17 November 2016
EMA/CHMP/611664/2016
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Minutes for the meeting on 10-13 October 2016

Chair: Tomas Salmonson – Vice-Chair: Pierre Demolis/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).

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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 pre-meeting list of participants and restrictions. See (current) October 2016 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 10-13 October 2016.

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

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

The Committee welcomed the new Slovakian member Nikola Moravcova and noted the new Bulgarian alternate member Assena Stoimenova.

1.2. Adoption of agenda

CHMP agenda for 10-13 October 2016

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 12-15 September 2016.

The CHMP adopted the minutes.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. dinutuximab beta - Orphan - EMEA/H/C/003918

APEIRON Biologics AG; treatment of neuroblastoma

Scope: Oral explanation

Action: Oral explanation to be held on Thursday 13 October 2016 at 09:00

List of Outstanding Issues adopted on 26.05.2016. List of Questions adopted on 24.09.2015.

An oral explanation was held on Thursday 13 October 2016 at 09:00

See also 3.2.5

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0020 & EMEA/H/C/002720/R/0022

MAH: PTC Therapeutics International Limited, treatment of Duchenne muscular dystrophy

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Sabine Straus,

Scope: Report from the SAG Neurology meeting held 29 September 2016. Oral explanation to be held on Tuesday 11 October 2016 at 14.00.

Type II variation

"Update of sections 4.4, 4.6, 4.7, 4.8, and 5.1 of the SmPC and Annex II in order to reflect the result from the submitted study TC124-GD-020-DMD object of SOB 001. The Package Leaflet and the RMP are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some minor editorial changes throughout the Product information."
Request for Supplementary Information adopted on 21.07.2016, 01.04.2016.

Renewal of Marketing Authorisation
Request for Supplementary Information adopted on 21.07.2016, 28.04.2016.

Action: For adoption

An oral explanation was held on Tuesday 11 October 2016 at 14.00.

See 9.1.1

2.3.2. Helicobacter Test INFAI - 13C-urea - EMEA/H/C/000140/II/0019

MAH: INFAI GmbH

Rapporteur: Andrea Laslop

Scope: "Update of the SmPC section 4.2, 4.3, 5.1 and 6.5 in order to add information on use of Refex test meal prior to the Helicobacter Test INFAI administration. The Package leaflet has

been updated accordingly. Additionally, the MAH has taken the opportunity to align the PI with the latest QRD template version 9.1."

Oral explanation to be held on Wednesday 12 October 2016 at 14.00.

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016, 21.07.2016, 23.06.2016, 01.04.2016, 28.01.2016.

An oral explanation was held on Wednesday 12 October 2016 at 14.00.

See 9.1.3

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Cystadrops - mercaptamine - Orphan - EMEA/H/C/003769

Orphan Europe S.A.R.L.; treatment of cystinosis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 19.11.2015, 22.10.2015, 25.06.2015. List of Questions adopted on 22.01.2015.

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 12.10.2016.

The summary of opinion was circulated for information.

3.1.2. Emtricitabine/Tenofovir disoproxil Mylan - emtricitabine / tenofovir disoproxil - EMEA/H/C/004050

MYLAN S.A.S; treatment of HIV

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 21.07.2016, 26.05.2016. List of Questions adopted on 19.11.2015.

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

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

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

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

The summary of opinion was circulated for information.

3.1.3. Emtricitabine/ Tenofovir disoproxil Krka - emtricitabine / tenofovir disoproxil - EMEA/H/C/004215

KRKA, d.d., Novo mesto; treatment of HIV-1 infection

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 15.09.2016. 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 restricted medical prescription.

The summary of opinion was circulated for information.

3.1.4. Ocaliva - obeticholic acid - Orphan - EMEA/H/C/004093

Intercept Pharma Ltd; treatment of primary biliary cirrhosis

Scope: Opinion

Action: For adoption

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

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

22.10.2015.

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

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

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

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

The CHMP noted the letter of recommendation dated 11.10.2016.

The summary of opinion was circulated for information.

3.1.5. Rekovelle - follitropin delta - EMEA/H/C/003994

Ferring Pharmaceuticals A/S; indicated for controlled ovarian stimulation

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 21.07.2016. List of Questions adopted on 25.02.2016.

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 Follitropin delta is not 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 12.10.2016.

The summary of opinion was circulated for information.

The CHMP adopted the BWP report.

3.1.6. SomaKit-TOC - edotreotide - Orphan - EMEA/H/C/004140

Advanced Accelerator Applications; Diagnosis of gastro-entero-pancreatic neuroendocrine tumours

Scope: Opinion

Action: For adoption

Well-established use application (Article 10a of Directive No 2001/83/EC)

2nd List of Outstanding Issues was adopted via written procedure on 15.09.2016. List of Outstanding Issues adopted on 21.07.2016. List of Questions adopted on 25.02.2016.

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 15.09.2016.

The summary of opinion was circulated for information.

3.1.7. Venclyxto - venetoclax - Orphan - EMEA/H/C/004106

AbbVie Ltd.; treatment of adult patients with chronic lymphocytic leukaemia (CLL)

Scope: Opinion

Action: For adoption

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

Oral explanation held on 15.09.2016. List of Outstanding Issues adopted on 21.07.2016. 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 conditional marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

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

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

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

The summary of opinion was circulated for information.

The CHMP adopted the CHMP assessment report on similarity

3.1.8. Tenofovir disoproxil Mylan - tenofovir disoproxil - EMEA/H/C/004049

MYLAN S.A.S.; treatment of HIV-1 infection and hepatitis B infection

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 21.07.2016, 26.05.2016. List of Questions adopted on 17.12.2015.

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 12.10.2016.

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. - pegfilgrastim - EMEA/H/C/004342

treatment of neutropenia

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 21.07.2016. 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 2nd list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.2. - trientine tetrahydrochloride - Orphan - EMEA/H/C/004005

GMP-Orphan SA; Wilson's disease

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 28.04.2016.

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

3.2.3. - pegfilgrastim - EMEA/H/C/004023

treatment of neutropenia

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 21.07.2016. 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 2nd list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.4. - prasterone - EMEA/H/C/004138

treatment of vulvovaginal atrophy

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 26.05.2016.

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.

3.2.5. dinutuximab beta - Orphan - EMEA/H/C/003918

APEIRON Biologics AG; treatment of neuroblastoma

Scope: Oral explanation

Action: Oral explanation to be held on Thursday 13 October 2016 at 09:00

List of Outstanding Issues adopted on 26.05.2016. List of Questions adopted on 24.09.2015.

An oral explanation was held on Thursday 13 October 2016 at 09:00. During the oral explanation the company presented the epidemiology and key features of neuroblastoma and answered the questions raised by the Committee.

The Committee discussed a 2nd list of outstanding issues which was adopted via written procedure on 19.10.2016 with a specific timetable.

The CHMP adopted the BWP report.

See also 2.1.1

3.2.6. - baricitinib - EMEA/H/C/004085

treatment of moderate to severe active rheumatoid arthritis (RA)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.06.2016.

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.

3.2.7. - pregabalin - EMEA/H/C/004277

treatment of neuropathic pain, epilepsy and Generalised Anxiety Disorder (GAD)

Scope: List of Outstanding Issues

Action: For adoption

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 list of outstanding issues with a specific timetable.

3.2.8. - insulin glargine / lixisenatide - EMEA/H/C/004243

treatment of type 2 diabetes mellitus

Scope: Day 180 list of outstanding issue

Action: For adoption

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 list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.9. - rituximab - EMEA/H/C/004112

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

Scope: Day 180 list of outstanding issues

Action: For adoption

List of Questions adopted on 25.02.2016.

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.

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

3.3.1. - carmustine - EMEA/H/C/004326

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

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.

3.3.2. - pegfilgrastim - EMEA/H/C/004262

treatment of neutropenia

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.

3.3.3. - tigecycline - EMEA/H/C/004419

treatment of: - complicated skin and soft tissue infections, excluding diabetic foot infections

- complicated intra-abdominal infections

should be used only in situations where it is known or suspected that other alternatives are not suitable.

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.

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

3.4.1. - adalimumab - EMEA/H/C/004212

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, paediatric Crohn's disease and Ulcerative colitis

Scope: Clockstop extension requested to respond to LoOI

Action: For adoption

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 28.04.2016.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted on 15.09.2016.

3.4.2. - adalimumab - EMEA/H/C/004373

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, paediatric Crohn's disease and Ulcerative colitis

Scope: Clockstop extension requested to respond to LoOI

Action: For adoption

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 28.04.2016.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted on 15.09.2016.

3.4.3. - miglustat - EMEA/H/C/004366

treatment of Gaucher disease

Scope: Assessment Report on similarity

Action: For adoption

The CHMP discussed the CHMP similarity Assessment Report and adopted a list of questions with a specific timetable.

3.4.4. - nitisinone - EMEA/H/C/004281

treatment of hepatorenal tyrosinemia type 1

Scope: Clockstop extension requested to respond to LoQ

Action: For adoption

List of Questions adopted on 21.07.2016.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted on 21.07.2016.

3.4.5. - nonacog beta pegol - Orphan - EMEA/H/C/004178

Novo Nordisk A/S; treatment of haemophilia B

Scope: Clockstop extension requested. List of Questions to ad-hoc expert group meeting.

Action: For adoption

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 26.05.2016.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted on 15.09.2016.

The CHMP adopted a list of questions to the ad-hoc expert group.

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

treatment of haemophilia A

Scope: List of Questions to ad-hoc expert group meeting

Action: For adoption

List of Questions adopted on 21.07.2016.

The CHMP adopted a list of questions to the ad-hoc expert group.

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

treatment of schizophrenia

Scope: Clockstop extension requested to respond to LoQ.

Action: For adoption

List of Questions adopted on 21.07.2016.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted on 21.07.2016

3.4.8. - bezlotoxumab - EMEA/H/C/004136

indicated for the prevention of Clostridium difficile infection (CDI) recurrence

Scope: Amended timetable and draft list of experts for the SAG meeting to be held on 3 November 2016.

Action: For adoption

List of Outstanding Issues adopted on 21.07.2016. List of Questions adopted on 01.04.2016.

The CHMP adopted the amended timetable and the draft list of experts for the SAG.

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

indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4

Scope: Clockstop extension requested to respond to LoQ

Action: For adoption

List of Questions adopted on 21.07.2016.

The CHMP did not agree to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted on 21.07.2016

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

treatment of schizophrenia

Scope: Letter from the applicant dated 5 October 2016 requesting an extension of clock stop to respond to the List of Questions adopted on 28.04.2016

Action: For information

List of Questions adopted on 28.04.2016.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted on 28.04.2016.

3.4.11. - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/004051

prevent invasive meningococcal disease caused by Neisseria meningitidis serogroup B

Scope: amended timetable

Action: For information

List of Questions adopted on 15.09.2016.

The CHMP noted the amended timetable.

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. Ertapenem Hospira - ertapenem - EMEA/H/C/004080

Hospira UK Limited; treatment of bacterial infections and prophylaxis of surgical site infection following elective colorectal surgery

Scope: Withdrawal of initial marketing authorisation application

Action: For information

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

The CHMP noted the letter from the applicant informing of the decision to withdraw the MAA.

3.7.2. Pemetrexed ditromethamine Hospira - pemetrexed - EMEA/H/C/004306

Hospira UK Limited; treatment of malignant pleural mesothelioma and non-small cell lung cancer

Scope: Withdrawal of initial marketing authorisation application

Action: For information

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

List of Questions adopted on 21.07.2016.

