for Supplementary Information adopted on 23.03.2017.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to Request for supplementary information adopted on 23.03.2017.

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. - budesonide - Orphan - H0004655

Dr. Falk Pharma GmbH, Treatment of active eosinophilic esophagitis (EoE) in adults (older than 18 years of age)

Scope: Briefing note and 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

Note: Products requesting eligibility under PRIME scheme are listed in the Annex G.

The CHMP noted the list of applications received.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

Note: Recommendation for PRIME are listed in the Annex G.

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 6 recommendations for eligibility to PRIME: 1 was accepted, 4 were denied and 1 was postponed. The individual outcomes are listed in PRIME Monthly Report on EMA website.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Hemoprostol - misoprostol - Article 58 - EMEA/H/W/002652

Linepharma International Limited; treatment and prevention of Post Partum Haemorrhage

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Menno van der Elst

Scope: Withdrawal of Article 58 scientific opinion

Action: For information

Article 58 of Regulation (EC) No 726/2004

The CHMP was updated on the withdrawal procedure of this Article 58 scientific opinion.

9.1.2. Flixabi - infliximab - EMEA/H/C/004020/II/0009

Samsung Bioepis UK Limited (SBUK)

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Submission of the final study report of study SB2-G31-RA: A Randomised, Double-blind, Parallel Group, Multicentre Clinical Study to Evaluate the Efficacy, Safety, Pharmacokinetics and Immunogenicity of SB2 Compared to Remicade® in Subjects with Moderate to Severe Rheumatoid Arthritis despite Methotrexate Therapy.

The RMP (v. 4) has been updated to reflects the results from the 78 weeks CSR, to exclude 2 of the 5 registries of the pharmacovigilance plan and update in the due date for the

prospective observational cohort study of Flixabi in AS (Ankylosing Spondylitis) and CD (Crohn's Disease) patients."

Opinion

Action: For adoption

Request for Supplementary Information adopted on 15.12.2016.

See also Annex to Minutes B.5.3.

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.

9.1.3. Glybera - Alipogene tiparvovec; Orphan; EMA/H/C/002145

UniQure; Indicated for the long term correction of lipoprotein lipase deficiency, to control or abolish symptoms and prevent complications in adult patients clinically diagnosed with lipoprotein lipase deficiency (LPLD)

CAT Rapporteur: Christiane Niederlaender; CAT Co-Rapporteur: Egbert Flory; CHMP Coordinators: Greg Markey, Jan Mueller-Berghaus

Scope: Formal notification letter by the MAH informing the EMA of the withdrawal of the 5 year renewal application in view of allowing the marketing authorisation to expire on 25 October 2017 based on economic reasons

Action: For information

The CHMP noted that the company withdrew the renewal application. The assessment of the data submitted will therefore not be required.

10. Referral procedures

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

No items

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

10.4.1. Alcover 750 mg, 1250 mg, 1750 mg Granulat im Beutel – Sodium oxybate – EMEA/H/A-29(4)/1451

D&A Pharma

Rapporteur: Andrea Laslop, Co-Rapporteur: Fatima Ventura

Scope: List of outstanding issues

Decentralised Procedure number: AT/H/0552/01-03/DC, notification by the Austrian Agency dated 22 December 2016 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC.

Action: For adoption

List of Questions adopted on 26.01.2017.

The Committee was reminded of the status of this application and its remaining outstanding issues. The members were informed about the data submitted by the applicant in response of the list of questions. The members discussed the data and agreed to request further clarification on the risks in patients with a very high drinking risk level, on the available evidence of efficacy in the proposed indication as well as on the overall benefit/risk ratio.

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

Submission of responses: 19.05.2017

Re-start of the procedure: 25.05.2017

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 07.06.2017

Comments: 12.06.2017

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 15.06.2017

CHMP opinion: June 2017 CHMP

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

10.5.1. Etopophos and associated names– etoposide - EMEA/H/A-30/1417

MAH: Bristol-Myers Squibb group of companies and associated companies

Rapporteur: Greg Markey, Co-Rapporteur: Paula Boudewina van Hennik,

Scope: Opinion

Harmonisation exercise for Etopophos and associated names

Action: For adoption

List of outstanding issues adopted 15.12.2016, 21.07.2016, 25.02.2016 CHMP, List of Questions adopted on 22.10.2015.

The CHMP adopted an opinion by consensus recommending that the above referred marketing authorisation(s) should be varied.

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

10.5.2. Vepesid and associated names - etoposide - EMEA/H/A-30/1425

MAH: Bristol-Myers Squibb group of companies and associated companies

Rapporteur: Greg Markey, Co-Rapporteur: Paula van Hennik

Scope: Opinion

Harmonisation exercise for Vepesid and associated names

Action: For adoption

List of outstanding issues adopted 15.12.2016, 21.07.2016, 25.02.2016 CHMP. List of Questions adopted on 22.10.2015.

The CHMP adopted an opinion by consensus recommending that the above referred marketing authorisation(s) should be varied.

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

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) (EC) No 1084/2003

No items

10.10. Procedure under Article 29 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) No 1234/2008)

No items

11. Pharmacovigilance issue

11.1. Early Notification System

April 2017 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

The CHMP noted the information.

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

Disclosure of 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

Action: For information

The CHMP noted the minutes.

13.2. Innovation Task Force briefing meetings

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

No items

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 3-6 April 2017

Action: For information

The CHMP noted the information.

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for April 2017

Action: For adoption

The CHMP noted the information.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 10-12 April 2017
Action: For information

The CHMP noted the minutes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 27-28 March 2017

Action: For information

The CHMP noted the information.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at April 2017 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 21-24 March 2017

Action: For information

The CHMP noted the report.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 10-12 April 2017
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 18-20 April 2017

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 28 March April 2017. Table of conclusions

Action: For information

The CHMP noted the report.

Scientific advice letters: See Annex G

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

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 29 March 2017.

Action: For adoption

The CHMP adopted the table of decisions.

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz,

Election of BWP Vice-Chair

Action: For adoption

The CHMP elected Nanna Aaby Kruse as Vice-Chair to BWP.

14.3.4. Vaccines Working Party (VWP)

Chair: Mair Powell

Election of VWP Vice-Chair

Nominations received

Action: For adoption

The CHMP elected Svein Rune Andersen as Vice-Chair to VWP.

VWP responses to a PDCO list of questions related to the PIP EMEA-001888-PIP01-15 , adopted by written procedure on 11 April 2017.

Action: For information

The CHMP noted the information.

14.3.5. Biosimilar Medicinal Product Working Party (BMWP)

Chair: Elena Wolff-Holz/Martina Weise

Nomination of additional PK expert to BMWP

Nominations received

Current list of members

Action: For adoption

The CHMP appointed Frederike Lentz (DE) and Rene Bouw (SE) as additional experts to BMWP.

14.3.6. Cardiovascular Working Party (CVSWP)

Chair: Pieter de Graeff/Kristina Dunder

Nomination of CVSWP member following resignation of Karsten Bruins Slot

Nominations received: Maciej Kostrubiec (PL)

Action: For adoption

The CHMP appointed Maciej Kostrubiec (PL) as member to the CVSWP.

14.3.7. Blood Product Working Party (BPWP)

Chair: Jacqueline Kerr

Nomination of Marie Louise S. Christiansen as member of BPWP

Action: For adoption

The CHMP appointed Marie Louise S. Christiansen as member to the BPWP.

14.3.8. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Alfredo Garcia-Arieta

Concept paper on the revision of the Guideline on the role of pharmacokinetics in the development of medicinal products in the paediatric population (EMA/CHMP/448599/2016)

Action: For adoption for 3 months public consultation

The CHMP adopted the concept paper for 3 months public consultation.

14.3.9. Infectious Diseases Working Party (IDWP)

Chair: Anders Lignell/Maria Jesus Fernandez Cortizo

Concept paper on a guideline on the evaluation of medicinal products indicated for treatment of influenza (EMA/CHMP/EWP/808940/2016)

Action: For adoption

The CHMP adopted the concept paper.

14.4. Cooperation within the EU regulatory network

14.4.1. Revision of the Commission Regulation (EC) No 847/2000 of April 2000 laying down the provisions for implementation of the Criteria for designation of a medicinal product as an orphan medicinal product and definitions of the Concept 'similar medicinal product and 'clinical superiority'

Action: For discussion

The CHMP was updated on the consultation on the Commission Regulation (EC) No 847/2000 and the comments received.

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

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 discussion

The CHMP noted the update.

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 18 – 21 April 2017 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	
Christophe Focke	Alternate	Belgium	No restrictions applicable to this meeting	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Katarina Vučić	Member	Croatia	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Hanne Lomholt Larsen	Alternate	Denmark	No interests declared	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Eleftheria Nikolaidi	Member	Greece	No interests declared	
Agnes Gyurasics	Member	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	Iceland	No interests declared	
David Lyons	Member	Ireland	No restrictions applicable to this meeting	
Patrick Salmon	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No restrictions applicable to this meeting	
Natalja Karpova	Alternate	Latvia	No interests declared	
Rugile Pilviniene	Alternate	Lithuania	No interests declared	
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Svein Rune Andersen	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No restrictions applicable to this meeting	
Piotr Fiedor	Member	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Nela Vilceanu	Member	Romania	No interests declared	
Eva Malikova	Alternate	Slovakia	No interests declared	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Arantxa Sancho-Lopez	Alternate	Spain	No restrictions applicable to this meeting	
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 participation in final deliberations and voting on:	3.3.17. - Herpes zoster vaccine (recombinant surface antigen, adjuvanted) - EMEA/H/C/004336 3.3.7. - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781 3.3.20. - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Jean-Louis Robert	Co-opted member	Luxembourg	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
María Escudero Galindo	Expert - in person*	Spain	No participation in discussions, final deliberations and voting on:	3.1.5. Febuxostat Mylan - febuxostat - EMEA/H/C/004374 3.3.3. - anagrelide - EMEA/H/C/004585 3.3.9. - fulvestrant - EMEA/H/C/004649

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				3.3.16. - rotigotine - EMEA/H/C/004286
Jorge Camarero Jiménez	Expert - in person*	Spain	No restrictions applicable to meetings	
Rúna Hauksdóttir Hvannberg	Expert - in person*	Iceland	No restrictions applicable to this meeting	
Anja Schiel	Expert - in person*	Norway	No interests declared	
Kristina Bech Jensen	Expert - in person*	Denmark	No interests declared	
Matthew Camilleri	Expert - in person*	Malta	No interests declared	
Tamás Szolyák	Expert - in person*	Hungary	No participation in discussions, final deliberations and voting on:	4.4.1. Tasigna - nilotinib - Orphan - EMEA/H/C/000798/X/0088/G 5.1.5. Tasigna - nilotinib - Orphan - EMEA/H/C/000798/II/0084/G 3.2.4. - ribociclib - EMEA/H/C/004213 3.2.8. - midostaurin - Orphan - EMEA/H/C/004095 4.3.2. Signifor - pasireotide - Orphan - EMEA/H/C/002052/X/0030/G
Patients' representative		Observer, in person	No interests declared	
Patients' representative		Observer, in person	No interests declared	
Sylvain Gueho	Expert - in person*	France	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Hatice Canan Bayar	Expert - in person*	Norway	No interests declared	
Nicolas Beix	Expert - in person*	France	No restrictions applicable to this meeting	
Amanda Shipman	Expert - in person*	UK	No restrictions applicable to this meeting	
Dominik Karres	Expert - in person*	UK	No interests declared	
Beatriz Flores	Expert - in person*	UK	No interests declared	
Miki Hew	Expert - in person*	Netherlands	No restrictions applicable to this meeting	
Yolanda Barbachano	Expert - in person*	UK	No interests declared	
Sabine Mayrhofer	Expert - via telephone*	Germany	No interests declared	
Vitalis Briedis	Expert - via telephone*	Lithuania	No interests declared	
Olivier Le Blaye	Expert - via telephone*	France	No restrictions applicable to meetings	
Macarena Rodriguez Mendizabal	Expert - via telephone*	Spain	No interests declared	
Philip Lange Møller	Expert - via telephone*	Denmark	No interests declared	
Bernardo Ratilal	Expert - via telephone*	Portugal	No interests declared	
Jan Neuhauser	Expert - via telephone*	Austria	No interests declared	
Per Harald Fuglerud	Expert - via telephone*	Norway	No restrictions applicable to this meeting	
Ingrid Wang	Expert - via telephone*	Norway	No interests declared	
George Aislaitner	Expert - via telephone*	Greece	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Paula Salmikangas	Expert - via telephone*	Finland	No interests declared	
Nathalie Morgensztejn	Expert - via telephone*	France	No interests declared	
Jonas Bergh	Expert - via telephone*	Sweden	No restrictions applicable to this meeting	
Giuseppe Rosano	Expert - via telephone*	Italy	No interests declared	
Anna Vikerfors	Expert - via telephone*	Sweden	No interests declared	
Cecilia Chisholm	Expert - via telephone*	UK	No interests declared	
John Johnston	Expert - via telephone*	UK	No interests declared	
Marie-Christine Bielsky	Expert - via telephone*	UK	No restrictions applicable to this meeting	
Swati Bhat	Expert - via telephone*	UK	No interests declared	
Martina Schüßler-Lenz	Expert - via telephone*	Germany	No interests declared	
João Manuel Lopes de Oliveira	Expert - via telephone*	Portugal	No interests declared	
Joao Freire	Expert - via telephone*	Portugal	No restrictions applicable to this meeting	
Niamh Buckley	Expert - via telephone*	Ireland	No interests declared	
Maia Uusküla	Expert - via telephone*	Estonia	No interests declared	
Bernhardt Sachs	Expert - via Adobe	Germany	No interests declared	
Ralf Meyer	Expert - via Adobe	Germany	No interests declared	
Christoph Unkrig	Expert - via Adobe	Germany	No interests declared	
Martin Mengel	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
Gabriele Schlosser-Weber	Expert - via Adobe	Germany	No interests declared	
Sylvia Kühn	Expert - via Adobe	Germany	No interests declared	
Nele Berthels	Expert - via Adobe	Belgium	No interests declared	
Flora Musuamba Tshinanu	Expert - via Adobe	Belgium	No interests declared	
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)*

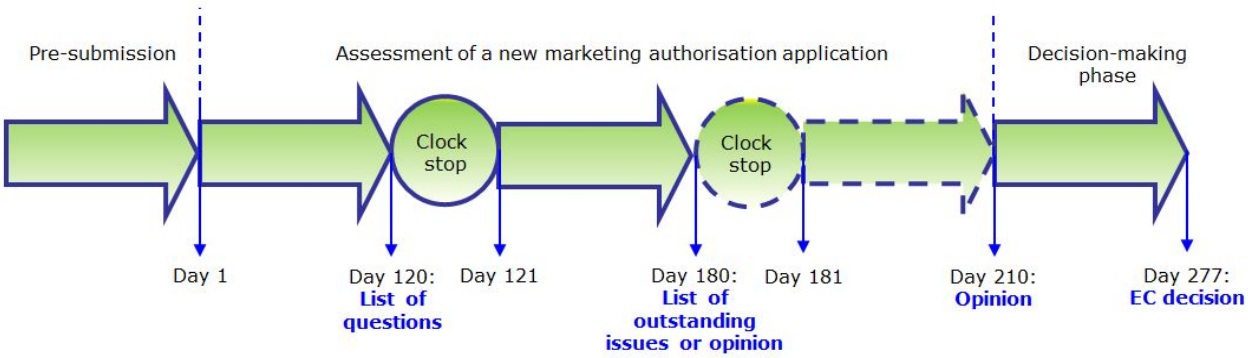
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

26 May 2017
EMA/317901/2017

Annex to April 2017 CHMP Minutes

Pre submission and post authorisations issues

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

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for April 2017: **For adoption**	Adopted.

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

Final Outcome of Rapporteurship allocation for April 2017: **For adoption**	Adopted.

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

Disclosure of information related to pre-submission of initial applications cannot be released at 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

Defitelio - defibrotide - EMEA/H/C/002393/S/0020, Orphan MAH: Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams	Positive Opinion adopted by consensus together with the CHMP assessment report. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
Kolbam - cholic acid - EMEA/H/C/002081/S/0020, Orphan MAH: Retrophin Europe Ltd, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Patrick Batty Request for Supplementary Information adopted on 23.03.2017.	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/0005, Orphan MAH: Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Carmela Macchiarulo Request for Supplementary Information adopted on 23.03.2017, 26.01.2017.	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.
SCENESSE - afamelanotide - EMEA/H/C/002548/S/0011, Orphan	Positive Opinion adopted by consensus together with the CHMP assessment report.

MAH: Clinuvel (UK) Limited, Rapporteur: Harald Enzmann, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Valerie Strassmann	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

B.2.2. Renewals of Marketing Authorisations for unlimited validity

alli - orlistat - EMEA/H/C/000854/R/0054 MAH: Glaxo Group Ltd, Informed Consent of Xenical, Rapporteur: Greg Markey, Co-Rapporteur: Eleftheria Nikolaidi, PRAC Rapporteur: Patrick Batty Request for Supplementary Information adopted on 23.02.2017.	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.
Atriance - nelarabine - EMEA/H/C/000752/R/0037, Orphan MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Torbjorn Callreus Request for Supplementary Information adopted on 23.02.2017.	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.
Capecitabine medac - capecitabine - EMEA/H/C/002568/R/0017 MAH: Medac Gesellschaft fuer klinische Spezialpraeparate m.b.H, Generic, Generic of Xeloda, Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that 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.
ECALTA - anidulafungin - EMEA/H/C/000788/R/0033 MAH: Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Sabine Straus Request for Supplementary Information adopted	Request for Supplementary Information adopted

on 21.04.2017.	
Increlex - mecasermin - EMEA/H/C/000704/R/0042, Orphan MAH: Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kirsti Villikka Request for Supplementary Information adopted on 23.02.2017.	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.
Revestive - teduglutide - EMEA/H/C/002345/R/0038, Orphan MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Torbjorn Callreus Request for Supplementary Information adopted on 23.03.2017.	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.

B.2.3. Renewals of Conditional Marketing Authorisations

Translarna - ataluren - EMEA/H/C/002720/R/0032, Orphan MAH: PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Sabine Straus	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.
Zalmoxis - allogeneic t cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ðlngfr) and the herpes simplex i virus thymidine kinase (hsv-tk mut2) - EMEA/H/C/002801/R/0003, Orphan, ATMP MAH: MolMed SpA, Rapporteur: Johannes Hendrikus Ovelgonne, PRAC Rapporteur: Brigitte Keller-Stanislawski Request for Supplementary Information adopted on 12.04.2017.	Request for Supplementary Information adopted

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection PRAC recommendations on signals adopted at the PRAC meeting held on 3-6 April 2017 PRAC:	
Albiglutide (EMEA/H/C/002735) (Eperzan); MAH: GlaxoSmithKline Trading Services Limited; Rapporteur: Kristina Dunder, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Julie Williams, Signal of acute kidney injury: **For adoption**	Adopted.
Lenflunomide; teriflunomide, (Arava, Lenflunomide Winthrop, Lenflunomide Medac, Aubagio); Rapporteur: , Co-Rapporteur:, PRAC Rapporteur: Sabine Straus, PM:, EPL: Signal of falsely decreased ionized calcium levels: **For adoption**	Adopted.
Temozolomide, (Temodal) MAH: Merck Sharp & Dohme Limited Rapporteur: Harald Enzmann, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber, Signal of meningoencephalitis Herpetic: **For adoption**	Adopted.
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its April 2017 meeting:	
EMEA/H/C/PSUSA/00000208/201609 (anagrelide) CAPS: **Xagrid** (EMEA/H/C/000480) (anagrelide), MAH: Shire Pharmaceutical Contracts Ltd., Rapporteur: Alexandre Moreau NAPS: **Thromboreductin 0,5 mg 16/0027/04-S SK** - AOP ORPHAN PHARMACEUTICALS AG **Thromboreductin 0,5 mg capsules 20060389 BG** - AOP ORPHAN PHARMACEUTICALS AG **Thromboreductin 0,5 mg cietās kapsulas 04-0076 LV** - AOP ORPHAN PHARMACEUTICALS AG **Thromboreductin 0,5 mg kapsule UP/I-530-09/08-01/408 HR** - AOP ORPHAN PHARMACEUTICALS AG **Thromboreductin 0,5 mg kemény kapszula OGYI-T-9545/01 HU** - AOP ORPHAN PHARMACEUTICALS AG **Thromboreductin 0,5 mg kietosios kapsules LT/1/03/2755/001 LT** - AOP ORPHAN PHARMACEUTICALS AG **THROMBOREDUCTIN 0,5 mg trde kapsule 5363-I-2767/10 SI** - AOP ORPHAN	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above-mentioned medicinal product, concerning the following changes: Update of section 4.4 of the SmPC to add a warning on pulmonary hypertension and section 4.8 to change the frequency of pulmonary hypertension to 'uncommon'. The Package leaflet is updated accordingly.

PHARMACEUTICALS AG **THROMBOREDUCTIN 0,5 mg tvrdé tobolky 16/123/04-C CZ** - AOP ORPHAN PHARMACEUTICALS AG **Thromboreductin, 0,5 mg kapsułki twarde 10331 PL** - AOP ORPHAN PHARMACEUTICALS AG **THROMBOREDUCTIN, capsule, 0,5 mg 7585/2015/01 RO** - AOP ORPHAN PHARMACEUTICALS AG **Thromboreductin® 0,5 mg Kapseln 1-24286 AT** - AOP ORPHAN PHARMACEUTICALS AG , PRAC Rapporteur: Caroline Laborde, "Update of section 4.4 of the SmPC to add a warning on pulmonary hypertension and section 4.8 to change the frequency of pulmonary hypertension to 'uncommon'. The Package leaflet is updated accordingly."	
EMEA/H/C/PSUSA/00000931/201609 (daptomycin) CAPS: **Cubicin** (EMEA/H/C/000637) (daptomycin), MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "Update of section 4.4 and 4.8 of the SmPC to add the term organising pneumonia as a recognised presentation of eosinophilic pneumonia. No changes to the package leaflet are required. The MAH also took the opportunity to implement minor editorial changes."	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above-mentioned medicinal product, concerning the following changes: Update of section 4.4 and 4.8 of the SmPC to add the term organising pneumonia as a recognised presentation of eosinophilic pneumonia. No changes to the package leaflet are required. The MAH also took the opportunity to implement minor editorial changes. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00000954/201609 (denosumab (indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer)) CAPS: **Prolia** (EMEA/H/C/001120) (denosumab), MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "27/09/2015-26/09/2016"	Based on the PRAC Rapporteur review of data on safety and efficacy, the PRAC Rapporteur considers that the risk-benefit balance of medicinal products containing denosumab remains unchanged but recommends that the terms of the marketing authorisation(s) should be varied as follows: Update of sections 4.4 and 4.8 of the SmPC to include osteonecrosis of external auditory canal as an adverse drug reaction and to introduce a relevant wording. The Package Leaflet is updated accordingly. A comprehensive Annual report was provided for ongoing PASS Study 20090522: Denosumab Global Safety Assessment Among Women With Postmenopausal Osteoporosis (PMO) and Men

	With Osteoporosis in Multiple Observational Databases. A detailed assessment of the report is not possible within this PSUR. The study started 2010 and the projected completion date is year 2023. It is reasonable to make one detailed interim assessment by the authorities prior to 2023. The MAH should therefore submit the next annual report as a LEG to be assessed in a separate procedure (6 months after finalisation of this PSUSA procedure). In addition, the MAH(s) should also address the following issues in the next PSUR: Regarding several important identified and potential risks, the MAH has summarized "time to onset" for reported events from the first dose of the treatment. Prolia is given as an injection every 6 months and several risks (such as skin infections, cardiovascular risks (focus on arrhythmia) due to transient hypocalcaemia) may be timely related to the latest dose. In the next PSUR, The MAH is asked to present "time to onset" also related to the latest dose of Prolia, when applicable. The next PSUR should be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.
EMEA/H/C/PSUSA/00002653/201609 (rivaroxaban) CAPS: **Xarelto** (EMEA/H/C/000944) (rivaroxaban), MAH: Bayer Pharma AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "16/09/2015 - 15/09/2016"	Based on the PRAC review of data on safety and efficacy, the PRAC considers by consensus that the risk-benefit balance of medicinal products containing rivaroxaban remains unchanged but recommends that the terms of the marketing authorisation(s) should be varied as follows: Update of sections 4.4 and 4.8 of the Summary of Product Characteristics (SmPC) to add information regarding Stevens-Johnson syndrome/Toxic Epidermal Necrolysis. The Package Leaflet is updated accordingly. Issues to be addressed in the next PSUR The MAH should address the following issues in the next PSUR: • a cumulative review of hearing disorders, DRESS syndromes, pancreatitis, reported with rivaroxaban • a cumulative safety review of arthralgia, back pain, musculoskeletal pain and myalgia • a careful review of any new cases of agranulocytosis and alopecia.

	• a cumulative assessment of cases in which rivaroxaban was administered together with fluconazole; • the topics (renal failure [not directly caused by bleeding], dyspnoea, and paraesthesia and hypoesthesia) should be followed and reported in future PSURs, especially if new cases emerge. The MAH should discuss the data and propose an update of the Product Information and/or the RMP if considered relevant. PSUR frequency The next PSUR should be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.
EMEA/H/C/PSUSA/00002880/201608 (telbivudine) CAPS: **Sebivo** (EMEA/H/C/000713) (telbivudine), MAH: Novartis Europharm Ltd, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Caroline Laborde, "01 Sep 2013 – 31 Aug 2016"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended , recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 of the SmPC to reinforce the current warning on lactic acidosis and update of section 4.8 of the SmPC to delete from the adverse drug reaction 'lactic acidosis' the reference to a secondary event often associated with serious conditions. The Package leaflet is updated accordingly.
EMEA/H/C/PSUSA/00003001/201609 (trabectedin) CAPS: **Yondelis** (EMEA/H/C/000773) (trabectedin), MAH: Pharma Mar, S.A., Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Torbjorn Callreus, "From 18 September 2015 to 17 September 2016"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): To update section 4.4 and 4.8 of the SmPC to introduce a warning on Capillary Leak Syndrome (CLS) with frequency uncommon. The PL has been updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

EMEA/H/C/PSUSA/00003149/201608 (zoledronic acid (indicated for cancer and fractures))
CAPS:
Zoledronic acid Hospira (EMEA/H/C/002365) (zoledronic acid), MAH: Hospira UK Limited, Rapporteur: Filip Josephson
Zoledronic acid medac (EMEA/H/C/002359) (zoledronic acid), MAH: medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Alar Irs
Zometa (EMEA/H/C/000336) (zoledronic acid), MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac
NAPS:
ACID ZOLEDRONIC SANDOZ 4 mg/100 ml soluţie perfuzabilă 5011/2012/01 RO - S.C. SANDOZ S.R.L.
ACID ZOLEDRONIC SANDOZ 4 mg/100 ml soluţie perfuzabilă 5011/2012/02 RO - S.C. SANDOZ S.R.L.
ACID ZOLEDRONIC SANDOZ 4 mg/100 ml soluţie perfuzabilă 5011/2012/03 RO - S.C. SANDOZ S.R.L.
ACIDE ZOLEDRONIQUE SANDOZ 4 mg/100 ml, solution pour perfusion 34009 224 088 9 7 FR - SANDOZ
ACIDE ZOLEDRONIQUE SANDOZ 4 mg/100 ml, solution pour perfusion 34009 582 943 0 3 FR - SANDOZ
ACIDE ZOLEDRONIQUE SANDOZ 4 mg/100 ml, solution pour perfusion 34009 582 944 7 1 FR - SANDOZ
ACIDE ZOLEDRONIQUE SANDOZ 4 mg/100 ml, solution pour perfusion 34009 586 953 0 8 FR - SANDOZ
Ácido zoledrónico Sandoz 4 mg/100 ml solución para perfusión 76505 ES - SANDOZ FARMACÉUTICA, S.A.
Ácido Zoledrónico Sandoz 5466867 PT - SANDOZ FARMACÊUTICA LDA.
Kyselina zoledrónová Sandoz 4 mg/100 ml infúzny roztok 87/0281/12-S SK - SANDOZ PHARMACEUTICALS D.D.
STEOZOL 4 mg/5 ml concentrado para solución para perfusión en jeringa precargada 76675 ES - CHEMI S.P.A.
STEOZOL 4 mg/5 ml pykno dialyma gia paraskeyn dialumatos pros egchysh 84684 GR - ITF HELLAS AE
STEOZOL 4 mg/5ml Konzentrat zur

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 sections 4.4 and 4.8 of the SmPC to add a warning on osteonecrosis of other anatomical sites and add this adverse reaction with a frequency very rare. The Package leaflet is updated accordingly.
The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