The CHMP noted the letter from the applicant informing of the decision to withdraw the MAA.

3.7.3. Zemfirza - cediranib - Orphan - EMEA/H/C/004003

AstraZeneca AB; treatment of platinum sensitive relapsed (PSR) ovarian cancer relapsed (PSR) ovarian cancer

Scope: Withdrawal of initial marketing authorisation application

Action: For information

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

The CHMP noted the letter from the applicant informing of the decision to withdraw the MAA.

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. Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/X/0050/G

Bial - Portela & Cª, S.A.

Rapporteur: Martina Weise, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Martin Huber

Scope: "An extension of the marketing authorisation for Zebinix concerning a new strength: 50 mg/ml and a new pharmaceutical form: oral suspension, grouped with an extension of indication to add treatment of adolescents and children aged above 6 years (adjunctive therapy in patients with partial-onset seizures with or without secondary generalisation).

Consequently, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.7, 4.8, 5.1, 5.2 and 5.3 of the SmPC have been updated and the Package Leaflet has been updated accordingly.

In addition, the MAH took the opportunity to make minor editorial changes and implement the latest QRD template in the SmPC, Annex II, labelling and Package Leaflet.

Furthermore, the list of local representatives in the Package Leaflet has been revised to amend contact details for the representative of Spain.

The application included a revised RMP version 18.0."

Action: For adoption

List of Outstanding Issues adopted on 21.07.2016. List of Questions adopted on 19.11.2015.

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.

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

No items

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. 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 4.4 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

The Committee discussed the issues identified in this application. The members discussed the presented data from the paediatric study and noted a low adherence to the therapy. This issue was discussed in general for paediatric programs for HIV products and it was agreed to consult the infectious disease working party on this general subject.

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

4.3.2. Humira - adalimumab - EMEA/H/C/000481/X/0157

AbbVie Ltd.

Rapporteur: Kristina Dunder

Scope: "Extension application to add a new strength of 80 mg (80 mg/0.8 ml) for adalimumab solution for injection in single-use pre-filled syringe, for subcutaneous injection."

Action: For adoption

The Committee discussed the issues identified in this application, which were related to the quality and clinical part.

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

4.3.3. Isentress - raltegravir - EMEA/H/C/000860/X/0059

Merck Sharp & Dohme Limited

Rapporteur: Greg Markey, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Julie Williams

Scope: "Extension application to add a new strength of 600mg film coated tablets."

Action: For adoption

The Committee discussed the issues identified in this application. The main issues discussed related to the pharmacokinetic data, but also other parts of the dossier.

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

4.3.4. Mimpara - cinacalcet - EMEA/H/C/000570/X/0055/G

Amgen Europe B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to introduce a new pharmaceutical form associated with new strengths (1 mg, 2.5 mg and 5 mg hard capsules) grouped with a type II variation (C.1.6.a) to include paediatric use in the approved indication. As a consequence, sections 4.2 and 4.4 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.

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."

Action: For adoption

The Committee discussed the issues identified in this application and noted that additional data is needed from the applicant.

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

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

No items

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

No items

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

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

5.1.1. Caprelsa - vandetanib - EMEA/H/C/002315/II/0016

Genzyme Europe BV

Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard

Scope: "Extension of Indication to include paediatric indication population for Caprelsa. As a consequence, sections 4.1, 4.2, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated in update the safety information. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 23.06.2016, 01.04.2016, 19.11.2015.

The Committee discussed the issues identified in this application. The Committee discussed the issues identified in this application which related to the MAH's request for a +1 year market protection.

The Committee adopted a 4th request for supplementary information with a specific timetable.

5.1.2. Humira - adalimumab - EMEA/H/C/000481/II/0158

AbbVie Ltd.

Rapporteur: Kristina Dunder

Scope: "Extension of Indication to include new indication for moderate to severe nail psoriasis in adult patients who are candidates for systemic therapy for Humira.
As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 9.1."

Action: For adoption

The Committee discussed the issues identified in this application, which were related to indication wording and respective SmPC sections.

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

5.1.3. Lucentis - ranibizumab - EMEA/H/C/000715/II/0061

Novartis Europharm Ltd

Rapporteur: Kristina Dunder, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur:

Ulla Wändel Liminga

Scope: “Extension of Indication to include treatment of visual impairment due to choroidal neovascularization (CNV) based on data from the pivotal study CRFB002G2301 (MINERVA). Consequential changes have been implemented in SmPC sections 4.1, 4.2, 4.4, 4.8 and 5.1 and the Package Leaflet has been updated accordingly. An updated RMP version 16.2 was agreed during the procedure.”

Action: For adoption

Request for Supplementary Information adopted on 26.05.2016.

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.

5.1.4. Opdivo - nivolumab - EMEA/H/C/003985/II/0012

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 adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL):
-after autologous stem cell transplant (ASCT) and treatment with brentuximab vedotin, or
-after at least two prior therapies in patients who are not candidates for ASCT,
for OPDIVO as monotherapy.
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 new indication, add a warning that patients with active autoimmune disease and symptomatic interstitial lung disease were excluded from clinical trials of cHL, and update the safety and pharmacodynamic information. The Package Leaflet is updated in accordance.
Furthermore, the PI is brought in line with the latest QRD template version 10.0.
Moreover, the updated RMP version 5.0 has been submitted”

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016, 23.06.2016.

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. Opdivo - nivolumab - EMEA/H/C/003985/II/0017

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 treatment of recurrent or metastatic squamous cell cancer of the head and neck (SCCHN) after platinum-based therapy in adults for Opdivo. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, of the SmPC are updated in order to add the proposed new indication, add a warning that patients with a baseline performance score ≥ 2, untreated brain metastasis, active autoimmune disease, or medical conditions requiring systemic immunosuppression were excluded from the SCCHN clinical trial and update the undesirable effect and safety information. Labelling is updated in accordance. Moreover, the updated RMP version 6.0 has been submitted"

Action: For adoption

The Committee discussed the issues identified in this application, which were related to the uncertainties regarding to some subgroup analysed, which should be further explored.

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

5.1.6. 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: "This grouped variation application consists of three Type II variation applications as follows:
- Update of the 150 mg SmPC sections 4.1, 4.2, 4.4, 4.8 and 5.1, and Package Leaflet 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.
- Update of the 150 mg and 200 mg Tasigna SmPC sections 4.1, 4.2, 4.4, 4.8 and 5.1, and Package Leaflet based on the results from 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.
- Update of the 200 mg Tasigna SmPC sections 4.8 and 5.1, based on the results from 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.
Additional changes to the labelling are proposed to comply with the latest QRD template version 10.
An updated RMP, version 16, is also provided in this application."

Action: For adoption

The Committee discussed the issues identified in this application, which related to the proposed indication wording and how best to reflect the new data in the SmPC. In addition the members discussed the proposed description risk for relapse and the criteria when to discontinue a tyrosine kinase inhibitor.

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

5.1.7. Trisenox - arsenic trioxide - EMEA/H/C/000388/II/0058

Teva B.V.

Rapporteur: Pierre Demolis, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Claire Ferard

Scope: "Extension of Indication to include induction of remission, and consolidation in adult patients with newly diagnosed low-to-intermediate risk acute promyelocytic leukaemia (APL) (white blood cell count, ≤ 10 x 10^3/µl) in combination with all trans retinoic acid (ATRA), characterised by the presence of the t(15;17) translocation and/or the presence of the Pro-Myelocytic Leukaemia/Retinoic-Acid-Receptor-alpha (PML/RAR-alpha) gene for Trisenox.
As a consequence, sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated regarding the posology, efficacy and safety information and warnings. In addition, a Risk Management Plan (version 1.3) is introduced. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 23.06.2016.

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.

5.1.8. Xgeva - denosumab - EMEA/H/C/002173/II/0045

Amgen Europe B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of Indication to include treatment of hypercalcemia of malignancy refractory to intravenous bisphosphonate for Xgeva.
As a consequence, sections 4.2, 4.3, 4.8, 5.1 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application, which were related to the proposed indication and which should be supported by other studies/external data. It was

agreed to ask the applicant for several clarifications.

The Committee adopted a request for supplementary information .

The CHMP agreed to the request by the MAH for an extension to the clock stop to respond to the RSI.

5.1.9. Trajenta Jentadueto - linagliptin linagliptin / metformin - EMEA/H/C/WS0915

Boehringer Ingelheim International GmbH

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

Scope: "Extension of Indication to include use of Trajenta as combination therapy with metformin and an SGLT-2 inhibitor and use of Jentadueto as combination therapy with an SGLT-2 inhibitor. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated based on studies 1245.30, 1275.10 and 1275.1. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make minor editorial changes in the SmPC for Jentadueto only. Moreover, the updated RMP version 10 (for Trajenta) and version 12 (for Jentadueto) have been submitted."

Action: For adoption

Request for Supplementary Information adopted on 26.05.2016.

The Committee discussed the issues identified in this application, which were related to the wording of SmPC section 4.1.

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

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

5.2.1. Jardiance - empagliflozin - EMEA/H/C/002677/II/0014

Boehringer Ingelheim International GmbH

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Dolores Montero Corominas

Scope: Clockstop extension requested.

"Extension of indication to include a new indication on prevention of cardiovascular events, based on the final data of the cardiovascular safety phase III clinical trial EMPA-REG OUTCOME. As a consequence, section 4.1 of the SmPC is updated. The Package Leaflet is also updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make some editorial changes."

Action: For adoption

Oral explanation was held on 14.09.2016, Request for Supplementary Information adopted on 15.09.2016, 23.06.2016, 25.02.2016.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the RSI adopted on 15.09.2016.

5.2.2. Synjardy - empagliflozin / metformin - EMEA/H/C/003770/II/0015

Boehringer Ingelheim GmbH

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Dolores Montero Corominas

Scope: Clockstop extension requested.

“Extension of Indication to include treatment with Synjardy as adjunct to standard care therapy in adult patients with type 2 diabetes mellitus and high cardiovascular risk when treatment with empagliflozin and metformin is appropriate and empagliflozin is needed to reduce the risk of all-cause mortality by reducing cardiovascular death and cardiovascular death or hospitalization for heart failure. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated based on the final CSR of study EMPA-REG OUTCOME. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes/corrections in the SmPC. Moreover, the updated RMP version 5.0 has been submitted.”

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016, 26.05.2016.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the RSI adopted on 15.09.2016.

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

6.1.1. - human serum albumin - EMEA/H/D/004287

Human serum albumin ancillary action prevents adsorption to the container of various amino acids, vitamins which may be present in trace quantities and acts as a carrier of these substances to support growth and maintenance of gametes and/or embryos. Scavenges embryotoxic components generated prevents adsorption to the container of various amino acids and vitamins, acts as a carrier of these substances to support growth and maintenance of gametes and/or embryos, Scavenges embryotoxic components generated during embryo's metabolism in vitro

Scope: List of outstanding issues, Clockstop extension requested

Action: For adoption

List of Questions adopted on 28.01.2016.

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.

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

The CHMP adopted the BWP report.

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. metreleptin - Orphan - H0004218

Aegerion Pharmaceuticals Limited;

Treatment of patients with generalised lipodystrophy and of a subset of patients with partial lipodystrophy with low leptin levels and metabolic abnormalities.

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

Action: For adoption

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.1.2. rucaparib - Orphan - H0004272

Clovis Oncology; Rucaparib is indicated as monotherapy treatment of advanced ovarian cancer in adult patients with deleterious BRCA-mutated tumours (inclusive of both germline and somatic BRCA mutations), and who have been treated with two or more prior lines of

chemotherapy.