Herstellung einer Infusionslösung in einer Fertigspritze 84927.00.00 DE - CHEMI S.P.A.
STEOZOL 4mg/5ml concentrato per soluzione per infusione 040982011 IT - ITALFARMACO S.P.A
STEOZOL 4mg/5ml concentrato per soluzione per infusione 040982023 IT - ITALFARMACO S.P.A
STEOZOL 4mg/5ml concentrato per soluzione per infusione 040982035 IT - ITALFARMACO S.P.A
STEOZOL 4mg/5ml concentrato per soluzione per infusione 040982047 IT - ITALFARMACO S.P.A
Zoledronic Acid Sandoz 4 mg / 100 ml infuusioneste, liuos 29715 FI - SANDOZ A/S
Zoledronic acid Sandoz 4 mg/100 ml 021979 CY - SANDOZ GMBH
Zoledronic acid Sandoz 4 mg/100 ml infusionsvätska, lösning 46101 SE - SANDOZ A/S
Zoledronic acid Sandoz 4 mg/100 ml oplossing voor infusie BE424715 BE - SANDOZ N.V.
Zoledronic acid Sandoz 4 mg/100 ml solution for infusion PL 04416/1307 UK - SANDOZ LTD
ZOLEDRONOVA KISELINA SANDOZ MG/100 ML INFUZIONEN RAZTVOR 20120593 BG - SANDOZ PHARMACEUTICALS D.D.
Zoledronsav Sandoz 4 mg/100 ml oldatos infúzió OGYI-T-22283/04 HU - SANDOZ HUNGÁRIA KFT
Zoledronsav Sandoz 4 mg/100 ml oldatos infúzió OGYI-T-22283/05 HU - SANDOZ HUNGÁRIA KFT
Zoledronsav Sandoz 4 mg/100 ml oldatos infúzió OGYI-T-22283/06 HU - SANDOZ HUNGÁRIA KFT
Zoledronsav Sandoz 4 mg/100 ml oldatos infúzió OGYI-T-22283/10 HU - SANDOZ HUNGÁRIA KFT
Zoledronsäure - 1 A Pharma 4 mg/100 ml Infusionslösung 84970.00.00 DE - 1 A PHARMA GMBH
Zoledronsäure Hexal 4 mg/100 ml – Infusionslösung 1-31351 AT - HEXAL PHARMA GMBH
Zoledronsäure Sandoz 4 mg/100 ml – Infusionslösung 1-31349 AT - SANDOZ GMBH
Zoledronska kislina Sandoz 4 mg/100 ml

raztopina za infundiranje H/12/01713/001 SI - SANDOZ PHARMACEUTICALS D.D. **Zoledronska kislina Sandoz 4 mg/100 ml raztopina za infundiranje H/12/01713/002 SI** - SANDOZ PHARMACEUTICALS D.D. **Zoledronska kislina Sandoz 4 mg/100 ml raztopina za infundiranje H/12/01713/003 SI** - SANDOZ PHARMACEUTICALS D.D. **Zoledronska kislina Sandoz 4 mg/100 ml raztopina za infundiranje H/12/01713/004 SI** - SANDOZ PHARMACEUTICALS D.D. **Zoledronsyre Sandoz 4 mg/100 ml infusjonsvæske, oppløsning 11-8739 NO** - SANDOZ A/S **Zoledronsyre Sandoz 48818 DK** - SANDOZ A/S , PRAC Rapporteur: Doris Stenver, "Update of sections 4.4 and 4.8 of the SmPC to add a warning on osteonecrosis of other anatomical sites and add this adverse reaction with a frequency very rare. The Package leaflet is updated accordingly. In addition, MAHs which have an RMP in place should address the issues, as detailed in section 2 of the Assessment report, in the next RMP update to be submitted within an upcoming regulatory procedure affecting the RMP."	
EMEA/H/C/PSUSA/00009119/201609 (denosumab (indicated for skeletal related events associated with bone metastases and for giant cell tumour of bone)) CAPS: **XGEVA** (EMEA/H/C/002173) (denosumab), MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "27 September 2015 - 26 September 2016"	Based on the PRAC review of data on safety and efficacy, the PRAC considers by consensus that the risk-benefit balance of medicinal products containing denosumab (indicated for skeletal related events associated with bone metastases and for giant cell tumour of bone) remains unchanged but recommends that the terms of the marketing authorisation(s) should be varied as follows: Update of sections 4.4 and 4.8 of the SmPC to include osteonecrosis of external auditory canal as an adverse drug reaction and to introduce a relevant wording. The Package Leaflet is updated accordingly. A comprehensive annual report was provided for ongoing PASS Study 20101102. A detailed assessment of the report is not possible within this PSUR. The study started in 2012 and the projected completion date is in the year 2021. It is reasonable to make one detailed interim assessment by the authorities prior to 2021. The MAH should therefore submit the next annual report as a LEG to be assessed in a separate procedure within 6 months after finalisation of

	this PSUSA procedure. In addition, the MAH(s) should also address the following issues in the next PSUR: It is noted that 'New primary malignancy' and 'Delay in diagnosis of PMGCTB (primary malignancy in giant cell tumour of bone)' are among the important potential risks for Xgeva. The MAH should discuss in detail whether there is a causal relationship with denosumab treatment. The next PSUR should be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.
EMEA/H/C/PSUSA/00010074/201609 (bedaquiline) CAPS: **SIRTURO** (EMEA/H/C/002614) (bedaquiline), MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue, "06 March 2016 to 05 September 2016"	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 together with the detailed explanation of the scientific grounds for the differences with the PRAC recommendation, recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change: Based on the PRAC Rapporteur review of data on safety and efficacy, the PRAC considers that the risk-benefit balance of medicinal product containing bedaquiline remains unchanged but recommends that the terms of the marketing authorisations should be varied as follows: Update of section 4.5 of the Summary of Product Characteristics to add information about bedaquiline exposure over 48 hours in subjects treated with bedaquiline as part of therapy for drug–resistant tuberculosis and lopanivir/ritonavir-based antiretroviral therapy. No change in bedaquiline dosing is recommended in case of co-treatment with lopinavir/ritonavir or other ritonavir-boosted HIV protease inhibitors.The Icelandic and the Norwegian CHMP members agreed with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010133/201609 (regorafenib) CAPS: **Stivarga** (EMEA/H/C/002573) (regorafenib), MAH: Bayer Pharma AG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine	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),

Straus, “27-Mar-2015 to 26-Sep-2016.”	concerning the following change(s): Update of section 4.8 of the SmPC to add ‘dehydration’ with the frequency ‘common’. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010135/201609 (teriflunomide) CAPS: **AUBAGIO** (EMEA/H/C/002514) (teriflunomide), MAH: sanofi-aventis groupe, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, “13-Mar-2015 - 12-Sep-2016”	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 include the adverse drug reactions interstitial lung disease (ILD), acute hepatitis, asthenia and nails disorders with a frequency ‘not known’. Furthermore, alanine aminotransferase (ALT) increase, gamma-glutamyl transferase (GGT) increase and aspartate aminotransferase increase are moved from the SOC ‘Investigations’ to the newly introduced SOC ‘Hepatobiliary disorders’ with the same frequencies as before. Finally, the existing warning on respiratory reactions in section 4.4 of the SmPC has been updated in relation to ILD. The Package leaflet is updated accordingly. In addition, certain side-effects in the Package leaflet have also been moved under ‘serious side-effects’. RMP version 4.0 has been submitted and agreed; however, the conclusions drawn from the assessment of the current PSUR warrant further changes to the RMP to be submitted at the next opportunity. The MAH has also taken the occasion to align the PI to QRD template version 10.0 and to update local representatives for Bulgaria, France and Hungary in the Package leaflet. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010311/201609 (dulaglutide) CAPS: **Trulicity** (EMEA/H/C/002825) (dulaglutide), MAH: Eli Lilly Nederland B.V., Rapporteur: Greg	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 together with the detailed explanation of the scientific grounds for

Markey, PRAC Rapporteur: Carmela Macchiarulo, "Based on the PRAC review of data on safety and efficacy, the PRAC considers that the risk-benefit balance of medicinal products containing dulaglutide remains unchanged but recommends that the terms of the marketing authorisation should be varied as follows: Update of section 4.8 of the SmPC to add 'hypersensitivity' as adverse reaction with a frequency 'uncommon'. 'Anaphylactic reaction' and 'angioedema' are also being added, with a frequency 'rare'. The Package leaflet is updated accordingly."	the differences with the PRAC recommendation, 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 'hypersensitivity' as adverse reaction with a frequency 'uncommon'. 'Anaphylactic reaction' and 'angioedema' are also being added, with a frequency 'rare'. 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/00010366/201609 (naltrexone / bupropion) CAPS: **Mysimba** (EMEA/H/C/003687) (naltrexone hydrochloride / bupropion hydrochloride), MAH: Orexigen Therapeutics Ireland Limited, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Martin Huber, "To introduce a warning in Section 4.4 and 4.8 of the SmPC on hepatotoxicity as drug-induced liver injury has been reported post-marketing associated with the use of the medicinal product as well as levels of elevated liver enzymes. In addition, the warning on suicidal behaviour in section 4.4 of the SmPC has also been updated to indicate that suicidality events does not predominantly concern younger patients below the age of 25 years but patients above the age of 40 years. In addition, the MAH took the opportunity to introduce amendments in the local representative for Poland in the Package Leaflet."	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 together with the detailed explanation of the scientific grounds for the differences with the PRAC recommendation, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): To introduce a warning in Section 4.4 and 4.8 of the SmPC on hepatotoxicity as drug-induced liver injury has been reported post-marketing associated with the use of the medicinal product as well as levels of elevated liver enzymes. In addition, the warning on suicidal behaviour in section 4.4 of the SmPC has also been updated to indicate that suicidality events does not predominantly concern younger patients below the age of 25 years but patients above the age of 40 years. In addition, the MAH took the opportunity to introduce amendments in the local representative for Poland in the Package Leaflet. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010403/201609 (pembrolizumab) CAPS: **Keytruda** (EMEA/H/C/003820) (pembrolizumab), MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, PRAC	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 together with the detailed explanation of the scientific grounds for the differences with the

Rapporteur: Sabine Straus, “04/03/2016 to 03/09/2016”	PRAC recommendation, 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): Based on the PRAC review of data on safety and efficacy, the PRAC considers that the risk-benefit balance of pembrolizumab remains unchanged but recommends that the terms of the marketing authorisation should be varied as follows: Update of section 4.8 of the SmPC to add sarcoidosis as an adverse drug reaction with frequency rare. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010413/201609 (guanfacine) CAPS: **Intuniv** (EMEA/H/C/003759) (guanfacine), MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia, “18/03/2016 to 17/09/2016”	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 the SmPC to add the adverse reaction ‘erectile dysfunction’ with a frequency ‘not known’. The Package leaflet is updated accordingly.

B.4. EPARs / WPARs

Axumin - fluciclovine (18F) - EMEA/H/C/004197 Applicant: Blue Earth Diagnostics Ltd, diagnostic agent for PET of adult men with suspected recurrence of prostate cancer, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Blectifor - caffeine citrate - EMEA/H/C/004100, Orphan Applicant: Viridian Pharma Ltd, indicated in preterm neonates for the prevention of bronchopulmonary dysplasia, Rapporteur: Milena Stain, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Leonor Chambel, Peer Reviewer: Greg MarkeyWell-established use application (Article 10a of Directive No 2001/83/EC)	adopted.

WPAR	
Dinutuximab beta Apeiron - dinutuximab beta - EMEA/H/C/003918, Orphan Applicant: APEIRON Biologics AG, treatment of neuroblastoma, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Elmiron - pentosan polysulfate sodium - EMEA/H/C/004246, Orphan Applicant: bene-Arzneimittel GmbH, treatment of Interstitial Cystitis, Well-established use application (Article 10a of Directive No 2001/83/EC)	adopted.
Ivabradine Accord - ivabradine - EMEA/H/C/004241 Applicant: Accord Healthcare Ltd, treatment of angina pectoris, Generic, Generic of Procoralan, Generic application (Article 10(1) of Directive No 2001/83/EC)	adopted.
Refixia - nonacog beta pegol - EMEA/H/C/004178, Orphan Applicant: Novo Nordisk A/S, treatment of haemophilia B, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Solithromycin Triskel EU Services - solithromycin - EMEA/H/C/004179 Applicant: Triskel EU Services Ltd, treatment of bacterial infections, New active substance (Article 8(3) of Directive No 2001/83/EC) **WPAR**	adopted.
Trumenba - meningococcal group b vaccine (recombinant, adsorbed) - EMEA/H/C/004051 Applicant: Pfizer Limited, prevent invasive meningococcal disease caused by Neisseria meningitidis serogroup B, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Advate - octocog alfa - EMEA/H/C/000520/II/0083/G MAH: Baxter AG, Rapporteur: Jan	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Mueller-Berghaus Opinion adopted on 21.04.2017.	recommendation.
Aflunov - prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - EMEA/H/C/002094/II/0032 MAH: Seqirus S.r.l, Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 06.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0001 MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 21.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Armisarte - pemetrexed - EMEA/H/C/004109/II/0008/G MAH: Actavis Group PTC ehf, Rapporteur: Alar Irs Request for Supplementary Information adopted on 21.04.2017, 09.03.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Azopt - brinzolamide - EMEA/H/C/000267/II/0064/G MAH: Alcon Laboratories (UK) Ltd, Rapporteur: Concepcion Prieto Yerro Request for Supplementary Information adopted on 06.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Cerezyme - imiglucerase - EMEA/H/C/000157/II/0099/G MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 30.03.2017. Request for Supplementary Information adopted on 16.02.2017.	Positive Opinion adopted by consensus on 30.03.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cetrotide - cetrorelix acetate - EMEA/H/C/000233/II/0056 MAH: Merck Serono Europe Limited, Rapporteur: Martina Weise Opinion adopted on 06.04.2017.	Positive Opinion adopted by consensus on 06.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cetrotide - cetrorelix acetate - EMEA/H/C/000233/II/0058 MAH: Merck Serono Europe Limited, Rapporteur: Martina Weise Opinion adopted on 21.04.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
CIAMBRA - pemetrexed - EMEA/H/C/003788/II/0002/G MAH: Menarini International Operations	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

Luxembourg S.A., Generic, Generic of Alimta, Rapporteur: Juris Pokrotnieks Request for Supplementary Information adopted on 06.04.2017.	
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0058/G MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder Opinion adopted on 06.04.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 06.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Darzalex - daratumumab - EMEA/H/C/004077/II/0005/G, Orphan MAH: Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac Opinion adopted on 06.04.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 06.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
ELOCTA - efmoroctocog alfa - EMEA/H/C/003964/II/0012/G MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 21.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Foclivia - influenza virus surface antigens (inactivated) of strain A/Vietnam/1194/2004 (H5N1) - EMEA/H/C/001208/II/0027 MAH: Seqirus S.r.l, Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 06.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Galafold - migalastat - EMEA/H/C/004059/II/0005, Orphan MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 06.04.2017.	Positive Opinion adopted by consensus on 06.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Herceptin - trastuzumab - EMEA/H/C/000278/II/0121 MAH: Roche Registration Limited, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 09.02.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0003/G, Orphan MAH: CSL Behring GmbH, Rapporteur: Jan	Positive Opinion adopted by consensus on 06.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Mueller-Berghaus Opinion adopted on 06.04.2017. Request for Supplementary Information adopted on 23.02.2017.	recommendation.
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0032/G, Orphan MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson Opinion adopted on 21.04.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Increlex - mecasermin - EMEA/H/C/000704/II/0046/G, Orphan MAH: Ipsen Pharma, Rapporteur: Outi Mäki-Ikola Opinion adopted on 30.03.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 30.03.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Inhixa - enoxaparin sodium - EMEA/H/C/004264/II/0005/G MAH: Techdow Europe AB, Duplicate, Duplicate of Thorinane, Rapporteur: Andrea Laslop Opinion adopted on 30.03.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 30.03.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Inhixa - enoxaparin sodium - EMEA/H/C/004264/II/0009/G MAH: Techdow Europe AB, Duplicate, Duplicate of Thorinane, Rapporteur: Andrea Laslop Opinion adopted on 21.04.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0026/G MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 21.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0013/G MAH: Orexigen Therapeutics Ireland Limited, Rapporteur: Hanne Lomholt Larsen Request for Supplementary Information adopted on 06.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Onivyde - irinotecan hydrochloride trihydrate - EMEA/H/C/004125/II/0002, Orphan MAH: Baxalta Innovations GmbH, Rapporteur: Filip Josephson Opinion adopted on 21.04.2017. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 23.02.2017.	
OPDIVO - nivolumab - EMEA/H/C/003985/II/0031/G MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez Opinion adopted on 30.03.2017.	Positive Opinion adopted by consensus on 30.03.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0018/G MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil Opinion adopted on 30.03.2017.	Positive Opinion adopted by consensus on 30.03.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
RotaTeq - rotavirus vaccine (live, oral) - EMEA/H/C/000669/II/0069/G MAH: MSD Vaccins, Rapporteur: Greg Markey Request for Supplementary Information adopted on 21.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Simponi - golimumab - EMEA/H/C/000992/II/0074/G MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 30.03.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
TachoSil - human thrombin / human fibrinogen - EMEA/H/C/000505/II/0077/G MAH: Takeda Austria GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 06.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0090 MAH: Genzyme Europe BV, Rapporteur: Patrick Salmon Request for Supplementary Information adopted on 06.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Vectibix - panitumumab - EMEA/H/C/000741/II/0084 MAH: Amgen Europe B.V., Rapporteur: Robert James Hemmings Opinion adopted on 21.04.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vimizim - elosulfase alfa - EMEA/H/C/002779/II/0017/G, Orphan MAH: BioMarin Europe Ltd, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 30.03.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

Xofigo - radium-223 - EMEA/H/C/002653/II/0022/G MAH: Bayer AG, Rapporteur: Harald Enzmann Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 19.01.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zevalin - ibritumomab tiuxetan - EMEA/H/C/000547/II/0046/G MAH: Spectrum Pharmaceuticals B.V., Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 30.03.2017, 19.01.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS1124 Fertavid-EMEA/H/C/001042/WS1124/0034 Puregon-EMEA/H/C/000086/WS1124/0092 MAH: Merck Sharp & Dohme Limited, Lead Rapporteur: Nithyanandan Nagercoil Opinion adopted on 21.04.2017.	Positive Opinion adopted by consensus on 21.04.2017. 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

Adempas - riociguat - EMEA/H/C/002737/II/0018/G, Orphan MAH: Bayer Pharma AG, Rapporteur: Johann Lodewijk Hillege, "C.I.13 Submission of the final clinical study report of study 12166: A multicentre, non-randomized, non-blinded, non-controlled study to investigate the impact of multiple doses of riociguat on safety, tolerability, pharmacokinetics and pharmacodynamics in patients with pulmonary hypertension in a 12 week 3 times a day individual dose titration scheme. C.I.13 Submission of the final clinical study report of study 16097: An open-label phase IIIb study of riociguat in patients with in-operable chronic thromboembolic pulmonary hypertension (CTEPH) or recurrent or persisting pulmonary hypertension after surgical treatment who are not satisfactorily treated and cannot participate in any other CTEPH trial." Opinion adopted on 30.03.2017. Request for Supplementary Information adopted on 26.01.2017.	Positive Opinion adopted by consensus on 30.03.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Azarga - brinzolamide / timolol - EMEA/H/C/000960/II/0034	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP

MAH: Alcon Laboratories (UK) Ltd, Rapporteur: Hanne Lomholt Larsen, “Update of sections 4.2, 4.4, 4.6 and 4.8 of the SmPC following a review of the safety profile taking into consideration data from clinical studies and post-marketing experience. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and Package Leaflet and to update the contact details for the local representative in Spain in the Package Leaflet.” Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 16.02.2017.	Members were in agreement with the CHMP recommendation.
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0057/G MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder B.II.e.6.a (Type IB) - to introduce an additional presentation which combines a Pre-filled Syringe (PFS) within a single-use, needle-safe Dose-dispenser Cartridge (DDC) (functional secondary packaging) (EU/1/09/544/008) B.II.e.5.a).1 (Type IAin) – To add an additional pack size of 6 (3 x 2) dose-dispenser cartridges (multipack) (EU/1/09/544/009) B.II.e.5.a).1 (Type IAin) - To add an additional pack size of 10 (5 x 2) dose-dispenser cartridges (multipack) (EU/1/09/544/010) C.I.4 (Type II) - amend the Product Information (PI) to add the Dose-dispenser Cartridge presentations.” Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Eperzan - albiglutide - EMEA/H/C/002735/II/0031 MAH: GlaxoSmithKline Trading Services, Rapporteur: Kristina Dunder, “Update of sections 4.4 and 4.8 of the SmPC in order to add angioedema with frequency ‘rare’ and to include a warning concerning hypersensitivity reactions in general. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder took the opportunity to implement minor editorial amendments throughout the Product Information.” Request for Supplementary Information adopted	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

on 21.04.2017.	
Glivec - imatinib - EMEA/H/C/000406/II/0108 MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, "Submission of the final CSR for study STI571A2405 - the International Study for Chronic Myeloid Leukemia (CML) in childhood and adolescents (I-CML-Ped Study). The provision of the study report addresses the post-authorisation measure MEA 162.8." Request for Supplementary Information adopted on 21.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0136 MAH: Merck Serono Europe Limited, Rapporteur: Nithyanandan Nagercoil, "Update of the SmPC section 4.8 to indicate that thromboembolism can occur both in association with and separate from ovarian hyperstimulation syndrome (OHSS). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.0." Opinion adopted on 30.03.2017. Request for Supplementary Information adopted on 02.02.2017.	Positive Opinion adopted by consensus on 30.03.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/II/0035 MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, "Update of sections 4.2 and 4.4 of the SmPC to revise dosing recommendations in patients with decompensated cirrhosis and to add a warning concerning infection with hepatitis C virus genotype 3 based on data from clinical studies SOLAR-1 and SOLAR-2. Furthermore, sections 4.8, 5.1 and 5.2 of the SmPC were updated in order to reflect on emerging clinical data from these two studies. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representative in the Package Leaflet." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017, 10.11.2016.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hetlioz - tasimelteon - EMEA/H/C/003870/II/0008, Orphan MAH: Vanda Pharmaceuticals Ltd., Rapporteur:	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

Greg Markey, “Update of section 4.5 of the SmPC with the deletion of the CYP2C19 statement and the removal of the commitment to conduct a human CYP2C19 Drug-Drug Interaction Study to evaluate the single-dose pharmacokinetics of tasimelteon 20 mg alone and in combination with a CYP2C19 inhibitor, omeprazole, at steady-state from the Risk Management Plan (RMP).” Request for Supplementary Information adopted on 06.04.2017.	
IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0005, Orphan MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, “Update of section 4.8 of the SmPC in order to change a previous report of low titre inhibitor to the correct high titre inhibitor development in a previously untreated patient (PUP) in the ongoing extension study CSL654-3003. The Package Leaflet is updated accordingly.” Opinion adopted on 21.04.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Increlex - mecasermin - EMEA/H/C/000704/II/0040, Orphan MAH: Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, “Update of section of 4.1 of the SmPC in order to re-word the recommendation to confirm diagnosis with an IGF-1 generation test used for diagnosis of Severe Primary IGFD” Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 26.01.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Incruse - umeclidinium bromide - EMEA/H/C/002809/II/0013 MAH: Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, “Update of section 4.8 of the SmPC and relevant section of the PL to add hypersensitivity reactions including rash, urticaria, pruritus as uncommon and anaphylaxis and angioedema as rare adverse reactions. The MAH is taking the opportunity to update the Local representative section in the PL.” Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 15.12.2016.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lenvima - lenvatinib - EMEA/H/C/003727/II/0008, Orphan MAH: Eisai Europe Ltd., Rapporteur: Bart Van der Schueren, “Submission of Clinical Study Report for Study E78080-J081-208”	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

Request for Supplementary Information adopted on 06.04.2017.	
Mimpara - cinacalcet - EMEA/H/C/000570/II/0056 MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, "Submission of the final report for Study 20090686, a study designed to determine the efficacy of cinacalcet compared with vitamin D therapy for management of secondary HPT (hyperparathyroidism) in haemodialysis subjects. This variation fulfils LEG 031." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0010 MAH: Orexigen Therapeutics Ireland Limited, Rapporteur: Hanne Lomholt Larsen, "Submission of study report NB-CVOT - Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Assessing the Occurrence of Major Adverse Cardiovascular Events (MACE) in Overweight and Obese Subjects with Cardiovascular Risk Factors Receiving Naltrexone SR/Bupropion SR. The product information remains unchanged." Request for Supplementary Information adopted on 21.04.2017, 23.02.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0014 MAH: Orexigen Therapeutics Ireland Limited, Rapporteur: Hanne Lomholt Larsen, "C.I.13: Submission of the final report from study NaltrexBuprop-1004; a Phase 1, Open-Label, Sequential Design Study to Evaluate the Potential Effect of Multiple Oral Doses of Extended-Release Combination of Naltrexone and Bupropion on the Pharmacokinetics of a Single Oral Dose of Metformin in Healthy Subjects. This study does not lead to changes in the product information." Request for Supplementary Information adopted on 21.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0015 MAH: Orexigen Therapeutics Ireland Limited,	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

Rapporteur: Hanne Lomholt Larsen, “Submission of the final report from study NB-404 A Multicenter, Randomized, Open-Label, Controlled, Method-of-Use Study Assessing the Effect of Naltrexone SR/Bupropion SR on Body Weight and Cardiovascular Risk Factors in Overweight and Obese Subjects. This study does not lead to changes in the product information.” Request for Supplementary Information adopted on 21.04.2017.	
Noxafil - posaconazole - EMEA/H/C/000610/II/0048 MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, “Update of sections 4.4 and 4.5 of the SmPC in order to strengthen the current warning on interaction of posaconazole with vincristine. The Package Leaflet is 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.” Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
SIRTURO - bedaquiline - EMEA/H/C/002614/II/0021, Orphan MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, “Update of section 4.4 of the SmPC in order to add delamanid as an example of a drug that prolongs the QT interval following the review of the global safety database for all serious cases received from 28 December 2012 to 30 September 2016. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.” Request for Supplementary Information adopted on 06.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Sutent - sunitinib - EMEA/H/C/000687/II/0064 MAH: Pfizer Limited, Rapporteur: Daniela Melchiorri, “Update of section 4.1 of the SmPC in order to remove the statement ‘Experience with SUTENT as first-line treatment is limited (see section 5.1)’ and update of section 5.1 of the SmPC based on the final CSR of study A6181202 in fulfilment of MEA 037.2. In addition, the MAH took the opportunity to make a minor editorial	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

change in the SmPC." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 26.01.2017.	
Travatan - travoprost - EMEA/H/C/000390/II/0053 MAH: Novartis Europharm Ltd, Rapporteur: Concepcion Prieto Yerro, "Following the submission of final CSR for study C-01-79 and a review of supporting clinical studies and post-marketing data, update to SmPC section 4.8 is proposed. The package leaflet is updated accordingly. In addition, MAH took the opportunity to update number of the Spanish representative in the PL." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 19.01.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Victrelis - boceprevir - EMEA/H/C/002332/II/0041 MAH: Merck Sharp & Dohme Limited, Rapporteur: Joseph Emmerich, "In line with the Latuda Product Information and following data obtained from the MAH continuous safety monitoring, update of sections 4.3 and 4.5 of the SmPC in order to add lurasidone in the list of contraindicated medications. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement QRD template version 10, including implementation of the 2D barcode in the PI." Opinion adopted on 21.04.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0173 MAH: Gilead Sciences International Ltd, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Caroline Laborde, "Submission of final long-term safety and efficacy data (480 weeks) from two completed Phase 3 studies in HBeAg-negative and HBeAg-positive patients with chronic hepatitis B (CHB), Studies GS-US-174-0102 and GS-US-174-0103." Opinion adopted on 30.03.2017. Request for Supplementary Information adopted on 26.01.2017.	Positive Opinion adopted by consensus on 30.03.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xagrid - anagrelide - EMEA/H/C/000480/II/0075 MAH: Shire Pharmaceutical Contracts Ltd., Rapporteur: Alexandre Moreau, "Update of	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

sections 4.4, 4.5 and 5.1 of the SmPC in order to change the terminology of myeloproliferative disorders to neoplasms, add text regarding platelet count rebound above baseline following dosage interruption, incorporate a section in drug interactions on Cyp 1A2 inducers and update information on the mode of action. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, correct typographical errors and bring the PI in line with the latest QRD template. No changes were proposed to the RMP." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 26.01.2017.	recommendation.
Xarelto - rivaroxaban - EMEA/H/C/000944/II/0050 MAH: Bayer Pharma AG, Rapporteur: Kristina Dunder, "Update of the Summary of Product Characteristics (SmPC) to add a new posology in the patients with non valvular atrial fibrillation and information on safety and efficacy in patients who undergo PCI (percutaneous coronary intervention) with stent placement based on the final results of study 16523 (PIONEER AF-PCI): An Open-label, Randomized, Controlled, Multicenter Study Exploring Two Treatment Strategies of Rivaroxaban and a Dose- Adjusted Oral Vitamin K Antagonist Treatment Strategy in Subjects With Atrial Fibrillation Who Undergo Percutaneous Coronary Intervention. Sections 4.2, 4.4 and 5.1 of the SmPC are updated. Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder took the opportunity to update the telephone number of local representatives for UK in the Package Leaflet." Request for Supplementary Information adopted on 21.04.2017.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Yondelis - trabectedin - EMEA/H/C/000773/II/0051, Orphan MAH: Pharma Mar, S.A., Rapporteur: Sinan B. Sarac, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update the safety information following submission of study report ET743-OVC-1004 "An Open-Label, Multicenter, Pharmacokinetic Study of Trabected in in Subjects with Advanced Malignancies and Hepatic Dysfunction"	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

listed in the RMP. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce editorial changes in the SmPC." Request for Supplementary Information adopted on 21.04.2017.	
Zepatier - elbasvir / grazoprevir - EMEA/H/C/004126/II/0005 MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, "Update of section 4.5 of the SmPC in order to update information regarding drug-drug interaction (DDI) of elbasvir/grazoprevir when co-administrated with sunitinib (tyrosine kinase inhibitor). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some editorial changes." Opinion adopted on 06.04.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 06.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1055 **Ebymect-EMEA/H/C/004162/WS1055/0016** **Edistride-EMEA/H/C/004161/WS1055/0012** **Forxiga-EMEA/H/C/002322/WS1055/0031** **Qtern-EMEA/H/C/004057/WS1055/0004** **Xigduo-EMEA/H/C/002672/WS1055/0027** MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to add rash as new skin and subcutaneous tissue adverse reactions occurring with the frequency of common. The Package Leaflet is updated accordingly. The ATC code was updated in section 5.1 of the SmPC. Section 6.1 was corrected regarding missing information on the differences in the list of excipients for the two existing strengths of Xigduo/Ebymect film coated tablets. Annex IIIA was updated in sections 17 and 18 to remove the unique identifier 2D barcode included by error." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 19.01.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1070 **Bretaris Genuair-EMEA/H/C/002706/WS1070/0032**	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Eklira **Genuair-EMEA/H/C/002211/WS1070/0032** MAH: AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, “Update of section 4.3 of the SmPC in order to modify the contraindication section deleting reference to hypersensitivity to atropine or its derivative providing justification for the claim that the chemical structure of aclidinium is unrelated to that of atropine or its derivatives. Moreover, a minor change is introduced in section 4.2 of the SmPC. The Package Leaflet is updated accordingly.” Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017.	recommendation.
WS1072 **Eucreas-EMEA/H/C/000807/WS1072/0060** **Galvus-EMEA/H/C/000771/WS1072/0051** **Icandra-EMEA/H/C/001050/WS1072/0061** **Jalra-EMEA/H/C/001048/WS1072/0051** **Xiliarx-EMEA/H/C/001051/WS1072/0050** **Zomarist-EMEA/H/C/001049/WS1072/0061** MAH: Novartis Europharm Ltd, Lead Rapporteur: Kristina Dunder, “Update of section 5.1 of the SmPC, subsection ‘cardiovascular risk’, with results from a new meta-analysis evaluating the cardiovascular safety of vildagliptin. In addition, the Worksharing applicant (WSA) took the opportunity to bring the annexes in line with the latest QRD template version 10, and to merge the two SmPCs into one single SmPC for Eucreas, Icandra and Zomarist. Moreover, the section on pregnancy and breast-feeding in the PL for Eucreas/Icandra/Zomarist has been aligned with the wording used for Galvus/Jalra/Xiliarx.” Opinion adopted on 21.04.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1077/G **Aluvia-EMEA/H/W/000764/WS1077/0101/G** **Kaletra-EMEA/H/C/000368/WS1077/0163/G** **Norvir-EMEA/H/C/000127/WS1077/0143/G** MAH: AbbVie Ltd., Lead Rapporteur: Joseph Emmerich, “Update of sections 4.3 and 4.5 of the	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