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

Action: For adoption

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.2. 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 9 recommendations for eligibility to PRIME: 3 were granted and 6 were denied. The individual outcomes are listed in PRIME Monthly Report on EMA website.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0020 & EMEA/H/C/002720/R/0022

MAH: PTC Therapeutics International Limited, treatment of Duchenne muscular dystrophy

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Sabine Straus,

Scope: Report from the SAG Neurology meeting held 29 September 2016. Oral explanation to be held on Tuesday 11 October 2016 at 14.00.

Type II variation

"Update of sections 4.4, 4.6, 4.7, 4.8, and 5.1 of the SmPC and Annex II in order to reflect the result from the submitted study TC124-GD-020-DMD object of SOB 001. The Package Leaflet and the RMP are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some minor editorial changes throughout the

Product information."
Request for Supplementary Information adopted on 21.07.2016, 01.04.2016.

Renewal of Marketing Authorisation
Request for Supplementary Information adopted on 21.07.2016, 28.04.2016.

Action: For adoption

The CHMP noted the report from the SAG held 29 September 2016 and the scientific advice on the clinical study design.

An oral explanation was held on Tuesday 11 October 2016 at 14.00. During the oral explanation the Company presented the overview of the proposed study – study population, primary analysis, duration and feasibility.

The Committee discussed the proposed study design and was questioning the lack of robustness of the totality of the data provided thus far, as well as the concerns were expressed about some of the key design features of the proposed RCT (to serve as a specific obligation in the context of the CMA) as presented by the MAH during the Oral explanation.

Furthermore, the CHMP noted that the MAH has new scientific data not assessed by the CHMP. The CHMP agreed to request the additional scientific data.

The CHMP adopted a 4th request for supplementary information with a specific timetable.

Post-meeting note: the final request for supplementary information with a specific timetable was adopted via written procedure on 18th October 2016.

See 2.3.1

9.1.2. Emtriva - emtricitabine - EMEA/H/C/000533/II/0113

MAH: Gilead Sciences International Ltd,

Rapporteur: Greg Markey,

Scope: Re-adoption of opinion due to change in administration time from 24-48 hours to 24 hours.

"Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to allow administration of Emtriva 200 mg hard capsule every 24 hours in patients with renal impairment (eGFRCG ≥ 30 mL/min) and corresponding update the SmPC for Emtriva 10mg/ml oral solution. The Package Leaflet is updated accordingly."

Action: For adoption

Opinion adopted on 15.09.2016. Request for Supplementary Information adopted on 23.06.2016.

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

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

The summary of opinion was circulated for information.

9.1.3. Helicobacter Test INFAI - 13C-urea - EMEA/H/C/000140/II/0019

MAH: INFAI GmbH

Rapporteur: Andrea Laslop

Scope: "Update of the SmPC section 4.2, 4.3, 5.1 and 6.5 in order to add information on use of Refex test meal prior to the Helicobacter Test INFAI administration. The Package leaflet has been updated accordingly. Additionally, the MAH has taken the opportunity to align the PI with the latest QRD template version 9.1."

Oral explanation to be held on Wednesday 12 October 2016 at 14.00.

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016, 21.07.2016, 23.06.2016, 01.04.2016, 28.01.2016.

An oral explanation was held on Wednesday 12 October 2016 at 14.00.

The oral explanation focused on the diagnostic performance measures and the simulation study.

The CHMP adopted a negative opinion by consensus recommending the refusal of the variation to the terms of the marketing authorisation together with the Assessment Report.

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

See 2.3.2

10. Referral procedures

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

10.1.1. Direct-acting antivirals (DAAV) indicated for the treatment of hepatitis C (interferon free - EMEA/H/A-20/1438

PRAC Rapporteur: Margarida Guimarães; PRAC Co-rapporteur: Dolores Montero Corominas

Scope: Final List of experts to the SAG HIV/viral meeting

Action: For information, the final list was adopted via written procedure on 7th October 2016.

The CHMP noted the list of experts adopted by the CHMP via written procedure.

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

10.2.1. Desloratadine-containing products - desloratadine - EMEA/H/A-5(3)/1431

Rapporteur: Koen Norga, Co-Rapporteur: Andrea Laslop,

Scope: amended timetable

Prescription status of desloratadine-containing products

Action: For adoption

List of outstanding issues adopted on 26 May 2016.

The CHMP adopted an amended timetable.

Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 13.10.2016

Comments: 27.10.2016

Updated Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 02.11.2016

CHMP discussion/opinion: November 2016 CHMP

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

No items

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

10.5.1. Haldol and associated names - haloperidol - EMEA/H/A-30/1393

Janssen-Cilag Group of companies and associated companies

Rapporteur: Martina Weise, Co-Rapporteur: Katarina Vučić,

Scope: List of outstanding issues, SAG report

Action: For adoption

List of outstanding issues adopted 01.04.2016, 26.03.2015. List of Questions adopted on 26.06.2014

The CHMP main discussion focused on the indication wordings taking into account the SAG report on the need and benefit/risk of haloperidol in the different indications.

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

Submission of responses: 15.12.2016

Re-start of the procedure: 29.12.2016

Joint assessment report circulated to CHMP: 11.01.2017

Comments: 16.01.2017

Updated joint assessment report circulated to CHMP: 19.01.2017

CHMP opinion: January 2017 CHMP

10.5.2. Haldol decanoate and associated names – haloperidol - EMEA/H/A-30/1405

Janssen-Cilag Group of companies and associated companies

Rapporteur: Martina Weise, Co-Rapporteur: Katarina Vučić,

Scope: List of outstanding issues

Action: For adoption

List of outstanding issues adopted 01.04.2016, 26.03.2015. List of Questions adopted on 26.06.2014

The CHMP main discussion focused on the indication wordings.

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

Submission of responses: 15.12.2016

Re-start of the procedure: 29.12.2016

Joint assessment report circulated to CHMP: 11.01.2017

Comments: 16.01.2017

Updated joint assessment report circulated to CHMP: 19.01.2017

CHMP opinion: January 2017 CHMP

10.5.3. Lovenox and associated names – enoxaparin - EMEA/H/A-30/1429

Sanofi Aventis group of companies and associated companies

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

Scope: List of outstanding issues

Harmonisation exercise for Lovenox and associated names. The review was triggered by France, due to the need of harmonisation of the Summary of Product Characteristics across Member States.

Action: For adoption

List of outstanding Issues adopted 28.04.2016. List of Questions adopted on 19.11.2015.

The members discussed amendments to the SmPC as well as a possible communication plan for these changes. On some aspects the CHMP considered literature searches appropriate.

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

Submission of responses: 03.11.2016

Re-start of the procedure: 17.11.2016

Rapporteur / co-rapporteur joint assessment report circulated to CHMP: 30.11.2016

Comments: 05.12.2016

Updated rapporteur / co-rapporteur joint assessment report circulated to CHMP: 08.12.2016

Adoption of list of outstanding issues / CHMP opinion: December 2016 CHMP

10.5.4. Saroten and associated names - amitriptyline - EMEA/H/A-30/1430

Lundbeck group of companies and associated companies

Rapporteur: George Aislaitner, Co-Rapporteur: Alar Irs,

Scope: List of Outstanding Issues

Harmonisation exercise for Saroten and associated names (amitriptyline). Review triggered by Greece due to the need to harmonise the product information across all Member States, including the therapeutic indication, the posology, the contra-indications, the adverse effects and the recommendations for use.

Action: For adoption

List of outstanding issues adopted on 23.06.2016, 01.04.2016. List of Questions adopted 17.12.2015

The CHMP discussed the indications and supporting data for Saroten and associated names .

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

Submission of responses: 03.11.2016

Re-start of the procedure: 17.11.2016

Rapporteur / co-rapporteur joint assessment report circulated to CHMP: 30.11.2016

Comments: 05.12.2016

Updated rapporteur / co-rapporteur joint assessment report circulated to CHMP: 08.12.2016

Adoption of list of outstanding issues / CHMP opinion: December 2016 CHMP

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

10.6.1. Metformin and metformin containing fixed-dose combinations – metformin containing products – EMEA/H/A-31/1432

Rapporteur: Kristina Dunder, Co-Rapporteur: Johann Lodewijk Hillege, Scope: Opinion

Review of use in patients with renal impairment and precautions regarding lactic acidosis

Action: For adoption

List outstanding issues adopted 23.06.2016. List of Questions adopted 28.01.2016.

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.

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

10.6.2. Symbioflor 2, Escherichia Coli bacteria (cells and autolysate) - EMEA/H/A-31/1441

Symbiopharm GmbH,

Rapporteur: Harald Enzmann, Co-rapporteur: Milena Stain;

Scope: List of question to Ad-hoc expert meeting

Article 31 triggered by the BfArM in Germany in March 2016 requesting the review of the benefit-risk balance for Symbioflor 2 and associated names following concerns that the effectiveness of the medicine(s) has not been adequately demonstrated.

Action: For adoption

The CHMP adopted the list of questions to the ad-hoc expert meeting.

10.6.3. Pharmaceutics International – EMEA/H/A-31/1444

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: David Lyons,

Scope: Request from the European Commission for clarification in relation to the Opinion adopted by the CHMP for Pharmaceutical International Article 31 referral at its September meeting.

Article 31 triggered by the European Commission

Action: For discussion

Opinion adopted on 15.09.2016. List of Questions adopted on 23.06.2016. List of Outstanding Issues adopted on 21 July 2016.

The CHMP noted the communication from the European Commission.

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

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

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

October 2016 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

The CHMP noted the ENS.

12. Inspections

12.1. GMP inspections

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 ITF minutes.

13.2. Innovation Task Force briefing meetings

Disclosure of information related to briefing meetings taking place with applicants cannot be released at present time as deemed to contain commercially confidential information

13.2.1. ITF Briefing Meeting

ITF Briefing Meeting Meeting date: 22 November 2016

Action: For adoption

The CHMP agreed to the meeting.

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Election of CHMP Vice-Chair

Action: For adoption

The CHMP elected Harald Enzmann as new CHMP Vice-chair.

14.1.2. Review of CHMP assessment reports templates for initial MAA, Generics, Ancillary (Autumn 2016 Roll out) (EMA/629410/2016)

Action: For adoption

The CHMP noted the review about the changes and adopted the templates.

The changes include updates to the D80 assessment reports (ARs) for quality, non-clinical and clinical and guidance documents, D120 list of questions (LoQ), D150 joint assessment report (JAR) templates, D180 list of outstanding issues (LoOI), D180 JAR templates. The D210 CHMP ARs have also been updated (templates and guidance documents). In addition, an update of the templates for the initial consultation procedure for ancillary substances included in medical devices is proposed.

It was agreed to include guidance to the template, rather than having separate Templates and Guidance documents (so that there is one document only). The information related to update of templates will be forwarded to specific contact person at the NCA.

The revised AR templates apply to new MAAs starting from November 2016 onwards.

The revised templates will be published on the EMA website labelled as Rev 10.16.

14.1.3. Pilot Project on a model for a pre-marketing risk-based model for product testing

Scope: Outcome report of pilot project

Action: For information

Comments should be provided by 31 October 2016. The CHMP noted the information.

14.1.4. Update on the NCA Dashboard

Scope: Presentation on the use of the NCA Dashboard

Action: For information

Postponed.

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 **26-29 September 2016**

Action: For information

The CHMP adopted the Summary of recommendations and advice of PRAC meeting.