SmPC in order to add information regarding the interaction of lopinavir/ritonavir and ritonavir with lurasidone and ranolazine. In addition, sections 4.4 and 4.5 of the SmPC are updated to add information regarding the interaction with triamcinolone. The Package Leaflet is updated accordingly." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017.	
WS1105 **IntronA-EMEA/H/C/000281/WS1105/0107** **PegIntron-EMEA/H/C/000280/WS1105/0128** **ViraferonPeg-EMEA/H/C/000329/WS1105/0121** MAH: Merck Sharp & Dohme Limited, Lead Rapporteur: Filip Josephson, "Update of sections 4.2 and 4.8 of the SmPC in order to update the safety information with information on HCV/HBV co-infection, and to add an ADR on hepatitis B reactivation in HCV/HBV co-infected patients as post marketing adverse experience respectively. The Package Leaflet and Labelling are updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10 including the implementation of the use of combined SmPCs and PLs for PegIntron and ViraferonPeg and the use of combined SmPCs for Intron A in multidose pen." Request for Supplementary Information adopted on 21.04.2017, 23.02.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS1110 **Kinzalkomb-EMEA/H/C/000415/WS1110/0100** **MicardisPlus-EMEA/H/C/000413/WS1110/0102** **PritorPlus-EMEA/H/C/000414/WS1110/0110** MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Daniela Melchiorri, "Update of sections 4.5 and 4.8 to align the hydrochlorothiazide component information with that of the originator. The Package Leaflet is updated accordingly. In addition, WorkSharing Applicant (WSA) took the opportunity of this procedure to bring the	Positive Opinion adopted by consensus on 06.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Product Information in line with the latest QRD version 9.1 and 10.0 templates, including combining the SmPC of the different strengths, as well as implement minor editorial changes and reformatting of some sections of the SmPC. The details of local representative (Portugal for MicardisPlus and United Kingdom for PritorPlus and Kinzalkomb) in the PL have been updated." Opinion adopted on 06.04.2017. Request for Supplementary Information adopted on 16.02.2017.	
WS1148/G **Hexacima-EMEA/H/C/002702/WS1148/0059/G** **Hexaxim-EMEA/H/W/002495/WS1148/0065/G** **Hexyon-EMEA/H/C/002796/WS1148/0063/G** MAH: Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus, "C.I.4 - Update of section 5.1 of the SmPC in order to include data on persistence of immunity following final results from studies: A3L47: Laboratory analysis on sera stored at Sanofi Pasteur Global Clinical Immunology laboratory and collected within the context of trial PNA19 and A3L49: Phase III, multi-center study in children vaccinated with Hep B vaccine at birth followed by three infant primary series doses of Hexaxim® or Infanrix® hexa in A3LI2 study in Thailand C.I.3.z – To include the information about sequential schedule of hexavalent and pentavalent vaccines in primary series in section 4.2 of SmPC following the assessment of A3L39 study." Opinion adopted on 21.04.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.3. CHMP-PRAC assessed procedures

Champix - varenicline - EMEA/H/C/000699/II/0064 MAH: Pfizer Limited, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Doris Stenver, "Update of sections 4.5 and 5.1 of the SmPC in order to update the safety information based on the final results from study Study A3051078, a Varenicline Pregnancy Cohort Study This is a prospective cohort study to compare	Weekly start timetable.

women who use varenicline while pregnant with women who smoke while pregnant with respect to birth outcomes The Package Leaflet is updated accordingly. The RMP version 10.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 06.04.2017.	
Edurant - rilpivirine - EMEA/H/C/002264/II/0024 MAH: Janssen-Cilag International NV, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus, "Update of sections 4.2, 4.4, 4.6, 5.1 and 5.2 of the SmPC in order to include information: use of rilpivirine in combination with a background regimen for the treatment of HIV-1 infection during pregnancy and postpartum, without dose adjustment following final results from study TMC114HIV3015 listed as a category 3 study in the RMP. This is a single arm, open-label trial to assess the pharmacokinetics of darunavir/ritonavir, etravirine, and rilpivirine in HIV-1-infected pregnant women. The Package Leaflet is updated accordingly. The RMP version 7.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce the latest renewal date in section 9 of the SmPC and the physical address of the Netherlands Local Operating Company in the PIL section 6." Request for Supplementary Information adopted on 06.04.2017.	Weekly start timetable.
Emtricitabine/Tenofovir disoproxil Mylan - emtricitabine / tenofovir disoproxil - EMEA/H/C/004050/II/0001 MAH: Mylan S.A.S, Generic, Generic of Truvada, Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Patrick Batty, "Update of sections 4.1, 4.2, 4.3, 4.4, 4.8, 4.9, 5.1, 5.2 and 5.3 the SmPC for emtricitabine/tenofovir disoproxil Mylan following the assessment of the extension of indication for the reference product, Truvada, for pre-exposure prophylaxis. The Annex II, Package Leaflet, Labelling and Risk Management plan (v.5.0) are updated in	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

accordance." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.03.2017.	
Erivedge - vismodegib - EMEA/H/C/002602/II/0032 MAH: Roche Registration Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 5.3 of the SmPC in order to reflect non-clinical carcinogenicity studies (MEA 003): - Study 13-0322 is a 26-Week Oral Gavage Carcinogenicity Study with Vismodegib in Hemizygous CByB6F1-Tg(HRAS)2Jic Mice. - Study 13-0323 is a 104-Week and 52-Week with a 12-Week Recovery Phase Oral Gavage Carcinogenicity Study with Vismodegib in Sprague Dawley Rats. The packaged leaflet section 2 Contraception was updated to include the correct wording agreed by the PRAC during procedure PSUSA/00010140/201601 and approved on 15 Sept 2016, and consistent with section 4.4 of the SmPC. The RMP (RMP 12.0) has been consequently updated. Furthermore, additional routine changes (including some resulting from the assessment of RMP version 11) have been introduced." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Flixabi - infliximab - EMEA/H/C/004020/II/0009 MAH: Samsung Bioepis UK Limited (SBUK), Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final study report of study SB2-G31-RA: A Randomised, Double-blind, Parallel Group, Multicentre Clinical Study to Evaluate the Efficacy, Safety, Pharmacokinetics and Immunogenicity of SB2 Compared to Remicade® in Subjects with Moderate to Severe Rheumatoid Arthritis despite Methotrexate Therapy. The RMP (v. 4) has been updated to reflects the results from the 78 weeks CSR, to exclude 2 of the 5 registries of the pharmacovigilance plan	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

and update in the due date for the prospective observational cohort study of Flixabi in AS (Ankylosing Spondylitis) and CD (Crohn's Disease) patients." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 15.12.2016.	
Ganfort - bimatoprost / timolol - EMEA/H/C/000668/II/0026 MAH: Allergan Pharmaceuticals Ireland, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Torbjorn Callreus, "Update of section 4.8 as per the PRAC recommendation following the PSUSA assessment. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the Product Information in line with the QRD template version 10.0, implement the unique identifier – 2D bar code and correct typographical errors. As per the PRAC recommendation, the updated RMP version 3.2 is also agreed." Opinion adopted on 06.04.2017.	Positive Opinion adopted by consensus. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0018/G MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus, "Update of section 5.1 of the SmPC to reflect the data from three post-authorisation efficacy studies (PAES) in melanoma, studies P001, P002 and P006; the Annex II has been revised to reflect that the relevant data have been submitted and that the Annex II conditions for the submission of the P002 and P006 CSRs, of a comparison between two dosing regimens and of biomarker analyses in the melanoma indication have been fulfilled. An updated RMP version 6.2 was agreed during the procedure." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 26.01.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0025 MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus, "Update of sections 4.2, 4.4 and 4.8 of the SmPC to add a warning for the risk of severe skin reactions and to	The Committee adopted a Request for Supplementary information together with a specific timetable.

communicate that Stevens - Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), including fatal cases, have been reported in patients treated with pembrolizumab. The Package Leaflet has been updated accordingly. The application included an updated RMP version 8.0, and a proposed DHPC and communication plan." Request for Supplementary Information adopted on 21.04.2017.	
Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0017 MAH: Genzyme Therapeutics Ltd, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Torbjorn Callreus, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and long term use information in the posology following final results from study CAMMS03409 - An Extension Protocol For Multiple Sclerosis Patients Who Participated in Genzyme-Sponsored Studies of Alemtuzumab (ongoing at the time of the initial MAA) to evaluate the long term safety and efficacy of alemtuzumab in MS patients who received alemtuzumab during prior company-sponsored studies. The RMP version 3.0 has also been submitted. The PL has been 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 introduce editorial corrections in the PI." Request for Supplementary Information adopted on 21.04.2017.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Levemir - insulin detemir - EMEA/H/C/000528/II/0084 MAH: Novo Nordisk A/S, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Doris Stenver, "Submission of the summary analysis report on the incidence of neoplasms with the combination of liraglutide and insulin detemir from the cardiovascular outcome trial for Victoza®, trial EX2211-3748 (LEADER®). As a consequence the following important potential risk of "malignant neoplasms following combination treatment with insulin detemir + liraglutide + metformin" is deleted from the updated RMP version 18." Request for Supplementary Information adopted	The Committee adopted a Request for Supplementary information together with a specific timetable.

on 21.04.2017, 23.02.2017.	
Nuwiq - simoctocog alfa - EMEA/H/C/002813/II/0017/G MAH: Octapharma AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga, "C.I.4: Update of sections 4.2, 4.8 and 5.1 of the SmPC to reflect avaialble data from Previously Untreated Patients (PUP) from GENA-05 (interim report) study. The Package Leaflet is updated accordingly. The RMP version 8.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the Product Information throughout to bring it in line with the Core summary of product characteristics for human plasma-derived and recombinant coagulation factor VIII products (EMA/CHMP/BPWP/1619/1999 rev. 2) and with the QRD version 10 (affects labelling only). Moreover the MAH is combining the SmPC for all strengths and updating Annex A with detailed information on the packaging. C.I.11: Submission of an updated RMP version 8.0 in order to align the content in a single harmonised worldwide version for simoctocog alfa (rFVIII)." Request for Supplementary Information adopted on 21.04.2017.	The Committee adopted a Request for Supplementary information together with a specific timetable.
OPDIVO - nivolumab - EMEA/H/C/003985/II/0024 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 5.1 of the SmPC in order to reflect the final overall survival and response data, including duration of response with longer follow-up, following completion of PAES CA209037 (Randomized, Open-Label, Phase 3 Trial of nivolumab vs Investigator's Choice in Advanced (Unresectable or Metastatic) Melanoma Patients Progressing Post Anti-CTLA-4 Therapy) and its addendum on predictability of efficacy with biomarkers. This application fulfils ANX 001 and 003.1. Annex II has been updated accordingly. RMP version 5.5 has been submitted within this application." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 23.03.2017, 26.01.2017.	
Prolia - denosumab - EMEA/H/C/001120/II/0062 MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the product information (SmPC sections 4.4, 4.8 and PL sections 3 and 4) as well as the Risk Management Plan (RMP) to update the safety information and reflect the multiple vertebral fractures (MVF) follwoing discontinuation of Prolia treatement as a new important risk. This variation follows a concluded analysis of osteoporosis-related fracture data in subjects who discontinued investigational product and remained on study in either the Prolia phase 3 pivotal fracture study (Study 20030216) or its study extension (Study 20060289) to better understand the incidence of fracture following treatment discontinuation. The results of this analysis conclude that multiple vertebral fractures may occur following discontinuation of Prolia treatment, particularly in patients with a history of vertebral fracture. In addition, the applicant took the opportunity to update the PI in line with the QRD template latest version, amend the PI previous version typographical errors from previous version, and implement minor changes in the Package leaflet local representatives." Request for Supplementary Information adopted on 21.04.2017, 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Prolia - denosumab - EMEA/H/C/001120/II/0063 MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the SmPC section 5.1 to provide information on the clinical study data experience in patients in treatment transition from an oral Bisphosphonate to desunomab, information resulting from the assessment on data of study report 20110153 and a discussion on the issue of long term antiresorptive treatment, in particular when long-term bisphosphonate treatment is followed by denosumab." Request for Supplementary Information adopted on 21.04.2017, 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Zavesca - miglustat - EMEA/H/C/000435/II/0056, Orphan MAH: Actelion Registration Ltd., Rapporteur:	The Committee adopted a Request for Supplementary information together with a specific timetable.

Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, “Submission of 8th NPC (Niemann-Pick type C) Registry report and update of Annex II-D to delete the NPC Registry listed as an obligation to the marketing authorisation. The RMP version 12.1 has also been submitted to reflect the above changes. In addition, the Marketing authorisation holder took the opportunity to introduce minor changes and bring the Product Information and Annex A in line with the latest QRD template version 10.” Request for Supplementary Information adopted on 21.04.2017.	
WS0992/G **Relvar Ellipta-EMEA/H/C/002673/WS0992/0022/G** **Revinty Ellipta-EMEA/H/C/002745/WS0992/0017/G** MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, “Type II C.I.4: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update the safety information and include data from the HZC113782 (SUMMIT) study (designed to investigate whether FF/VI-Furoate/Vilanterol could improve survival in patients with moderate chronic obstructive pulmonary disease (COPD) who had, or were at increased risk for cardiovascular disease (CV)). The Package Leaflet and Labelling are updated accordingly. The RMP v.9 is updated accordingly. Type II C.I.4: Update of section 4.8 of the SmPC in order to add "paradoxical bronchospasm" to the list of adverse reactions. The Package Leaflet and Labelling are updated accordingly. Type IB C.I.z: Update of section 5.1 the SmPC in order to correct an error identified in the pharmacodynamics section.” Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017, 13.10.2016.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1026 **Rasilez-EMEA/H/C/000780/WS1026/0110** **Rasilez HCT-EMEA/H/C/000964/WS1026/0080** MAH: Novartis Europharm Ltd, Lead Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur:	The Committee adopted a Request for Supplementary information together with a specific timetable.

Carmela Macchiarulo, “Update of section 5.1 of the SmPC in order to reflect the results of study SPP100F2301 (ATMOSPHERE) a multicenter, randomized, doubleblind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (NYHA Class II - IV). The RMP (v 13) has also been updated to reflect the study results.” Request for Supplementary Information adopted on 21.04.2017, 15.12.2016.	
WS1101 **Relvar Ellipta-EMEA/H/C/002673/WS1101/0029** **Revinty Ellipta-EMEA/H/C/002745/WS1101/0025** MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, “Submission of HZC115151 study (A 12-month, open label, randomised, effectiveness study to evaluate fluticasone furoate (FF, GW685698)/vilanterol (VI, GW642444) Inhalation Powder delivered once daily via a Novel Dry Powder Inhaler (NDPI) compared with the existing COPD maintenance therapy alone in subjects with Chronic Obstructive Pulmonary Disease (COPD)) in order to update the safety information. Consequently the Annex II of the Product Information and the RMP version 9.0 are updated.” Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1117/G **Stocrin-EMEA/H/C/000250/WS1117/0110/G** **Sustiva-EMEA/H/C/000249/WS1117/0139/G** MAH: Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, “C.I.4 (Type II) - Update of sections 4.4, 4.5 and 5.1 of the SmPC in order to add a warning and update the safety information on QTc prolongation based on the final results from study AI266959; this is an interventional study to determine the	Weekly start timetable.

concentration-electrocardiographic effects of efavirenz in healthy subjects enriched for cyp2b6 polymorphisms; the Package Leaflet is updated accordingly. The RMP version 8 has also been submitted. C.I.4 (Type II) – Update of sections 4.4 and 4.8 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)." Request for Supplementary Information adopted on 06.04.2017.	
WS1130/G **Efficib-EMEA/H/C/000896/WS1130/0081/G** **Janumet-EMEA/H/C/000861/WS1130/0081/G** **Ristfor-EMEA/H/C/001235/WS1130/0068/G** **Velmetia-EMEA/H/C/000862/WS1130/0084/G** MAH: Merck Sharp & Dohme Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, "C.I.11.b: Submission of an updated RMP version 7 in order to add a targeted questionnaire related to lactic acidosis as part of the outcome of the referral procedure EMEA/H/A-31/1432. C.I.3.b: Update of sections 4.4 of the SmPC in order to add Bullous pemphigoid as a warning following the PRAC assessment outcome EMEA/H/C/PSUSA/2711/201408; the Labelling is being updated accordingly." Request for Supplementary Information adopted on 06.04.2017.	Weekly start timetable.
WS1133/G **Atripla-EMEA/H/C/000797/WS1133/0121/G** **Descovy-EMEA/H/C/004094/WS1133/0015/G** **Eviplera-EMEA/H/C/002312/WS1133/0081/G** **Genvoya-EMEA/H/C/004042/WS1133/0029/G** **Odefsey-EMEA/H/C/004156/WS1133/0011/G** **Stribild-EMEA/H/C/002574/WS1133/0080/G**	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Truvada-EMEA/H/C/000594/WS1133/0136/G **Viread-EMEA/H/C/000419/WS1133/0174/G** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Amelia Cupelli, “The group of Workshare variations includes: Updates of sections 4.4 and 4.5 of the SmPC for the tenofovir disoproxil fumarate (TDF)-containing products (Viread, Truvada, Atripla, Eviplera, Stribild) which includes the results from Study GS-US-342-1167 and Study GS-US-342-1326. Update of section 4.5 for the tenofovir alafenamide (TAF)-containing products (Genvoya, Descovy, Odefsey) which include the results from Study GS-US-342-1167. Study GS-US-342-1167 is a Phase I Study to Evaluate the Pharmacokinetic Drug-Drug Interactions between Sofosbuvir/GS-5815 Fixed Dose Combination (FDC) Tablets and Antiretrovirals Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate (EFV/FTC/TDF; Atripla), Emtricitabine/Riplivirine/Tenofovir Disoproxil Fumarate (FTC/RPV/TDF; Complera), Dolutegravir (DTG; Tivicay) o Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Fumarate (EVG/COBI/FTC/TAF) in Healthy Subjects. Study GS-US-342-1326, a Phase I Study to Evaluate the Pharmacokinetic Drug-Drug Interaction Potential between Sofosbuvir/GS-5816 (SOF/GS-5816) Fixed-Dose Combination (FDC) Tablet and HIV Antiretroviral Regimens Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Disoproxil Fumarate (EVG/COBI/FTC/TDF), Ritonavir-boosted Darunavir (DRV/r) plus Emtricitabine/Tenofovir Disoproxil Fumarate (FTC/TDF), Ritonavir-boosted Atazanavir (ATV/r) plus FTC/TDF, Ritonavir/boosted Lopinavir (LPV/r) plus FTC/TDF or Raltegravir plus FTC/TDF. The Package Leaflet and Risk Managent Plan (RMP) are updated accordingly.” Opinion adopted on 21.04.2017.	
WS1134	Positive Opinion adopted by consensus on

Truvada-EMEA/H/C/000594/WS1134/0137 **Viread-EMEA/H/C/000419/WS1134/0175** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Joseph Emmerich, Lead PRAC Rapporteur: Caroline Laborde, "Update of section 4.5 of the SmPC for Viread and Truvada with interactions between emtricitabine (FTC), tenofovir disoproxil fumarate (TDF), ledipasvir, sofosbuvir and dolutegavir based on new clinical pharmacology data from study GS-US-377-1501. This is a Phase 1, open-label, multiple-dose study that evaluated the pharmacokinetic drug-drug interaction potential between Harvoni (ledipasvir [LDV]/sofosbuvir [SOF]) and FTC/TDF+dolutegravir (DTG). The RMP version 22 for Viread and version 14 for Truvada have also been submitted." Opinion adopted on 21.04.2017.	21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1141 **Januvia-EMEA/H/C/000722/WS1141/0056** **Ristaben-EMEA/H/C/001234/WS1141/0048** **TESAVEL-EMEA/H/C/000910/WS1141/0056** **Xelevia-EMEA/H/C/000762/WS1141/0060** MAH: Merck Sharp & Dohme Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 of the SmPC in order to add Bullous pemphigoid as a warning following the PRAC assessment outcome EMEA/H/C/PSUSA/2711/201408; the Labelling is being updated accordingly. Consequently, the RMP version 7 is updated accordingly." Request for Supplementary Information adopted on 06.04.2017.	Weekly start timetable.

B.5.4. PRAC assessed procedures

PRAC Led **Bydureon - exenatide - EMEA/H/C/002020/II/0042** MAH: AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, , "Submission of the updated RMP version 25 following closure and final summary of Exenatide Pregnancy Registry (a prospective, observational	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

study conducted in the United States that actively collected information on exposure to antidiabetic medication during pregnancy and the associated pregnancy outcomes in patients with Type 2 diabetes mellitus). Moreover, the MAH included additional minor updates to the RMP." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017.	
PRAC Led **Halaven - eribulin - EMEA/H/C/002084/II/0033** MAH: Eisai Europe Ltd., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, , "Update of the RMP version 4.2 following the revision of the protocol for a post-authorisation study to capture data on the frequency of resolution and time to resolution of eribulin-induced or -aggravated peripheral neuropathy in patients from a phase 3 study, E7389-A001-303 (ACCRU); the MAH will instead conduct an observational study, E7389-M044-504 (IRENE)." Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017, 15.12.2016.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0013** MAH: CSL Behring GmbH, PRAC Rapporteur: Eva A. Segovia, , "Submission of an updated RMP version 3.1 in order to include the final safety data from study CE1226_3001, which were assessed in the type II variation EMEA/H/C/002739/II/0002 and adjustments in the Non-Clinical Safety specification part (Part II, Module SII) with non-clinical information from local tolerability trials." Opinion adopted on 06.04.2017.	Positive Opinion adopted by consensus. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Tysabri - natalizumab - EMEA/H/C/000603/II/0101** MAH: Biogen Idec Ltd, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, , "Submission of the final clinical study report for TYGRIS, a post-marketing safety observational cohort program designed to obtain long-term safety data (approximately 5 years) in subjects with MS	Weekly start timetable.

treated with natalizumab, and comprising parallel studies 101MS402 (United States and Canada) and 101MS403 (Rest of World). The application included an updated RMP version 23." Request for Supplementary Information adopted on 06.04.2017.	
PRAC Led **Tysabri - natalizumab - EMEA/H/C/000603/II/0102** MAH: Biogen Idec Ltd, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final clinical study report for study STRATIFY-2 (101JC402), an observational, longitudinal cohort study designed to gather post-marketing data on the incidence of progressive multifocal leukoencephalopathy (PML) in natalizumab-treated subjects with MS. An updated RMP version 23 was provided accordingly." Opinion adopted on 06.04.2017.	Positive Opinion adopted by consensus. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Xiapex - collagenase clostridium histolyticum - EMEA/H/C/002048/II/0089** MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, , "Submission of the final clinical study report for study B1531005, a non-interventional study to evaluate the outcomes (clinical treatment success measured by goniometry assessment, recurrence rate measured by goniometry assessment, subject and physician global assessment of treatment satisfaction, complications resulting from the procedure based on the Adverse Event/Serious Adverse Event (AE/SAE)) of 3 various treatment options for Dupuytren's contracture, listed as a category 3 study in the RMP. The RMP (version 13.0) is updated accordingly." Request for Supplementary Information adopted on 06.04.2017.	Weekly start timetable.
PRAC Led **WS0943** **Saxenda-EMEA/H/C/003780/WS0943/0009** **Victoza-EMEA/H/C/001026/WS0943/0041** MAH: Novo Nordisk A/S, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur:	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Menno van der Elst, , “Submission of the final results from the Optum Database study (NN2211-3784, RMP category 3 study); this was a post-marketing safety surveillance study to observe the safety profile of liraglutide and to compare it with that of other antidiabetic medications when used in a real-life setting in the U.S. The study included a sub-study specifically addressing the safety concern of breast cancer. The updated RMP version 26 has been submitted.” Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 26.01.2017, 15.09.2016.	
PRAC Led **WS1088** **Eucreas-EMEA/H/C/000807/WS1088/0057** **Galvus-EMEA/H/C/000771/WS1088/0048** **Icandra-EMEA/H/C/001050/WS1088/0058** **Jalra-EMEA/H/C/001048/WS1088/0048** **Xiliarx-EMEA/H/C/001051/WS1088/0047** **Zomarist-EMEA/H/C/001049/WS1088/0058** MAH: Novartis Europharm Ltd, Lead PRAC Rapporteur: Qun-Ying Yue, “Following the outcome of an Article 31 referral procedure for metformin and metformin-containing products (Procedure EMEA/H/A-31/1432), the Applicant was requested toupdate the Risk Management Plan (RMP) for galvus, Jalra, Xiliarx, Eucreas, Icandra and Zomarist to implement a targeted questionnaire for cases of lactic acidosis.” Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.5. CHMP-CAT assessed procedures

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0008, ATMP MAH: Amgen Europe B.V., Rapporteur: Olli Tenhunen, CHMP Coordinators: Tuomo Lapveteläinen, Opinion adopted on 21.04.2017, 12.04.2017. Request for Supplementary Information adopted on 17.02.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

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

WS0921 **Ebymect-EMEA/H/C/004162/WS0921/0019** **Edistride-EMEA/H/C/004161/WS0921/0015** **Forxiga-EMEA/H/C/002322/WS0921/0034** **Qtern-EMEA/H/C/004057/WS0921/0005** **Xigduo-EMEA/H/C/002672/WS0921/0030** MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder Opinion adopted on 06.04.2017.	Positive Opinion adopted by consensus on 06.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1030 **ANORO-EMEA/H/C/002751/WS1030/0015** **Incruse-EMEA/H/C/002809/WS1030/0014** **Laventair-EMEA/H/C/003754/WS1030/0017** **Relvar Ellipta-EMEA/H/C/002673/WS1030/0028** **Revinty Ellipta-EMEA/H/C/002745/WS1030/0024** MAH: Glaxo Group Ltd, Lead Rapporteur: Nithyanandan Nagercoil Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1081 **Hexacima-EMEA/H/C/002702/WS1081/0055** **Hexaxim-EMEA/H/W/002495/WS1081/0062** **Hexyon-EMEA/H/C/002796/WS1081/0059** MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 21.04.2017, 16.02.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS1085 **Ceprotin-EMEA/H/C/000334/WS1085/0098** **HyQvia-EMEA/H/C/002491/WS1085/0034**	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Kiovig-EMEA/H/C/000628/WS1085/0076 MAH: Baxalta Innovations GmbH, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 23.02.2017.	
WS1112 **Hexacima-EMEA/H/C/002702/WS1112/0057** **Hexaxim-EMEA/H/W/002495/WS1112/0063** **Hexyon-EMEA/H/C/002796/WS1112/0061** MAH: Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 30.03.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS1126 **Gardasil-EMEA/H/C/000703/WS1126/0070** **Silgard-EMEA/H/C/000732/WS1126/0061** MAH: MSD Vaccins, Lead Rapporteur: Kristina Dunder Opinion adopted on 21.04.2017. Request for Supplementary Information adopted on 16.03.2017.	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1131 **Januvia-EMEA/H/C/000722/WS1131/0055** **Ristaben-EMEA/H/C/001234/WS1131/0047** **TESAVEL-EMEA/H/C/000910/WS1131/0055** **Xelevia-EMEA/H/C/000762/WS1131/0059** MAH: Merck Sharp & Dohme Limited, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 30.03.2017.	Positive Opinion adopted by consensus on 30.03.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1146 **Hexacima-EMEA/H/C/002702/WS1146/0058** **Hexaxim-EMEA/H/W/002495/WS1146/0064** **Hexyon-EMEA/H/C/002796/WS1146/0062** MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus	Positive Opinion adopted by consensus on 21.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 21.04.2017.

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

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

WS1092 **Ebymect-EMEA/H/C/004162/WS1092/0017** **Edistride-EMEA/H/C/004161/WS1092/0013** **Forxiga-EMEA/H/C/002322/WS1092/0032** **Xigduo-EMEA/H/C/002672/WS1092/0028** MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "Update of sections 4.4 and 5.1 of the SmPC in order to reflect the results of the Phase 3 study D5553C00003: 28-week safety and efficacy, randomised, double-blind comparison of simultaneous administration of exenatide once weekly 2 mg an dapagliflozin once daily 10 mg to exenatide once weekly 2 mg alone and dapagliflozin once daily 10 mg alone in patients with type 2 diabetes with inadequate glycaemic control on metformin. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflets for Ebymect and Edistride and to introduce minor editorial changes throughout the Product Informations." Letter from the applicant dated 13 April 2017 requesting an extension of clock stop to respond to Request for Supplementary Information. Request for Supplementary Information adopted on 23.03.2017.	The Committee agreed to a Request for extension of clock stop to respond to Supplementary information together 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

- fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781 , treatment of adult patients with chronic obstructive pulmonary disease (COPD), List of Questions adopted on 21.04.2017.

- fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363
, treatment of adult patients with chronic obstructive pulmonary disease (COPD),
List of Questions adopted on 21.04.2017.

- letermovir - EMEA/H/C/004536, Orphan **Accelerated review**
Applicant: Merck Sharp & Dohme Limited,
prophylaxis of cytomegalovirus (CMV) reactivation and disease

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

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

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

Firdapse - amifampridine - EMEA/H/C/001032/S/0049, Orphan
MAH: BioMarin Europe Ltd

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

Forxiga - dapagliflozin - EMEA/H/C/002322/R/0035
MAH: AstraZeneca AB, Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Qun-Ying Yue

Glubrava - pioglitazone / metformin hydrochloride - EMEA/H/C/000893/R/0054
MAH: Takeda Pharma A/S, Informed Consent of Competact, Rapporteur: Patrick Salmon, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Almath Spooner

NexoBrid - concentrate of proteolytic enzymes enriched in bromelain - EMEA/H/C/002246/R/0031, Orphan
MAH: MediWound Germany GmbH, Rapporteur: Harald Enzmann, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Valerie Strassmann,

Zoledronic acid Hospira - zoledronic acid - EMEA/H/C/002365/R/0026
MAH: Hospira UK Limited, Rapporteur: Filip

Josephson, PRAC Rapporteur: Doris Stenver,

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

Alecensa - alectinib -
EMEA/H/C/004164/II/0001
MAH: Roche Registration Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Julie WilliamsExtension of Indication to extend the indication of Alecensa (alectinib) to first line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC); as a consequence, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP are updated in accordance."