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for September 2016

Action: For adoption

The CHMP adopted the list.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 05-07 October 2016
Action: For information

The CHMP noted the minutes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 19-20 September 2016

Action: For information

The CHMP noted the report.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at October 2016 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 14-15 September 2016

Action: For information

The CHMP noted the report.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 04-06 October 2016
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 10-12 October 2016

Action: For information

The CHMP noted the report.

Letter from the CMDh dated 5th July 2016 to the PGWP on applicability of Art. 31 referral outcome on codeine-containing medicinal products to medicinal products containing morphine derivatives

Action: For information

The CHMP noted the letter.

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 26-29 September 2016. Table of conclusions

Action: For information

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.

The CHMP noted the report.

Scope: SA new initiative: Biosimilar Pilot

Action: For adoption

Postponed.

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 21 September 2016.

Action: For adoption

The CHMP adopted the Table of Decisions.

14.3.3. Biosimilar Medicinal Product Working Party (BMWP)

Vice-Chair: Martina Weise

Scope: Election of BMWP Chair

Action: For adoption

The CHMP elected Elena Wolff-Holz (DE) as Chair to BMWP.

Scope: Appointment of new core member to BMWP

Action: For adoption

The CHMP appointed Leon van Aerts as a new core member to BMWP.

Scope: Nomination of new observer Sandra Bright (IE) to BMWP

Action: For adoption

The CHMP nominated Sandra Bright (IE) as observer to BMWP.

14.3.4. Vaccines Working Party (VWP)

Scope: Election of VWP Chair

Action: For adoption

The CHMP elected Mair Powell as Chair to the VWP.

14.3.5. Pharmacogenomics Working Party (PGWP)

Scope: Election of PGWP Chair

Action: For adoption

The CHMP elected Krishna Prasad as Chair to the PGWP.

14.3.6. Quality Working Party (QWP)

Chair: Jean-Louis Robert

Scope: Q&As on quality requirements for orally inhaled products

Action: For adoption

Postponed.

14.3.7. Central Nervous System Working Party (CNSWP)

Chair: Karl Broich

Scope: Concept paper on the need for revision of the guideline on clinical investigation of medicinal product for the treatment of migraine (EMA/179671/2016)

Action: For adoption for 3 months public consultation

The CHMP adopted the concept paper for 3 months public consultation. The current guideline does not address the evidence needed to support a claim of treatment of chronic migraine, which is a relatively new concept. Chronic migraine has been accepted in the International Classification of Headache Disorders (3rd edition). Recently a number of scientific advice procedures have been considered for development programs of medicinal products for the treatment of chronic migraine. The other parts of the guideline still apply and are up to date although a slight adaptation may be discussed.

Scope: Concept paper on the need for revision of the guideline on clinical investigation of medicinal products in the treatment of epileptic disorders (EMA/CHMP/179692/2016).

Action: For adoption for 3 months public consultation

The CHMP adopted the concept paper for 3 months public consultation. The need for evaluating the full efficacy spectrum of newly developed anti-epileptic agents should be highlighted and the way to foster further development needs to be re-visited. Also the guideline may be adapted according to the revised and ongoing terminology and classification of seizures and seizure syndromes (Engel 2006; Berg et al., 2010; Scheffer et al., 2016).

Scope: Nomination of new observer Ewa Balkowiec Iskra (PL) to CNSWP

Action: For adoption

The CHMP nominated Ewa Balkowiec Iskra (PL) as observer to CNSWP.

14.3.8. Radiopharmaceutical Drafting Group (RadDG)

Chair: Anabel Cortes

Scope: Guideline on core SmPC and Package Leaflet for nanocolloidal technetium (99mTc) albumin

Action: For adoption

Postponed.

Scope: Guideline on core SmPC and Package Leaflet for sodium iodide (131I) therapy capsule

Action: For adoption and release for 4 months public consultation

Postponed.

14.3.9. Pharmacokinetics Working Party (PKWP)

Scope: Election of PKWP Chair

Action: For adoption

The CHMP elected Jan Welink as Chair to the PKWP.

14.3.10. Rheumatology/Immunology Working Party (RIWP)

Scope: Election of RIWP Chair

Action: For adoption

The CHMP elected Jan Mueller-Berghaus as Chair to the RIWP.

14.3.11. Oncology Working Party (ONCWP)

Chair: Pierre Demolis

Scope: Election of Vice-Chair

Action: For adoption

The CHMP elected Paolo Foggi (IT) as Vice-Chair to ONCWP.

14.3.12. Extrapolation Working Group

Report on Public Workshop on extrapolation of efficacy and safety in medicine development across age groups

Action: For information

The CHMP noted the information. The report summarises the main ideas and solutions proposed during the Public Workshop, the outcome will contribute to the further development of the draft reflection paper which is expected to be released for public consultation by the end of 2016 and to the implementation of the Extrapolation Framework in relevant procedures.

14.3.13. Respiratory Drafting Group (RDG)

Chair: Karolina Törneke Respiratory Drafting Group letter to CHMP and PDCO - Request for advice on how to address issues related to therapeutic equivalence for orally inhaled products for children

Action: For discussion

Follow-up from October ORGAM meeting.

The CHMP noted the need to form a small CHMP/PDCO task force to work on this request. The CHMP nominated membersto represent the CHMP as part of this task force.

14.3.14. Biostatistics Working Party (BSWP)

Chair: Thomas Lang (acting)

Call for nomination of a new core member following resignation of David Jonathan Wright (UK)

Action: For information

Expertise sought: professionally qualified senior assessor within the European regulatory network, with relevant expertise in the field of biostatistics.

Nominations should be sent by **21 October 2016**.

Appointment is going to take place at the November 2016 CHMP Plenary meeting.

The CHMP noted the information. The deadline was extended and nominations should be sent by 21 October 2016.

The CHMP noted the information.

14.3.15. Cardiovascular Working Party (CVSWP)

Chair: Pieter de Graeff

Scope: Appointment of new core member Bart Van der Schueren (BE) to CVSWP

Action: For adoption

The CHMP appointed new core member Bart Van der Schueren (BE) to CVSWP.

14.3.16. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan / Sonja Beken,

Scope: Election of Vice-Chair

Action: For adoption

The CHMP elected Mikael Andersson (SE) as Vice-Chair to the SWP.

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

14.9.1. Adaptive pathways

Scope: Workshop and report

Action: For information

The CHMP noted the report and next steps. The Workshop will be held on 8th December 2016. The final report on lessons learned was published in August 2016. Adaptive Pathways concept will be further explored as an approach to bringing promising medicines to patients with an unmet need in a timely manner.

Future discussions on adaptive pathways will be incorporated into the existing operational platform of EMA parallel regulatory-HTA scientific advice, with the inclusion of other stakeholders (patients, interested HTAs and, if relevant, payers will also be invited) relevant to the specific issues under discussion. An additional pre-submission meeting (two for SMEs) will be granted as compared to the parallel regulatory-HTA scientific advice.

15. Any other business

15.1. AOB topic

15.1.1. Revision of the 'Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products'

CHMP Rapporteur: Harald Enzmann

Scope: The concept paper was adopted at the July 2016 CHMP Plenary. The public consultation ended on 30 September. The guideline is being revised.

Action: For information

The CHMP noted that further discussions will be held during November Plenary.

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 10 – 13 October 2016 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Bart Van der Schueren	Member	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Ines Baotic	Member	Croatia	No restrictions applicable to this meeting	
Katarina Vučić	Alternate	Croatia	No interests declared	
Panayiotis Triantafyllis	Member	Cyprus	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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Pierre Demolis	Member (Vice-Chair)	France	No interests declared	
Joseph Emmerich	Alternate	France	No interests declared	
Harald Enzmann	Member	Germany	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Dimitrios Kouvelas	Member	Greece	No interests declared	
George Aislaitner	Alternate	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 interests declared	
Natalja Karpova	Alternate	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No restrictions applicable to this meeting	
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Karsten Bruins Slot	Member	Norway	No interests declared	
Piotr Fiedor	Member	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Nikola Moravcova	Member	Slovakia	No interests declared	
Jana Schweigertova	Alternate	Slovakia	No restrictions applicable to this meeting	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member- via telephone*	Spain	No interests declared	
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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Koenraad Norga	Co-opted member	Belgium	No interests declared	
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	
Theis Moeslund Jensen	Expert - in person*	Denmark	No restrictions applicable to this meeting	
Jana Jeřábková	Expert - in person*	Czech Republic	No interests declared	
Jorge Camarero Jimenez	Expert - in person*	Spain	No restrictions applicable to this meeting	
Maria Escudero Galindo	Expert - in person*	Spain	No participation in discussion, final deliberations and voting on:	3.1.2. Emtricitabine/Tenofovir disoproxil Mylan - emtricitabine / tenofovir disoproxil - EMEA/H/C/004050 3.1.8. Tenofovir disoproxil Mylan - tenofovir disoproxil - EMEA/H/C/004049 3.3.2. - pegfilgrastim - EMEA/H/C/004262
Valerie Lescrainier	Expert - in person*	Belgium	No interests declared	
Julien Gaudas	Expert - in person*	France	No interests declared	
David Owens	Expert - via telephone*	United Kingdom	No restrictions applicable to this meeting	
Serge Bakchine	Expert - via telephone*	France	No restrictions applicable to	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			this meeting	
Nele Berthels	Expert - via telephone*	Belgium	No interests declared	
Alicia Perez	Expert - via telephone*	Spain	No interests declared	
Marta Soler	Expert - via telephone*	Spain	No interests declared	
Christine Greiner	Adobe presenter	Germany	No interests declared	
Johanna Wernsperger	Adobe presenter	Austria	No interests declared	
Tanja Zahlner	Expert - via telephone*	Austria	No interests declared	
Marie-Christine Bielsky	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Nele Steens	Adobe presenter	Belgium	No interests declared	
Christian Gartner	Expert - via telephone*	Austria	No restrictions applicable to this meeting	
Stefan Bonné	Adobe presenter	Belgium	No interests declared	
Agustin Portela Moreira	Expert - via telephone*	Spain	No interests declared	
Andre Elferink	Expert - via telephone*	Netherlands	No interests declared	
Marek Surowiec	Expert - via telephone*	Poland	No interests declared	
Macarena Rodriguez Mendizabal	Expert - via telephone*	Spain	No interests declared	
Violeta Stoyanova-Beninska	Expert - via telephone*	Netherlands	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Aghadiuno Olaperi	Expert - via telephone*	United Kingdom	No interests declared	
Azijada Srkalovic Imsiragic	Expert - via telephone*	Croatia	No restrictions applicable to this meeting	
Mirjam Hinterleitner	Expert - via telephone*	Austria	No interests declared	
Stephan Lehr	Expert - via telephone*	Austria	No restrictions applicable to this meeting	
Sabine Mayrhofer	Expert - in person*	Germany	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)*

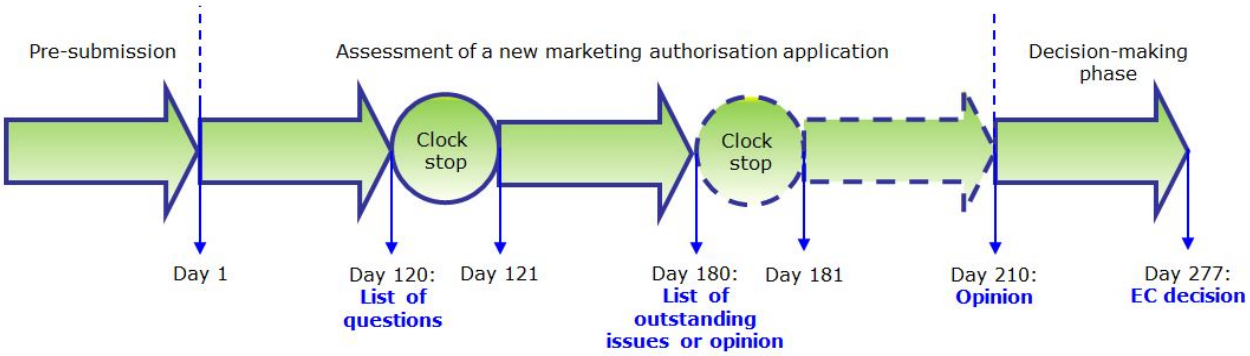
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

17 November 2016
EMA/738770/2016

Annex[1] to October 2016 CHMP Minutes

PRE SUBMISSION AND POST AUTHORISATIONS ISSUES

[1] From October 2016 onwards Annexes to CHMP Agendas and Minutes will be published

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A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for October 2016: **For adoption**	Adopted.