BLINCYTO - blinatumomab -
EMEA/H/C/003731/II/0011, Orphan
MAH: Amgen Europe B.V., Rapporteur: Alexandre Moreau, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Jana Mladá, "Extension of Indication to include the treatment of adults with minimal residual disease (MRD) positive B-cell precursor acute lymphoblastic leukaemia (ALL)for BLINCYTO;
as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, and to update the safety information. The Labelling is updated in accordance.
RMP version 4.0 is included in this submission."

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0027
MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus, "Extension of Indication to include 1st line treatment of metastatic non-squamous non-small cell lung cancer (NSCLC) in combination with platinum-pemetrexed chemotherapy based on the results from study KEYNOTE-021 (cohort G); a Phase 1/2, open-label trial of pembrolizumab in combination with chemotherapy or immunotherapy in patients with locally advanced or metastatic NSCLC.
As a consequence sections 4.1, 4.2, 4.4, 4.8 and

5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly. An updated RMP version 9.0 was provided as part of the application."

Prolia - denosumab - EMEA/H/C/001120/II/0068

MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga, "Treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk of fracture. Prevention of osteoporosis in women and men at increased risk of fracture who are starting or have recently started long-term glucocorticoid therapy." for Prolia; as a consequence, sections 4.1 and 5.1 of the SmPC are updated to reflect the new indications or are consequential to the analysis of the data from the pivotal study. The Package Leaflet is updated in accordance. The Risk Management Plan version 19.0 has also been updated to capture the new indications. The variation proposed amendments to the Summary of Product Characteristics and Package Leaflet."

Yervoy - ipilimumab - EMEA/H/C/002213/II/0044

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus,"Extension of indication to include the treatment of advanced (unresectable or metastatic) melanoma in children and adolescents 12 years of age and older for Yervoy. As a consequence sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 15) are updated in accordance."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0006/G, Orphan

MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop,

Apidra - insulin glulisine - EMEA/H/C/000557/II/0074/G

MAH: Sanofi-Aventis Deutschland GmbH, Rapporteur: Greg Markey

Betaferon - interferon beta-1b -
EMEA/H/C/000081/II/0114
MAH: Bayer AG, Rapporteur: Greg Markey,

Elonva - corifollitropin alfa -
EMEA/H/C/001106/II/0036/G
MAH: Merck Sharp & Dohme Limited,
Rapporteur: Paula Boudewina van Hennik

Extavia - interferon beta-1b -
EMEA/H/C/000933/II/0084
MAH: Novartis Europharm Ltd, Informed Consent
of Betaferon, Rapporteur: Greg Markey,

Flixabi - infliximab -
EMEA/H/C/004020/II/0013/G
MAH: Samsung Bioepis UK Limited (SBUK),
Rapporteur: Jan Mueller-Berghaus,

Ganfort - bimatoprost / timolol -
EMEA/H/C/000668/II/0027/G
MAH: Allergan Pharmaceuticals Ireland,
Rapporteur: Hanne Lomholt Larsen,

GONAL-f - follitropin alfa -
EMEA/H/C/000071/II/0138/G
MAH: Merck Serono Europe Limited, Rapporteur:
Nithyanandan Nagercoil,

Humira - adalimumab -
EMEA/H/C/000481/II/0167
MAH: AbbVie Ltd., Rapporteur: Kristina Dunder,

Memantine ratiopharm - memantine -
EMEA/H/C/002671/II/0008
MAH: ratiopharm GmbH, Generic, Generic of
Ebixa, Rapporteur: Bart Van der Schueren,

Praluent - alirocumab -
EMEA/H/C/003882/II/0022/G
MAH: sanofi-aventis groupe, Rapporteur: Johann
Lodewijk Hillege,

Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) -
EMEA/H/C/001104/II/0156
MAH: Pfizer Limited, Rapporteur: Kristina Dunder

Simponi - golimumab -
EMEA/H/C/000992/II/0075/G
MAH: Janssen Biologics B.V., Rapporteur:
Kristina Dunder,

Sustiva - efavirenz -
EMEA/H/C/000249/II/0142/G
MAH: Bristol-Myers Squibb Pharma EEIG,

Rapporteur: Bruno Sepodes

Vihuma - simoctocog alfa -
EMEA/H/C/004459/II/0001/G
MAH: Octapharma AB, Rapporteur: Jan Mueller-Berghaus,

Xultophy - insulin degludec / liraglutide -
EMEA/H/C/002647/II/0019
MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder,

Zepatier - elbasvir / grazoprevir -
EMEA/H/C/004126/II/0007
MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey

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

Alecensa - alectinib -
EMEA/H/C/004164/II/0003
MAH: Roche Registration Limited, Rapporteur: Filip Josephson"Update of section 4.8 of the SmPC in order to add "Increased blood alkaline phosphatase" as new Adverse Drug Reaction with a common frequency. The package leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some formatting changes in the Product Information."

Arzerra - ofatumumab -
EMEA/H/C/001131/II/0050, Orphan
MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac,, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add a recommendation to permanently discontinue Arzerra in case of anaphylactic reaction and revise the adverse drug reaction profile based on safety pool data analysis and updated Company Core Data Sheet.

The Package Leaflet is updated accordingly."

Arzerra - ofatumumab -
EMEA/H/C/001131/II/0051, Orphan
MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac,"Update to Section 4.6 Fertility, pregnancy and lactation and section 5.3 Preclinical safety data following implementation of the new Novartis Core Data Sheet (CDS) template.

Update to the Section 4.5 Interaction with other

medicinal products and other forms of interaction to reflect the results of a clinical study OMB113603 investigating the potential pharmacokinetic interactions between ofatumumab and bendamustine. Update to the Section 5 Pharmacological properties to update the information on immunogenicity for precision, addition of a table summarizing main pharmacokinectic (PK) parameters for brevity and to facilitate understanding, simplification of the PK section. Editorial changes for Arzerra 100 mg and Arzerra 1000 mg concentrate for solution for infusion consisting of updates to Sections 2 Qualitative and quantitative composition, 6.5 Nature and contents of container, and 6.6 Special precautions for disposal and other handling. Editorial changes to clarify the doses for various indications have been added to Section 4.2 Posology and method of administration. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10."	
Cosentyx - secukinumab - EMEA/H/C/003729/II/0020 MAH: Novartis Europharm Ltd, Rapporteur: Tuomo Lapveteläinen, "Update of section 4.5 of the SmPC in order to revise general information on CYP450/CYP3A4 as a result of data provided by study A2110 demonstrating that enzyme activity in moderate to severe psoriasis patients at baseline is similar to the activity observed in healthy volunteers."	
Cosentyx - secukinumab - EMEA/H/C/003729/II/0021/G MAH: Novartis Europharm Ltd, Rapporteur: Tuomo Lapveteläinen, , "Update of section 5.1 of the SmPC in order to add long term 52 week data from CLEAR study (CAIN457A2317) and to add new data from a scalp psoriasis study (CAIN457US01) . In addition the MAH has taken the occasion to include correction in section 4.2 to avoid medication errors and the Package leaflet has been updated accordingly, and in section 5.1 to align the information PsARC definition to the EMA guideline. The MAH has also implemented the latest QRD version 10.0."	
Eviplera - emtricitabine / rilpivirine /	

tenofovir disoproxil -
EMEA/H/C/002312/II/0082

MAH: Gilead Sciences International Ltd, Rapporteur: Johann Lodewijk Hillege"Update of section 4.5 of the SmPC with Drug-Drug Interaction information for Eviplera based on the results from Study TMC435-TiDP16-C114; this is a Phase I, 2-panel, open-label, randomized, cross-over trial in healthy subjects to investigate the pharmacokinetic interaction between TMC435 and antiretroviral agents, TMC278 and tenofovir disoproxil fumarate (TDF), at steady-state.

The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor administrative changes in the SmPC and to update the list of local representatives in the Package Leaflet for Estonia, Latvia and Lithuania.

Minor linguistic amendments (MLAs) have been implemented to the translations of the product information annexes: CS, DE, ES, FR, IS, IT, NL, NO, PT, SE and SK."

Halaven - eribulin -
EMEA/H/C/002084/II/0038

MAH: Eisai Europe Ltd., Rapporteur: Filip Josephson"Update of the SmPC section 5.1 with additional information on the mechanism of action of eribulin. Furthermore, the MAH has taken the opportunity to include in the package leaflet the name of the manufacturer responsible for batch release to align with the Annex II of the Product Information, and to update information related to the local representatives."

Harvoni - ledipasvir / sofosbuvir -
EMEA/H/C/003850/II/0052

MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson,"Submission of the final report from study GS-US-337-0115 listed as a category 3 study in the RMP. This is a phase 3, multicentre, randomized, open-label study to investigate the efficacy and safety of sofosbuvir/ledipasvir fixed-dose combination ± ribavirin for 12 or 24 weeks in Subjects with chronic genotype hepatitis C virus (HCV) and human immunodeficiency virus (HIV)-1 co-infection."

Humira - adalimumab -

EMEA/H/C/000481/II/0168
MAH: AbbVie Ltd., Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to update information on the long-term safety, tolerability, and efficacy of adalimumab in subjects with moderate to severe hidradenitis suppurativa after finalization of phase III open-label extension studyM12-555."

Imbruvica - ibrutinib - EMEA/H/C/003791/II/0034, Orphan
MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson"Submission of the final report from non-clinical study 17-008-Sal-X-MU (AMES assays for major human metabolites M21 + M34) listed as a category 3 studies in the RMP.
The in vitro metabolism report (FK10269) in Mod. 4.2.2.4 is amended to document the production of the metabolites M21 and M34."

IntronA - interferon alfa-2b - EMEA/H/C/000281/II/0110
MAH: Merck Sharp & Dohme Limited, Rapporteur: Koenraad Norga"Update of section 4.8 of the SmPC in order to add pericarditis as an adverse reaction based on continuous monitoring of the safety profile; the Package Leaflet is updated accordingly."

MULTAQ - dronedarone - EMEA/H/C/001043/II/0038
MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege,"Submission of the final results of a single historic prospective observational study to evaluate the efficacy of dronedarone in clinical practice (EFFECT-AF study). The product information and RMP remain unchanged."

Odomzo - sonidegib - EMEA/H/C/002839/II/0010
MAH: Novartis Europharm Ltd, Rapporteur: Paula Boudewina van Hennik,"Submission of the final results from the clinical pharmacology study CLDE225A2112, which was a Phase Ib, multi-center, two parallel groups, open-label, drug-drug interaction study to assess the effect of sonidegib on the pharmacokinetics of bupropion and warfarin in patients with advanced solid tumors. This study is listed as a measure in the RMP. The SmPC section 4.5 has been updated to reflect that the results of a drug-drug interaction study in cancer patients demonstrate

that the systemic exposure of bupropion (a CYP2B6 substrate) and warfarin (a CYP2C9 substrate) is not altered when co-administered with sonidegib. The PIL has been amended accordingly."

Selincro - nalmefene - EMEA/H/C/002583/II/0020/G

MAH: H. Lundbeck A/S, Rapporteur: Martina Weise, "Update of section 4.7 of the SmPC in order to state that Selincro may influence the ability to drive and use machines.
Update of section 4.8 of the SmPC in order to add the adverse drug reaction "diarrhoea" with frequency "common".
The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."

Sprycel - dasatinib - EMEA/H/C/000709/II/0055

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Sinan B. Sarac,"Update of section 4.8 of the SmPC in order to add nephrotic syndrome as an adverse reaction based on the results of routine pharmacovigilance activities.
The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the date of latest renewal (Section 9, SmPC) along with the phone number of the local representative in Croatia and the name of local representative in Ireland listed in the PIL."

Strensiq - asfotase alfa - EMEA/H/C/003794/II/0018, Orphan

MAH: Alexion Europe SAS, Rapporteur: Greg Markey, "Update of section 4.5 of the SmPC in order to update the information on Asfotase alfa interaction with the Alkaline Phosphatase (ALP), used as the detection reagent in many routine laboratory assays, which may leading to abnormal values reports. The Package Leaflet is updated accordingly."

Tarceva - erlotinib - EMEA/H/C/000618/II/0051

MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, , "Submission of the Real World Data Reports (BIOMARQUEURS FRANCE CSR and ESCAP-2011-CPHG CSR) and a new CSR Addendum of the previously submitted pivotal

study BR.21, in order to discuss the currently available evidence supporting the use of erlotinib for treatment of patients with locally advanced or metastatic NSCLC without EGFR-activating mutations after failure of at least one prior chemotherapy regimen, as requested in recommendation originating from variation EMEA/H/C/000618/II/0043."

Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0138/G

MAH: Gilead Sciences International Ltd, Rapporteur: Greg Markey, "Submission of the final report from studies GS-US-276-0101 and GS-US-276-0105, listed as a category 3 studies in the RMP.

GS-US-276-0101 - This is a A Prospective, Observational Study of Pregnancy Outcomes among Women Exposed to Truvada for PrEP Indication Nested in the Antiretroviral Pregnancy Registry

GS-US-276-0105 – This is a A Prospective, Observational, Drug Utilization Study of Subjects Taking Truvada for Pre-exposure Prophylaxis in the USA."

Venclyxto - venetoclax - EMEA/H/C/004106/II/0003, Orphan

MAH: AbbVie Ltd., Rapporteur: Filip Josephson, , "Submission of the final report from study R&D 16/1398: Assessment of Cytochrome P450 mRNA Induction by A-1195425 in Cultured Human Hepatocytes to evaluate CYP1A2 and CYP2B6 induction response which is included as a Post Authorisation Measure (Category 3) in RMP 2.0."

Ventavis - iloprost - EMEA/H/C/000474/II/0055

MAH: Bayer Pharma AG, Rapporteur: Alexandre Moreau, "Update of sections 4.9 of the SmPC in order to update the safety information related to overdose following a cumulative review of overdose cases. The Package Leaflet (PIL) is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the PIL, to align the PIL with the SmPC for children and adolescents and to adjust the labelling of the inner carton without blue box."

XGEVA - denosumab -

EMEA/H/C/002173/II/0054

MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga“Submission of an updated RMP version 25 in order to include that cataracts are no longer considered to be a potential risk associated with denosumab therapy supported by the Study 20080560 completed recently where results showed no difference between the risk of developing cataracts in the denosumab and placebo groups.”

Zostavax - shingles (herpes zoster) vaccine (live) - EMEA/H/C/000674/II/0112

MAH: MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, “Update of section 5.1 of the SmPC in order to add information on long-term effectiveness of Zostavax on herpes zoster and postherpetic neuralgia in individuals 50 years of age or older following the first interim results from the post-licensure observational study (Protocol 024) listed as category 3 study in the RMP. In addition, the marketing authorisation holder took the opportunity to bring the product information in line with the latest QRD template version 10.”

WS1135
Glyxambi-EMEA/H/C/003833/WS1135/0003
Jardiance-EMEA/H/C/002677/WS1135/0030
Synjardy-EMEA/H/C/003770/WS1135/0026

MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, “Update of section 5.2 of the SmPC in order to reflect the results from PK/PD study 1245.87 `An open-label, randomised, multicentre, single-dose, parallel group trial to evaluate pharmacokinetics and pharmacodynamics of empagliflozin in children and adolescents from 10 to less than 18 years of age with type 2 diabetes mellitus', previously assessed as Article 46 submission for Jardiance [EMEA/H/C/002677/P46-007].”

WS1162
Glyxambi-EMEA/H/C/003833/WS1162/0004
Jentadueto-EMEA/H/C/002279/WS1162/0038

Trajenta-EMEA/H/C/002110/WS1162/0028

MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 5.2 of the SmPC in order to reflect the results from PK/PD study 1218.56 `A randomised, double-blind, placebo-controlled parallel group dose-finding study of linagliptin (1 mg or 5 mg administered orally once daily) over 12 weeks in children and adolescents, from 10 to 17 years of age, with type 2 diabetes mellitus', previously assessed as Article 46 submission for Trajenta [EMEA/H/C/002110/P46/016]."

B.6.10. CHMP-PRAC assessed procedures

Abasaglar - insulin glargine - EMEA/H/C/002835/II/0014

MAH: Eli Lilly Regional Operations GmbH, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Carmela MacchiaruloEPL: Eberhard Blind, "Submission of the final report from study I4L-MC-ABER(ABER). This is a Prospective, Randomized, Open-Label Comparison of a Long-Acting Basal Insulin Analog LY2963016 to LANTUS® in Adult Patients with Type 2 Diabetes Mellitus: the ELEMENT 5 Study. This study was conducted in non European countries. This study replaces the cancelled studies that were planned to be conducted in China and other countries and that were described in the RMP.
An updated RMP version 1.6 is submitted accordingly."

Champix - varenicline - EMEA/H/C/000699/II/0066

MAH: Pfizer Limited, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Doris Stenver, "Update of section 5.1 of the SmPC in order to update the safety information based on final results from Clinical Study A3051148 (A Phase 4, Non-Treatment Follow-Up for Cardiac Assessments Following Use of Smoking Cessation Treatments in Subjects With and Without a History of Psychiatric Disorders), a non-interventional category 3 Post-authorisation safety study (PASS) in the RMP.

The primary objective of this study relates to understanding the potential safety risk for cardiovascular events. It is a non-treatment

extension to study A3051123, to collect data on cardiovascular safety for all participants in the A3051123 trial for an additional 28 weeks, allowing for a total of 52 weeks of cardiovascular safety data collection.

The RMP version 10.1 has also been submitted."

Imbruvica - ibrutinib - EMEA/H/C/003791/II/0033/G, Orphan

MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty"C.I.4 (Type II) - Update of sections 4.4 and 5.1 of the SmPC in order to update the safety information related to bleeding related events based on final results from study PCYC-1132-NT listed as a category 3 (MEA 004.1) study in the RMP; this is an in-vitro study to evaluate the effect of ibrutinib on platelet aggregation ;The Package Leaflet is updated accordingly.

C.I.4 (Type II) - Update of section 4.4 and 4.5 of the SmPC in order to update the safety information based on final) results from study LYM1003 listed as a category 3 study in the RMP (MEA 009.1); this is a drug-drug interaction study to assess steady state PK of repeated oral doses of ibrutinib alone in patients with B-cell malignancies and when combined with a moderate and strong CYP3A inhibitor; The Package Leaflet is updated accordingly.

C.I.4 (Type II) - Update of section 4.5 of the SmPC in order to update the safety information based on final results from study FK12024; this is a DDI study with CYP3A inhibitor posaconazole, in simulated subjects; The Package Leaflet is are updated accordingly.

C.I.4 (Type II) - Update of section 4.4 of the SmPC in order to update the safety information on antimicrobial prophylaxis following routine pharmacovigilance activity.

C.I.11.z (Type IB) - Submission of an updated RMP in order to extend the closure date of study PCYC-1112-CA (ANX 003.2) to Q2 2019. Yearly updates will be submitted in Q2 2017 and Q2 2018. Annex II has been updated accordingly.

C.I.11.a (Type Iain) - To update the RMP to include an additional action for Study PCI-32765 CAN3001 (MEA017) to provide a "further interim

report in 5 years' from time from the cut-off date of the current report (12 November 2015)". This change has been agreed by the CHMP in the outcome of EMA/H/C/ 003791/MEA/017. The RMP version 6.8 has been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."	
Neulasta - pegfilgrastim - EMEA/H/C/000420/II/0093/G MAH: Amgen Europe B.V., Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams,"- B.IV.1.a.3 (type II) – To add a new device which may have a significant impact on the delivery of the product: the on-body injector (Onpro kit) to be used with Neulasta, 6mg solution for injection, pre-filled syringe - B.II.e.5.c (type II) – To change the fill volume from 0.6 to 0.64 mL for Neulasta, 6 mg, solution for injection pre-filled syringe co-packed with the new on-body injector (Onpro kit) In addition the MAH took the opportunity to introduce editorial changes to module 3.2.P.2.4 Container Closure System Update of sections 3, 4.2, 5.1, 6.4, 6.5, 6.6 and 8 of the SmPC. The Labelling, Package Leaflet and the RMP (version 4.2) are updated accordingly. In addition the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet, to include some editorial changes and correct some typos throughout the product information, and to bring the product information in line with the latest QRD template version 10."	
Odomzo - sonidegib - EMEA/H/C/002839/II/0011 MAH: Novartis Europharm Ltd, Rapporteur: Paula Boudewina van Hennik, "Submission of the final results from studies CLDE225C2301 and CLDE225X2104. Study CLDE225C2301 is a phase II, multi-center, open-label, single-arm study of the efficacy and safety of oral LDE225 in patients with Hhpathway activated relapsed medulloblastoma. Study CLDE225X2104 is a Phase I/II study of LDE225 in pediatric patients with recurrent or refractory medulloblastoma or other tumors potentially dependent on the Hedgehog-signaling pathway and adult patients with recurrent or	

refractory
medulloblastoma. The RMP has been updated accordingly. The product information remains unchanged."

Prolia - denosumab -
EMEA/H/C/001120/II/0069
MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga"Change(s) in the Summary of Product Characteristics and Package Leaflet due to new clinical/pharmacovigilance data from study 20080560 (Variation category C.I.4)
Update of section 4.8 of the SmPC in order to update the safety information as cataracts are no longer considered to be a potential risk and/or adverse reaction associated with denosumab herapy, relevant changes to the SmPC, package leaflet and RMP are proposed supported by the final data report from study/studies (20080560) category 3 study in the RMP (Multicentre, randomized, double blind, placebo-controlled study in men with nonmetastatic prostate cancer receiving androgen deprivation therapy cataract development and progression study using a slit-lamp-based evaluation system (Lens Opacities Classification System III (LOCS III).)
In addition the RMP has been updated to remove the important potential risk "cataract in men with prostate cancer receiving androgen deprivation therapy"."

Reyataz - atazanavir / atazanavir sulfate -
EMEA/H/C/000494/II/0111
MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Caroline Laborde"Update of sections 4.4 and 4.8 of the SmPC to add a warning on chronic kidney disease observed in HIV infected patients during treatment with atazanavir (with or without ritonavir). This update is based on a review of the MAH safety database, a cohort study of patients with laboratory values from a large US administrative claims database and a review of published scientific literature. The Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted."

Yervoy - ipilimumab -
EMEA/H/C/002213/II/0047/G
MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van

Hennik“Update of section 4.4 to revised the current warning on concurrent administration with vemurafenib to enhance awareness on the potential of hypersensitivity reactions when ipilimumab is used sequentially with vemurafenib as requested by the PRAC following the assessment of PSUSA/00009200/201603. Update of sections 4.8 of the SmPC to amend the frequency of the adverse drug reaction ‘Vogt-Konyanagi-Haranda syndrome’ from ‘not know’ to ‘very rare’. The RMP (version 16) has been updated accordingly.]In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some editorial changes to sections 4.2 and 4.4 of the SmPC to update the dose modification information for hepatotoxicity management guidelines in line with National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) recommendations (version 4).”

B.6.11. PRAC assessed procedures

PRAC Led

Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0088

MAH: GSK Biologicals SA, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Bart Van der Schueren“Submission of the final report from the pregnancy registry data (study EPI-HPV-067). This study is a Post Approval Safety Study (PASS), and information related to the use of Cervarix during pregnancy was identified as important missing information in the Risk Management Plan (RMP).”

PRAC Led

Iclusig - ponatinib - EMEA/H/C/002695/II/0038, Orphan

MAH: Incyte Biosciences UK Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey“Submission of an updated RMP (version 17) in order to provide the statistical analysis plan for the study AP24534-14-401 (included in the pharmacovigilance plan of the RMP), as per the PRAC request made in the framework of MEA 015.”

PRAC Led

Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0020

MAH: GSK Biologicals SA, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Bart Van der Schueren"Update of the RMP (version 3.0) in order to 1) add cerebral malaria as an important potential risk, 2) add mortality by gender as missing information, 3) add the WHO Pilot Implementation Programme as a category 3 study, 4) change the study dates for studies Malaria-073 (200596, Phase IIIb randomized, open, controlled study to evaluate the immunogenicity and safety of Mosquirix, when administered as primary vaccination at 6, 7.5 and 9 months of age with or without coadministration of measles and rubella and yellow fever vaccines to children living in sub-Saharan, Africa), EPI-MAL-002(115055, an observational cohort study to estimate the incidence of AESI, of meningitis and of other AE leading to hospitalisation or death, in children, prior to implementation of Mosquirix), EPI-MAL-003 (115056, a prospective surveillance study to evaluate the safety, the effectiveness and the impact of Mosquirix in infants and young children in sub-Saharan Africa), EPI-MAL-005 (116682, an epidemiology study to assess Plasmodium falciparum parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post-Mosquirix introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit-risk in children in sub-Saharan Africa), EPI-MAL-010 (205071, a longitudinal, cross-sectional ancillary study of the EPI-MAL-005 study to evaluate the genetic diversity in circumsporozoite sequences before and after the implementation of Mosquirix in malaria-positive subjects ranging from 6 months to less than 5 years of age), 5) amend the protocol of study EPI-MAL-002, 6) update the draft protocol of study EPI-MAL-003, 7) provide a new draft of the protocol of study EPI-MAL-010, 8) provide a new protocol for the Pilot Implementation Programme."

PRAC Led

Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0062

MAH: Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Caroline Laborde, PRAC-CHMP liaison: Pierre Demolis“Submission of the final study report of non-interventional, non-imposed PASS study “Myozyme (alglucosidase alfa) Safety Information Packet effectiveness evaluation: a healthcare professional survey” (Myozyme SIP EU HCP Survey, ALGMYC08432). In addition, updated RMP version 8.0 has been submitted as part of this application.”

PRAC Led

Suliqua - insulin glargine / lixisenatide - EMEA/H/C/004243/II/0002

MAH: sanofi-aventis groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey“Submission of the final report from a pharmacoepidemiology study listed as a category 3 study in the RMP. This is retrospective database study of GLP-1 receptor agonists and risk of Acute Pancreatitis, Pancreatic Cancer and Thyroid Cancer, in Particular Medullary Thyroid Cancer, which primary objective was to estimate the incidence rates of acute pancreatitis, pancreatic and thyroid cancer among adult T2DM patients treated with GLP-1 receptor agonists (i.e. Exenatide & liraglutide) versus the ones treated with other antidiabetics.”

PRAC Led

Xyrem - sodium oxybate - EMEA/H/C/000593/II/0066

MAH: UCB Pharma Ltd., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes“Submission of the final report from study (C00302) listed as a category 3 study in the RMP. This is a post marketing non-interventional surveillance pharmacoepidemiology study (PMSS) to evaluate long-term safety, tolerability and compliance in administration of Xyrem (sodium oxybate) oral solution in patients who receive treatment with this medication in regular clinical practice.”

PRAC Led

WS1163

Harvoni-EMEA/H/C/003850/WS1163/0051

Sovaldi-EMEA/H/C/002798/WS1163/0041

MAH: Gilead Sciences International Ltd, Lead

PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey“To provide updated RMPs for Sovaldi and Harvoni following the CHMP opinion, endorsing a PRAC recommendation, issued on 15 December 2016 (EMA/CHMP/847450/2016) on the Article 20 procedure for Direct-acting antivirals (DAAs) indicated for the treatment of hepatitis C (interferon free). The PRAC requested `hepatitis B reactivation' to be considered as important identified risk for all direct-acting antivirals. In addition, `emergence of hepatocellular carcinoma' and `recurrence of hepatocellular carcinoma' have been included as important potential risks. `Patients with previous HCC' have been reflected as missing information in the RMP of the DAAs, since this population was excluded from existing clinical trials. The requested studies have also been reflected in the RMPs.”

PRAC Led

WS1169

Exviera-EMEA/H/C/003837/WS1169/0028

Viekirax-EMEA/H/C/003839/WS1169/0032

MAH: AbbVie Ltd., Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto YerroEPL: Radu Botgros, “To provide updated RMPs for Exviera and Viekirax following the CHMP opinion, endorsing a PRAC recommendation, issued on 15 December 2016 (EMA/CHMP/847450/2016) on the Article 20 procedure for Direct-acting antivirals (DAAs) indicated for the treatment of hepatitis C (interferon free). The PRAC requested `hepatitis B reactivation' to be considered as important identified risk for all direct-acting antivirals. In addition, `emergence of hepatocellular carcinoma' and `recurrence of hepatocellular carcinoma' have been included as important potential risks. `Patients with previous HCC' have been reflected as missing information in the RMP of the DAAs, since this population was excluded from existing clinical trials. The requested studies have also been reflected in the RMPs.”

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

WS1154
Rotarix-EMEA/H/C/000639/WS1154/0097
MAH: GlaxoSmithKline Biologicals S.A., Lead Rapporteur: Bart Van der Schueren

WS1161
Kisplyx-EMEA/H/C/004224/WS1161/0005
Lenvima-EMEA/H/C/003727/WS1161/0009
MAH: Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren

WS1170
Aflunov-EMEA/H/C/002094/WS1170/0036
Foclivia-EMEA/H/C/001208/WS1170/0031
MAH: Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri

WS1174
Hexacima-EMEA/H/C/002702/WS1174/0062
Hexaxim-EMEA/H/W/002495/WS1174/0068
Hexyon-EMEA/H/C/002796/WS1174/0066
MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus

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

Disclosure of information related to plasma master files cannot be released at 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):

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

Qualification of Biomarkers:

HTA:

G.2. Ongoing procedures

G.3. PRIME

Disclosure of some information related to PRIME cannot be released at present time as these contain commercially confidential information.

G.3.1. List of procedures concluding at 18-21 April 2017 CHMP plenary:

Haematology-haemostaseology		
1.	Adeno-associated viral vector serotype 5 containing human factor IX gene (AAV5-hFIX) (AMT-060);. (SME); ATMP;Treatment of severe haemophilia B	The CHMP granted eligibility to PRIME and adopted the critical summary report.
Oncology		
2.	Treatment of patients with advanced or metastatic ALK-positive non-small cell lung cancer	In view of the advanced stage of development, the CHMP denied eligibility to PRIME and adopted the critical summary report.
3.	(SME); ; ATMPTreatment of metastatic melanoma	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Cardiovascular Diseases		
4.	ATMP;Treatment of chronic cardiac ischemia	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Neurology		
5.	Treatment of Rett syndrome	The CHMP denied eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in April 2017 for May 2017 CHMP adoption of outcomes

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