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

Final Outcome of Rapporteurship allocation for October 2016: **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

Evoltra - clofarabine - EMEA/H/C/000613/S/0050 MAH: Genzyme Europe BV, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard	Positive Opinion adopted by consensus. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. Marketing Authorisation remains under exceptional circumstances.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Zoledronic acid Actavis - zoledronic acid - EMEA/H/C/002488/R/0017 MAH: Actavis Group PTC ehf, Generic, Generic of Zometa, Rapporteur: Milena Stain, PRAC Rapporteur: Doris Stenver	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information the CHMP was of the opinion that an additional five-year renewal was required. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Ecansya - capecitabine - EMEA/H/C/002605/R/0018 MAH: KRKA, d.d., Novo mesto, Generic, Generic of Xeloda, Rapporteur: Kristina Dunder, PRAC Rapporteur: Martin Huber	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Committee concluded that the renewal can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pioglitazone Accord - pioglitazone hydrochloride - EMEA/H/C/002277/R/0011 MAH: Accord Healthcare Ltd, Generic, Generic of Actos, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Committee concluded that the renewal can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pioglitazone Teva - pioglitazone - EMEA/H/C/002297/R/0016 MAH: Teva B.V., Generic, Generic of Actos, Glustin, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner Request for Supplementary Information adopted on 13.10.2016.	Request for Supplementary Information adopted together with a specific timetable.
Pioglitazone Teva Pharma - pioglitazone - EMEA/H/C/002410/R/0013 MAH: Teva B.V., Generic, Generic of Actos, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner Request for Supplementary Information adopted on 13.10.2016.	Request for Supplementary Information adopted together with a specific timetable.
Sebivo - telbivudine - EMEA/H/C/000713/R/0045 MAH: Novartis Europharm Ltd, Rapporteur: Joseph Emmerich, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Claire Ferard	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Committee concluded that the renewal can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.2.3. Renewals of Conditional Marketing Authorisations

Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - EMEA/H/C/002450/R/0008, Orphan, ATMP MAH: Chiesi Farmaceutici S.p.A., Rapporteur: Egbert Flory, Co-Rapporteur: Paolo Gasparini, CHMP Coordinators: Jan Mueller-Berghaus, , PRAC Rapporteur: Julie Williams	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 Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Tagrisso - osimertinib - EMEA/H/C/004124/R/0007 MAH: AstraZeneca AB, Rapporteur: Aranzazu Sancho-Lopez, 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 Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Translarna - ataluren - EMEA/H/C/002720/R/0022, Orphan MAH: PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus Request for Supplementary Information adopted on 28.04.2016.	See main agenda 9. Post-authorisation Issues

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection PRAC recommendations on signals adopted at the PRAC meeting held on 26-29 September 2016 PRAC:	
Levetiracetam - **Keppra (EMEA/H/C/000277)** MAH: UCB Pharma S.A., Rapporteur: Koenraad Norga, Co-Rapporteur: Filip Josephson, (treatment of epileptic seizures,treatment of epileptic seizures), Complete application (stand-alone) - Council Directive 81/851/EEC Medication errors associated with accidental overdoses with Levetiracetam oral solution • PRAC recommendation on a signal, DHPC and communication plan: **For adoption**	Adopted.
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its 26-29 September meeting:	
EMEA/H/C/PSUSA/00000390/201602 (betaine anhydrous (centrally authorised product only)) CAPS: **Cystadane** (EMEA/H/C/000678) (betaine anhydrous), MAH: Orphan Europe S.A.R.L., Rapporteur: Harald Enzmann, PRAC Rapporteur: Valerie Strassmann, "01/03/2015 - 28/02/2016"	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 4.2 of the SmPC to change dose recommendations. 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/00000756/201602 (cinacalcet) CAPS: **Mimpara** (EMEA/H/C/000570) (cinacalcet), MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "(01 March 2013 to 28 February 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 4.5 to add information regarding the use of CYP2D6 substrates together with cinacalcet. The Package leaflet is updated accordingly.
EMEA/H/C/PSUSA/00001393/201602 (fingolimod) CAPS: **Gilenya** (EMEA/H/C/002202) (fingolimod), MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, "01-Mar-2015 to 28-Feb-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 add thrombocytopenia with a frequency uncommon and Kaposi's sarcoma with a frequency not known. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010073/201603 (bosutinib) CAPS: **Bosulif** (EMEA/H/C/002373) (bosutinib), MAH: Pfizer Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, "04/03/2015-03/03/2016"	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 sections 4.8 and 4.4 of the SmPC to add the adverse reaction Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) with a frequency not known and the adverse reaction tumour lysis syndrome (TLS) with the frequency 'uncommon' and to add relevant warnings, respectively. The package leaflet is updated accordingly.
EMEA/H/C/PSUSA/00010175/201603	The CHMP, having considered in accordance with

(albiglutide) CAPS: **Eperzan** (EMEA/H/C/002735) (albiglutide), MAH: GlaxoSmithKline Trading Services, Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams, "22 September 2015 to 21 March 2016"	Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change(s): Update of section 4.8 of the SmPC to add decreased appetite with a frequency of unknown. The Package leaflet is updated accordingly.The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010180/201603 (cabozantinib) CAPS: **Cometriq** (EMEA/H/C/002640) (cabozantinib), MAH: Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "22 September 2015 to 21 March 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 for the above mentioned medicinal product, concerning the following change(s): Update of section 4.5 of the SmPC to include a new warning on the risk of drug-drug interaction between cabozantinib and warfarin and the need to monitor the INR with such combination. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010311/201603 (dulaglutide) CAPS: **Trulicity** (EMEA/H/C/002825) (dulaglutide), MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Carmela Macchiarulo, "19th September 2015 to 18th March 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 for the above mentioned medicinal product, concerning the following change(s): Update of section 4 of the PL to add the adverse reaction Whole body allergic reactions (e.g swelling, raised itchy skin rash (hives)) with a frequency uncommon. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010338/201603 (apremilast) CAPS: **Otezla** (EMEA/H/C/003746) (apremilast), MAH: Celgene Europe Limited, Rapporteur: Patrick Salmon, PRAC Rapporteur: Dolores Montero Corominas, "September 21- March 20 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 for the above mentioned medicinal product, concerning the following change(s): Update of 4.8 of the

	SmPC to add the adverse reaction depression and suicidal ideation and behaviour and to add a warning on section 4.4 of SmPC. The Package leaflet is to be updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

B.4. EPARs / WPARs

Chenodeoxycholic acid sigma-tau - chenodeoxycholic acid - EMEA/H/C/004061, Orphan Applicant: Sigma-tau Arzneimittel GmbH, treatment of inborn errors of primary bile acid synthesis, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	adopted.
Emtricitabine/Tenofovir disoproxil Zentiva - emtricitabine / tenofovir disoproxil - EMEA/H/C/004137 Applicant: Zentiva k.s., treatment of HIV-1 infection, Generic, Generic of Truvada, Generic application (Article 10(1) of Directive No 2001/83/EC)	adopted.
Glyxambi - empagliflozin / linagliptin - EMEA/H/C/003833 Applicant: Boehringer Ingelheim International GmbH, treatment of type 2 diabetes mellitus, Fixed combination application (Article 10b of Directive No 2001/83/EC)	adopted.
Granpidam - sildenafil - EMEA/H/C/004289 Applicant: Accord Healthcare Ltd, treatment of patients with pulmonary arterial hypertension, Generic, Generic of Revatio, Generic application (Article 10(1) of Directive No 2001/83/EC)	adopted.
Ibrance - palbociclib - EMEA/H/C/003853 Applicant: Pfizer Limited, treatment of breast cancer, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Ivabradine JensonR - ivabradine - EMEA/H/C/004217 Applicant: JensonR+ Limited, treatment of angina pectoris, Generic, Generic of Procoralan, Generic application (Article 10(1) of Directive No 2001/83/EC)	adopted.

Ivabradine Zentiva - ivabradine - EMEA/H/C/004117 Applicant: Zentiva k.s., treatment of angina pectoris, Generic, Generic of Procoralan, Generic application (Article 10(1) of Directive No 2001/83/EC)	adopted.
Lartruvo - olaratumab - EMEA/H/C/004216, Orphan Applicant: Eli Lilly Nederland B.V., treatment of soft tissue sarcomaNew active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Ninlaro - ixazomib - EMEA/H/C/003844, Orphan Applicant: Takeda Pharma A/S, multiple myeloma, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Parsabiv - etelcalcetide - EMEA/H/C/003995 Applicant: Amgen Europe B.V., treatment of secondary hyperparathyroidism (SHPT) in adult patients with chronic kidney disease (CKD) on haemodialysis therapy, treatment of secondary hyperparathyroidism (SHPT) in adult patients with chronic kidney disease (CKD) on haemodialysis therapy., New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Pemetrexed ditromethamine Hospira - pemetrexed - EMEA/H/C/004306 Applicant: Hospira UK Limited, treatment of malignant pleural mesothelioma and non-small cell lung cancer , Generic, Generic of Alimta, Generic application (Article 10(1) of Directive No 2001/83/EC) **WPAR**	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

BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0138 MAH: Pfizer Limited, Rapporteur: Jan Mueller-Berghaus, Request for Supplementary Information adopted	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

on 06.10.2016.	
Elocta - efmoroctocog alfa - EMEA/H/C/003964/II/0008/G MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Empliciti - elotuzumab - EMEA/H/C/003967/II/0003 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 13.10.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Flixabi - infliximab - EMEA/H/C/004020/II/0003 MAH: Samsung Bioepis UK Limited (SBUK), Rapporteur: Jan Mueller-Berghaus	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0013/G, Orphan MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 13.10.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
NexoBrid - bromelain enriched proteolytic enzyme preparation from Ananas comosus - EMEA/H/C/002246/II/0027/G, Orphan MAH: MediWound Germany GmbH, Rapporteur: Harald Enzmann Request for Supplementary Information adopted on 29.09.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
NutropinAq - somatropin - EMEA/H/C/000315/II/0065 MAH: Ipsen Pharma, Rapporteur: Hanne Lomholt Larsen Opinion adopted on 13.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nuwiq - simoctocog alfa - EMEA/H/C/002813/II/0012/G MAH: Octapharma AB, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.10.2016, 14.07.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Obizur - susoctocog alfa - EMEA/H/C/002792/II/0005 MAH: Baxalta Innovations GmbH, Rapporteur: Nithyanandan Nagercoil, , Opinion adopted on 29.09.2016.	Positive Opinion adopted by consensus on 29.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Orencia - abatacept - EMEA/H/C/000701/II/0103/G MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 06.10.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Orencia - abatacept - EMEA/H/C/000701/II/0104/G MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola Opinion adopted on 13.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0106/G MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 22.09.2016.	Positive Opinion adopted by consensus on 22.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Scintimun - besilesomab - EMEA/H/C/001045/II/0010/G MAH: CIS BIO International, Rapporteur: Greg Markey Opinion adopted on 22.09.2016.	Positive Opinion adopted by consensus on 22.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Unituxin - dinutuximab - EMEA/H/C/002800/II/0008, Orphan MAH: United Therapeutics Europe Ltd, Rapporteur: Robert James Hemmings, Opinion adopted on 06.10.2016. Request for Supplementary Information adopted on 04.08.2016.	Positive Opinion adopted by consensus on 06.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vimpat - lacosamide - EMEA/H/C/000863/II/0064/G MAH: UCB Pharma S.A., Rapporteur: Filip Josephson Request for Supplementary Information adopted on 29.09.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS0898/G Vfend-EMEA/H/C/000387/WS0898/0120/G MAH: Pfizer Limited, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 22.09.2016. Request for Supplementary Information adopted on 28.07.2016.	Positive Opinion adopted by consensus on 22.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0922/G Hexacima-EMEA/H/C/002702/WS0922/0052/G Hexaxim-EMEA/H/W/002495/WS0922/0059/G	The Committee adopted a Request for Supplementary information together with a specific timetable.

Hexyon-EMEA/H/C/002796/WS0922/0055/G MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.10.2016.	
WS0967 **Hexacima-EMEA/H/C/002702/WS0967/0048** **Hexaxim-EMEA/H/W/002495/WS0967/0055** **Hexyon-EMEA/H/C/002796/WS0967/0051** MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 21.07.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0969 **Infanrix hexa-EMEA/H/C/000296/WS0969/0204** MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 13.10.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS0976/G **Infanrix hexa-EMEA/H/C/000296/WS0976/0205/G** MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
WS0977 **Tivicay-EMEA/H/C/002753/WS0977/0021** **Triumeq-EMEA/H/C/002754/WS0977/0029** MAH: ViiV Healthcare UK Limited, Lead Rapporteur: Filip Josephson Opinion adopted on 06.10.2016.	Positive Opinion adopted by consensus on 06.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0983 **ProQuad-EMEA/H/C/000622/WS0983/0110** **Zostavax-EMEA/H/C/000674/WS0983/0106** MAH: Sanofi Pasteur MSD SNC, Lead Rapporteur: Jan Mueller-Berghaus	Positive Opinion adopted by consensus on 06.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 06.10.2016.	

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

Cerdelga - eliglustat - EMEA/H/C/003724/II/0008, Orphan MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, "Update of SmPC section 5.1 to include 2, 3 and 4 years composite stability endpoint data based on the final results of the ENCORE study." Request for Supplementary Information adopted on 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0075 MAH: GSK Biologicals SA, Rapporteur: Bart Van der Schueren, "Variations that do not affect the PI (C.I.13) Submission of study HPV-015 (MEA 083): A phase III, double-blind, randomized, controlled study to evaluate the safety, immunogenicity and efficacy of GlaxoSmithKline Biologicals' HPV_16/18 L1/AS04 vaccine administered intramuscularly according to a three-dose schedule (0, 1, 6 month) in healthy adult female subjects aged 26 years and above. At final analysis (M84) of study HPV-015, a new medical review of new onset of adverse events (NOADs) collected up to M48 was performed at M84. An additional analysis on potential immune mediated diseases (pIMDs) and pregnancy outcomes collected at M48 was also done at M84. No changes in the PI are proposed" Request for Supplementary Information adopted on 13.10.2016, 23.06.2016, 25.02.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Deltyba - delamanid - EMEA/H/C/002552/II/0014, Orphan MAH: Otsuka Novel Products GmbH, Rapporteur: Greg Markey, "Update of section 5.1 of the SmPC further to the submission of final clinical study report for trial 242-12-244 "Determination of Delamanid MIC Values and Sub-species Analysis of Mycobacterium tuberculosis Complex Isolates". Moreover the MAH has taken the occasion to implement version 10.0 of the QRD template. The date of the latest renewal has been	Positive Opinion adopted by consensus on 06.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

included as well." Opinion adopted on 06.10.2016. Request for Supplementary Information adopted on 04.08.2016.	
Evotaz - atazanavir / cobicistat - EMEA/H/C/003904/II/0010 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, "Proposed changes to the EVOTAZ SmPC to aling with the current Company Core Data Sheet (CCDS). During the EVOTAZ MAA procedure, an interim Week 144 CSR for Gilead study GS-US-216-0114 was submitted and the SmPC efficacy and safety data were updated and approved accordingly. However, the resistance data were not updated at that time. As a result, the MAH proposes to update the resistance sub-section in SmPC section 5.1 with study GS-US-216-0114 Week 144 resistance data that were submitted in the context of the MAA. In addition, for clarification purposes, the MAH proposes to use the specific designation of tenofovir disoproxil fumarate throughout the EVOTAZ Product Information (PI) to differentiate this pharmaceutical entity from the tenofovir alafenamide (for which no studies with EVOTAZ have been conducted). Finally, the MAH would like to take this opportunity to implement QRD version 10." Request for Supplementary Information adopted on 29.09.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Exjade - deferasirox - EMEA/H/C/000670/II/0048, Orphan MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, "Update of section 4.4 and 4.8 of the SmPC in order to add information on paediatric population from the final results of study A2411 from the Paediatric Investigation Plan EMEA-001103-PIP01-10-M02. This submission serves to comply with Article 46 of the Regulation (EC) No 1901/2206 on medicinal products for paediatric use. Consequently, the RMP v.12.2 is presented." Opinion adopted on 06.10.2016. Request for Supplementary Information adopted on 01.04.2016.	Positive Opinion adopted by consensus on 06.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Firdapse - amifampridine - EMEA/H/C/001032/II/0042, Orphan MAH: BioMarin Europe Ltd, Rapporteur: Greg	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Markey, “Submission of the clinical study report LMS-002 to support the efficacy of Firdapse in patient with Lambert-Eaton myasthenic syndrome (LEMS).” Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 23.06.2016.	recommendation.
Galafold - migalastat - EMEA/H/C/004059/II/0001, Orphan MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege, “Submission of 30 month data for Study AT1001-012, with updates to sections 4.8 and 5.1 of SmPC. Study AT1001-012 is a randomized, open-label study to compare the efficacy and safety of migalastat HCl and ERT in patients with Fabry disease and migalastat HCl-responsive GLA mutations, who were previously treated with ERT Please note that this variation meets a post approval commitment, Cat 3 : 01 as defined in the risk management plan. The variation also includes some editorial changes to product information (contact details of country representtives).” Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 15.09.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Galafold - migalastat - EMEA/H/C/004059/II/0002, Orphan MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege, “Submission of updates to the Galafold SmPC section 5.1 Pharmacodynamic properties; specifically, addition of guidance related to searching the mutation tables, moving text from below the tables to above the tables and new and updated mutations in Table 2: Galafold amenability table and Table 3: Mutations not amenable to Galafold. Changes introduced into the tables are based on a) a direct physician request for Amicus to confirm a mutation, b) a new nucleotide change or protein sequence change identified in the literature or 3) a mutations that does not qualify for testing being added to the non-amenable table 3. Individual Mutant Form Summary of Results (IMFSR) are included in the application for the new mutations. Editorial changes are also highlighted in the tables, which result from a thorough check of the	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

tables/mutations against the source documents. Updates to the contact details in the PIL have been included." Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 15.09.2016.	
Gilenya - fingolimod - EMEA/H/C/002202/II/0039 MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, "Update of sections 4.4 and 4.8 of the SmPC to add an approximate time of onset of multifocal leukoencephalopathy (PML) and for cryptococcal meningitis (CM), and to remove the term isolated from "isolated cases of CM"." Request for Supplementary Information adopted on 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Giotrif - afatinib - EMEA/H/C/002280/II/0017 MAH: Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, "Update of sections 4.2 and 5.2 of the SmPC in order to update the information regarding renal impairment, which has been introduced following completing of the Phase I study 1200.2016. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement editorial changes in the SmPC and to update the labelling (Annex IIIA) in line with QRD template, version 9.1." Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 14.07.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Helicobacter Test INFAI - 13C-urea - EMEA/H/C/000140/II/0019 MAH: INFAI GmbH, Rapporteur: Andrea Laslop, "Update of the SmPC section 4.2, 4.3, 5.1 and 6.5 in order to add information on use of Refex test meal prior to the Helicobacter Test INFAI administration. The Package leaflet has been updated accordingly. Additionally, the MAH has taken the opportunity to align the PI with the latest QRD template version 9.1." Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 15.09.2016, 21.07.2016, 23.06.2016, 01.04.2016, 28.01.2016.	Negative Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Instanyl - fentanyl -	Positive Opinion adopted by consensus on

EMEA/H/C/000959/II/0040 MAH: Takeda Pharma A/S, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, "Submission of PASS Study (Instanyl-5001: An Evaluation of the Effectiveness of Risk Minimisation Measures: A Survey among Health Care Professionals to Assess their Knowledge and Attitudes on Prescribing Conditions of Instanyl in France and the Netherlands) included in the RMP." Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 21.07.2016.	13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Intuniv - guanfacine - EMEA/H/C/003759/II/0003/G MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Johann Lodewijk Hillege"In compliance with requests in the RMP adopted at the time of MA, the MAH submitted final results of 4 completed non-clinical studies as follows: • Study V7613M-SPD503 (Secondary Pharmacodynamics) • Study V7089M-SPD503 (Drug Interaction) • Study V7400M-SPD503 and Study V7401M-SPD503 (Metabolism) This group of variations leads to amendments of the Product Information: sections 4.5 and 5.2 of the SmPC were updated to reflect the findings four studies submitted." Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 15.09.2016, 23.06.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Intuniv - guanfacine - EMEA/H/C/003759/II/0004 MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 (Posology and Method of Administration), 4.4 (Special Warnings and Precautions for Use), and 4.8 (Undesirable Effects) of the SmPC in order to include a warning and update the safety information as a result of a post-marketing case of hypertensive encephalopathy upon abrupt discontinuation of Intuniv (guanfacine hydrochloride). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 13.10.2016, 23.06.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Iressa - gefitinib - EMEA/H/C/001016/II/0026	The Committee adopted a Request for Supplementary information together with a

MAH: AstraZeneca AB, Rapporteur: Filip Josephson, , “Submission of final study report for IMPRESS study (D791LC00001) and discussion to address one of the ‘PRAC Recommendations as per procedure regarding the gefitinib Periodic Safety Update Report (PSUR: EMA/PRAC/4284/2016). No Changes in the PI and in the RMP are proposed” Request for Supplementary Information adopted on 13.10.2016.	specific timetable.
Isentress - raltegravir - EMEA/H/C/000860/II/0061 MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, “Update of section 4.2 of the SmPC of Isentress 100 mg granules for oral suspension, upon request by PRAC following the assessment of the latest PSUR for raltegravir (EMEA/H/C/PSUSA/00010373/201509), to add information relating to the maximum dose of Isentress being 100 mg twice a day, and that each single-use packet for oral suspension is suspended in 5mL of water giving a final concentration of 20mg/ml. In addition, the MAH took the opportunity to implement minor editorial changes in the annexes, to update the contact details of the local representative in Luxembourg in the Package Leaflet and to align the annexes with the latest QRD templates (versions 9.1 and 10).” Opinion adopted on 29.09.2016.	Positive Opinion adopted by consensus on 29.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kalydeco - ivacaftor - EMEA/H/C/002494/II/0050, Orphan MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Concepcion Prieto Yerro, “Update of sections 4.6 and 5.3 of the SmPC following a revision of the animal:human exposure ratio. 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 10.0 and to align the PIL text with the current SmPC.” Opinion adopted on 13.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
NovoRapid - insulin aspart - EMEA/H/C/000258/II/0114 MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, “Update of sections 4.4 and 4.8 of the SmPC with additional information regarding avoidance of accidental mix-ups and medication errors.”	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 13.10.2016.	
NovoSeven - eptacog alfa / eptacog alfa (activated) - EMEA/H/C/000074/II/0092 MAH: Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.4 of the SmPC in order to delete sucrose warning. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes/corrections in the SmPC and Package Leaflet and to bring the PI in line with the latest QRD template version 10 (combined SmPC has been introduced)." Request for Supplementary Information adopted on 06.10.2016, 04.08.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Plenadren - hydrocortisone - EMEA/H/C/002185/II/0022, Orphan MAH: Shire Services BVBA, Rapporteur: Kristina Dunder, "To update the SmPC section 4.8 (Undesirable Effects) and PIL section 4 (Possible side effects) of the Plenadren 5mg and 20 mg (hydrocortisone) modified release tablets." Opinion adopted on 13.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Praluent - alirocumab - EMEA/H/C/003882/II/0009/G MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege"Update of section 4.2 of the SmPC to include a 300 mg Q4W dosing regimen as a starting dose, based on the results of study CHOICE I (MEA 005). Section 4.8, 5.1 and 5.2 of the SmPC and the PL have also been updated to reflect the study results. In addition, the MAH submitted the final study report of study CHOICE II (MEA 009) and additional analysis of the two studies." Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 21.07.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0145 MAH: Pfizer Limited, Rapporteur: Kristina Dunder, "Update of the SmPC section 5.1 with information on Prevenar 13 effects on invasive pneumococcal disease, antimicrobial resistance and otitis media caused by nontypeable H. influenzae. Editorial changes have also been proposed throughout the SmPC."	The Committee adopted a Request for Supplementary information together with a specific timetable.

Request for Supplementary Information adopted on 13.10.2016.	
Saxenda - liraglutide - EMEA/H/C/003780/II/0010 MAH: Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.2 and 5.1 of the SmPC in order to update the documented treatment effect currently limited to 1 year. The proposed update of the current labelling for long-term efficacy, safety and tolerable use in the management of obesity is based on 3-year data from trial 1839. In addition, the Marketing authorisation holder took the opportunity to bring the PI in line with the latest QRD template version 10 and implement minor linguistic updates.” Request for Supplementary Information adopted on 29.09.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Stivarga - regorafenib - EMEA/H/C/002573/II/0018 MAH: Bayer Pharma AG, Rapporteur: Paula Boudewina van Hennik, “Update the SmPC section 4.2 and 5.2 based on results from phase 1 study which evaluated the pharmacokinetics and safety of regorafenib in cancer subjets with severe renal impairment compared to cancer subjects without or mild renal impairment. The package leaflet is updated accordingly.” Request for Supplementary Information adopted on 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0008, Orphan MAH: Alexion Europe SAS, Rapporteur: Greg Markey, , “Update of sections 4.4 and 4.8 of the SmPC in order to reinforce the wording on the risk of anaphylaxis. The Package Leaflet is updated accordingly. The MAH took th eopportunity to include the Pharmacotherapeutic group in section 5.1.” Request for Supplementary Information adopted on 13.10.2016, 21.07.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0031 MAH: ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, “Update of section 4.4 of the SmPC with revised wording related to mitochondrial dysfunction, and section 4.2 of the SmPC with an amended recommendation related to dose reduction in patients with hepatic	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

impairment, in line with the SmPCs of other abacavir containing products. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement minor changes in Annex II and the labelling in line with the latest QRD template." Opinion adopted on 13.10.2016.	
WS0990 **Actos-EMEA/H/C/000285/WS0990/0074** **Competact-EMEA/H/C/000655/WS0990/0061** **Glubrava-EMEA/H/C/000893/WS0990/0046** **Glustin-EMEA/H/C/000286/WS0990/0072** **Tandemact-EMEA/H/C/000680/WS0990/0050** MAH: Takeda Pharma A/S, Lead Rapporteur: Patrick Salmon, Lead PRAC Rapporteur: Almath Spooner, "Submission of final study results from Pioglitazone_5019, a Drug Utilisation Study (DUS) conducted in Denmark to further investigate prescribing patterns and the effectiveness of risk minimization measures for heart failure, uninvestigated macroscopic hematuria, bladder cancer and off-label 1st line use, in fulfilment of a request from PSUSA/00002417/201307 (Period covered: 01.02.13 - 31.07.13)." Opinion adopted on 13.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.3. CHMP-PRAC assessed procedures

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0054 MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Final clinical study report for study AS001 is submitted. Sections 4.8 and 5.1 of the Summary of Product Characteristics (SmPC) are revised in order to update the efficacy and safety information (Week 204) for study AS001. The package leaflet remains unchanged. A revised RMP (version 11.0) is also submitted." Request for Supplementary Information adopted on 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0055 MAH: UCB Pharma S.A., Rapporteur: Kristina	The Committee adopted a Request for Supplementary information together with a specific timetable.

Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Final clinical study report for study PsA001 is submitted to provide data on long-term use of Cimzia in psoriatic arthritis subjects up to 216 weeks of treatment. Sections 4.8 and 5.1 of the Summary of Product Characteristics (SmPC) are revised in order to update the efficacy and safety information (Week 216) for study PsA001. The package leaflet remains unchanged. A revised RMP (version 11) is also submitted. This corresponds to MEA 027" Request for Supplementary Information adopted on 13.10.2016.	
Gilenya - fingolimod - EMEA/H/C/002202/II/0040 MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, "Update of section 4.6 of the SmPC to add information on the use of the product in pregnancy. In addition, update of section 5.3 of the SmPC to include information about the dose correspondence between human and the species used for the preclinical tests of teratogenicity. An updated RMP is submitted (version 12.0). The MAH took the opportunity to make minor editorial changes in sections 4.4, 4.5, 4.6 and 5.2 and also in Annex II.D." Request for Supplementary Information adopted on 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Jakavi - ruxolitinib - EMEA/H/C/002464/II/0031 MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information for melofibrosis following the completion of two 5-year follow up studies INCB 18424-351 and INC424A2352, thereby addressing one of the outstanding Obligations in Annex II." Request for Supplementary Information adopted on 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Jetrea - ocriplasmin - EMEA/H/C/002381/II/0026 MAH: ThromboGenics NV, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "Update of sections 4.4, 4.8 and 5.1 of the SmPC to reflect new long-term safety and efficacy data	The Committee adopted a Request for Supplementary information together with a specific timetable.

based on the final CSR for study TG-MV-014 in fulfilment of the post-authorisation measure MEA 002. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the annexes, to align the annexes with the latest QRD templates (v9.1 and 10) and to update the contact details of the local representative in Spain in the Package Leaflet. An updated RMP version 7 was included as part of the application." Request for Supplementary Information adopted on 13.10.2016, 26.05.2016.	
Odomzo - sonidegib - EMEA/H/C/002839/II/0005 MAH: Novartis Europharm Ltd, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Julie Williams, "To submit the results from the pivotal registration study CLDE225A2201 and related analyses (correlative analysis of Gli1 data and molecular analysis in tumor material) with the aim to resolve two post-authorisation measures (PAES) listed in the Annex II.D of the Marketing Authorisation. Sections 4.8 and 5.1 of the SmPC and the Annex II are updated accordingly. Also the RMP is updated (version 4.0) to reflect the most recent 30-month data." Request for Supplementary Information adopted on 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Opdivo - nivolumab - EMEA/H/C/003985/II/0018 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update the safety information for toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), myositis, myocarditis and rhabdomyolysis based on findings from routine pharmacovigilance activities. The Package Leaflet is updated accordingly. In addition, the RMP is updated to version 4.5 to reflect this new safety information." Request for Supplementary Information adopted on 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Prolia - denosumab - EMEA/H/C/001120/II/0057 MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.6 of the SmPC in order to	The Committee adopted a Request for Supplementary information together with a specific timetable.

delete references to the Pregnancy and Lactation Surveillance programs. The Package Leaflet is updated accordingly. The RMP has been revised to remove all references to the Pregnancy and Lactation Program. In addition, the Marketing authorisation holder took the opportunity to make minor editorial updates to the SmPC and Package Leaflet." Request for Supplementary Information adopted on 13.10.2016.	
Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0032 MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Dolores Montero Corominas, "Update of the SmPC sections 4.4 and 4.8 with new information on the drug-induced liver injury. Consequently, the key elements to be included in the educational material section of the Annex II have been updated. The RMP (v. 42) has been revised accordingly." Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 21.07.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0035/G MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Dolores Montero Corominas"Submission of the final study report of study TRC112765 assessing safety of eltrombopag in subjects with solid tumours receiving gemcitabine monotherapy or gemcitabine plus cisplatin or carboplatin; the RMP version 42 has been updated accordingly. In addition, the MAH took the opportunity to revise due dates for submission of final reports for two studies in the Pharmacovigilance Plan." Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 21.07.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0036/G MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Eva A. Segovia"Update to the Annex II of the Product Information based on the study assessing Effectiveness of eltrombopag Educational Materials for Hepatitis C associated	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

thrombocytopenia; update of the RMP (v. 41) to remove the PASS Study PLATELET from the Pharmacovigilance Plan; submission of the ENABLE-TEE final study report, an Observational Follow-up Study of Patients who Experienced Thromboembolic Events in the ENABLE studies." Opinion adopted on 13.10.2016.	
Simponi - golimumab - EMEA/H/C/000992/II/0067 MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, Update of the SmPC sections 4.8 and 5.1 as a result of new data from the Phase 3 extension studies of Simponi in ulcerative colitis and non-radiographic axial spondyloarthritis (C0524T18 and P07642, respectively). Moreover, the updated RMP version 17 has been submitted. Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 26.05.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Torisel - temsirolimus - EMEA/H/C/000799/II/0063, Orphan MAH: Pfizer Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, "Submission of final results from Study 3066K1-4438-WW (B1771007) titled "A Randomized Phase 4 Study Comparing 2 Intravenous Temsirolimus (TEMSR) Regimens in Subjects with Relapsed, Refractory Mantle Cell Lymphoma" and fulfilment of obligation to conduct post authorisation measure ANX 027.2. The MAH also evaluate the toxic effects of interest [e.g., bleeding, infection- and mucositis-related events] for study 3066K1-4438-WW (Post-Marketing Commitment MEA 028) together with a review discussing potential new safety concerns arising from the results. The RMP (v.3.0) is updated accordingly to add myocardial infarction and cardiovascular events in patient with coexisting cardiovascular conditions as important potential risks, and anaemia, thrombocytopenia, hypercholesterolemia, and hypertriglyceridemia as important identified risks. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."	The Committee adopted a Request for Supplementary information together with a specific timetable.

Request for Supplementary Information adopted on 13.10.2016.	
Translarna - ataluren - EMEA/H/C/002720/II/0020, Orphan MAH: PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus, "Update of sections 4.4, 4.6, 4.7, 4.8, and 5.1 of the SmPC and Annex II in order to reflect the result from the submitted study TC124-GD-020-DMD object of SOB 001. The Package Leaflet and the RMP are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some minor editorial changes throughout the Product information." Request for Supplementary Information adopted on 13.10.2016, 21.07.2016, 23.06.2016, 01.04.2016. Oral explanation held on 13.10.2016. SAG meeting held on 29.09.2016, 16.06.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable. See main agenda 9.1. Post-authorisation issues.
Trulicity - dulaglutide - EMEA/H/C/002825/II/0012 MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Carmela Macchiarulo, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information to reflect findings from a recently completed phase 3b study (Study H9X-MC-GBDG (GBDG)) concerning the use of dulaglutide in combination with sulphonylurea alone. 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 13.10.2016. Request for Supplementary Information adopted on 21.07.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Trulicity - dulaglutide - EMEA/H/C/002825/II/0013 MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Carmela Macchiarulo, "Update of sections 4.2, 4.7, 4.8 and 5.1 of the Summary of Product Characteristics (SmPC) for Trulicity following completion of a phase 3b Study (Study H9X-MCGBDI (GBDI)) to reflect the study's findings concerning the use of dulaglutide in combination with basal insulin. The Package Leaflet is updated in accordance." Opinion adopted on 13.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Request for Supplementary Information adopted on 21.07.2016.	
Ventavis - iloprost - EMEA/H/C/000474/II/0051/G MAH: Bayer Pharma AG, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard"Grouped application to introduce the new additional nebulizer "FOX Bavent" for application of Ventavis 10 µg/ mL and Ventavis 20 µg/mL, nebulizer solution: - Type IB variation to add the additional nebulizer; - Type IAIN variation for change of pack sizes within the range of current approved pack sizes; - Type II variation to implement consequential changes to SmPC sections 4.2, 4.4, 6.5 and 8, as well as to the labelling and Package Leaflet. In addition, the MAH took the opportunity to delete reference in the product information to nebulizers which are no longer available by the device manufacturer (ProDose and HaloLite), to merge the texts for Ventavis 10 µg/ mL and Ventavis 20 µg/ mL,nebulizer solution into one SmPC and one Package Leaflet text, to update the list of local representatives in the Package Leaflet, to implement minor editorial changes in the annexes and to bring the annexes in line with the latest QRD template version 9.1. An updated RMP version 7.0 was provided as part of the application." Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 21.07.2016, 25.02.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Votrient - pazopanib - EMEA/H/C/001141/II/0038 MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Update of SmPC section 4.6 to add male contraception wording following a review of pazopanib according to the MAH's guideline on prevention of pregnancies. The Package Leaflet is proposed to be updated accordingly. An updated RMP version 16 is agreed. In addition, the MAH took the opportunity to bring the Product Information in line with the latest QRD template version 10 and combine the SmPC of the 2 tablets strengths." Opinion adopted on 13.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xgeva - denosumab -	The Committee adopted a Request for

EMEA/H/C/002173/II/0046 MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.6 of the SmPC in order to delete references to the Pregnancy and Lactation Surveillance programs. The Package Leaflet is updated accordingly. The RMP has been revised to remove all references to the Pregnancy and Lactation Program. In addition, the Marketing authorisation holder took the opportunity to make minor editorial updates to the SmPC and Package Leaflet." Request for Supplementary Information adopted on 13.10.2016.	Supplementary information together with a specific timetable.
WS0991 **Actos-EMEA/H/C/000285/WS0991/0075** **Competact-EMEA/H/C/000655/WS0991/0062** **Glubrava-EMEA/H/C/000893/WS0991/0047** **Glustin-EMEA/H/C/000286/WS0991/0073** **Tandemact-EMEA/H/C/000680/WS0991/0051** MAH: Takeda Pharma A/S, Lead Rapporteur: Patrick Salmon, Lead PRAC Rapporteur: Almath Spooner, "Submission of the final study report for the Clinical Practice Research Datalink (CPRD) GOLD linkage study (Pioglitazone_5018) conducted to investigate a possible association of the use of pioglitazone with prostate cancer and data on the incidence of adjudicated prostate cancer in patients receiving pioglitazone in the long-term Insulin Resistance Intervention after Stroke (IRIS) trial." Request for Supplementary Information adopted on 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
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)	The Committee adopted a Request for Supplementary information together with a specific timetable.

study (designed to investigate whether FF/VI-Furoate/Vilanterol could improve survival in patients with moderate COPD- chronic obstructive pulmonary disease who had, or were at increased risk for CV-cardiovascular disease). The Package Leaflet and Labelling are updated accordingly. The RMP v.8.1 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 pharmacodynamic section." Request for Supplementary Information adopted on 13.10.2016.	

B.5.4. PRAC assessed procedures

PRAC Led **Angiox - bivalirudin - EMEA/H/C/000562/II/0068** MAH: The Medicines Company UK Ltd, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, , "Submission of the drug utilization study Eurovision 2. The RMP has been amended to refine the additional risk minimisation measures in line with the findings of the study." Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 23.06.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Defitelio - defibrotide - EMEA/H/C/002393/II/0019, Orphan** MAH: Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, , "Submission of a revised RMP in order to include information regarding the additional risk minimisation measures (i.e. Healthcare professional material that highlights the existence of the Registry as well as the means to patients into the registry) as outlined in Annex II. In addition, the MAH took the opportunity to add administrative changes to the protocol of the registry study, to add information about the renal pharmacokinetics study, to add updated information about off-label use during postmarketing experience and to include further	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

administrative changes to the RMP." Opinion adopted on 13.10.2016.	
PRAC Led **Eliquis - apixaban - EMEA/H/C/002148/II/0040** MAH: Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, , "Submission of the final study report of the AEGEAN study (CV185-220) which assess the education and guidance programme for Eliquis (apixaban) adherence in non-valvular atrial fibrillation patients. The updated risk management plan is also submitted to reflect the results of the study." Opinion adopted on 13.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Enbrel - etanercept - EMEA/H/C/000262/II/0199** MAH: Pfizer Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Rafe Suvarna, , "Submission of a revised RMP (version 6.1) in order to remove 'injection site reactions' as an important potential risk and 'use in pregnant women' , 'use in hepatic and renal impaired subjects' and 'use in different ethnic origins' as missing information. In addition the MAH has taken the opportunity to amend the due dates of several category 3 studies, to align the RMP with GVP module V on Risk Management Systems (revision 1), to review the list of studies included in the Pharmacovigilance plan and to update the clinical trials and post-marketing experience." Opinion adopted on 13.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Glivec - imatinib - EMEA/H/C/000406/II/0103** MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Dolores Montero Corominas, , "Submission of an updated RMP version 9.0 in order to add Hepatitis B reactivation as a new important identified risk." Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 21.07.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Noxafil - posaconazole - EMEA/H/C/000610/II/0040** MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, PRAC Rapporteur:	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Rafe Suvarna, , “Submission of a Type II variation C.I.11.b Type II to provide the updated Risk Management Plan (RMP), version 12.0 for the medicinal product Noxafil (40 mg / mL Oral Suspension, 100 mg Tablet and 300 mg concentrate for solution for infusion). The RMP is updated with the study results showing a lack of interaction effect of OATP1B1 and OATP1B3 substrates and inhibitors.” Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 26.05.2016, 25.02.2016.	
PRAC Led **Tasigna - nilotinib - EMEA/H/C/000798/II/0083, Orphan** MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, , “Submission of a revised RMP version 15 in order to add the new important identified risk “Hepatitis B reactivation”.” Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 21.07.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS0973** **Levitra-EMEA/H/C/000475/WS0973/0053** **Vivanza-EMEA/H/C/000488/WS0973/0049** MAH: Bayer Pharma AG, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, , “To include in the RMP a safety concern (identified risk) already assessed and implemented in the Levitra/Vivanza product information (EMEA/H/C/xxxx/WS/0861 (eCTD seqs 55/45), positive CHMP Opinion dated 17 December 2015 and EC Decisions dated 22 Jan 2016, respectively; that concomitant use of riociguat with PDE5 inhibitors, including vardenafil, is contraindicated” Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 15.09.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1011** **Abseamed-EMEA/H/C/000727/WS1011/0057** **Binocrit-EMEA/H/C/000725/WS1011/0058** **Epoetin alfa**	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Hexal-EMEA/H/C/000726/WS1011/0056 MAH: SANDOZ GmbH, Lead PRAC Rapporteur: Claire Ferard, , “To update the RMP following the PRAC PSUR Assessment Report (EMEA/H/C/PSUSA/00001237/201508) dated 14 April 2016. PRAC requested the change in the risk classification for “hyperkalemia” and “hypersensitivity reactions (including anaphylactic reactions)” from important potential risks to important identified risks and the review of the table of safety concerns accordingly. Furthermore the MAH took the opportunity to update RMP to include changes related to the approval of the variation to add the subcutaneous route of administration in nephrology indications (EMEA/H/C/725-727/WS/0877) dated 31 Mar 2016. Appropriate minor updates of RMP have also been made as needed in order to reflect period covered since the last update of RMP (01 Sep 2015 until 29 Feb 2016).” Opinion adopted on 13.10.2016.	
PRAC Led **WS1015** **Ariclaim-EMEA/H/C/000552/WS1015/0065** **Cymbalta-EMEA/H/C/000572/WS1015/0069** **Duloxetine Lilly-EMEA/H/C/004000/WS1015/0005** **Xeristar-EMEA/H/C/000573/WS1015/0072** **Yentreve-EMEA/H/C/000545/WS1015/0055** MAH: Eli Lilly Nederland B.V., Duplicate, Duplicate of Yentreve, Lead Rapporteur: Aranzazu Sancho-Lopez, Lead PRAC Rapporteur: Dolores Montero Corominas, , “To update the RMP to add a new Observational Study to Assess Maternal and Fetal Outcomes Following Exposure to Duloxetine (F1J-MC-B057), and to update the plans for the existing pregnancy registry (F1JMC-B034) in section III.4.3 of the RMP.” Opinion adopted on 13.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1037** **Daliresp-EMEA/H/C/002398/WS1037/0029** **Daxas-EMEA/H/C/001179/WS1037/0033** **Libertek-EMEA/H/C/002399/WS1037/003**	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

0 MAH: Takeda GmbH, Lead PRAC Rapporteur: Dolores Montero Corominas, , “To update the due date for FUM 004 in the RMP for a phase 3 clinical study (study number: RO-2455-302-RD) from 'Q3 2016' to 'Q2 2017'.” Opinion adopted on 13.10.2016.	

B.5.5. CHMP-CAT assessed procedures

Glybera - alipogene tiparvovec - EMEA/H/C/002145/II/0056, Orphan, ATMP MAH: uniQure biopharma B.V., Rapporteur: Christiane Niederlaender, CHMP Coordinators: Greg Markey, Opinion adopted on 13.10.2016, 07.10.2016. Request for Supplementary Information adopted on 09.09.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - EMEA/H/C/003854/II/0001/G, Orphan, ATMP MAH: GlaxoSmithKline Trading Services, Rapporteur: Christiane Niederlaender, CHMP Coordinators: Robert James Hemmings, Opinion adopted on 13.10.2016, 07.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. 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

Cosentyx - secukinumab - EMEA/H/C/003729/II/0011 MAH: Novartis Europharm Ltd, Rapporteur: Tuomo Lapveteläinen Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 21.07.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0945/G Herceptin-EMEA/H/C/000278/WS0945/0115/G Kadcyla-EMEA/H/C/002389/WS0945/0026/G	Positive Opinion adopted by consensus on 22.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

MAH: Roche Registration Limited, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 22.09.2016.	
WS0970 **Infanrix hexa-EMEA/H/C/000296/WS0970/0203** MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren This WS also includes NAP products." Opinion adopted on 22.09.2016.	Positive Opinion adopted by consensus on 22.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0979 **Anoro-EMEA/H/C/002751/WS0979/0012** **Incruse-EMEA/H/C/002809/WS0979/0012** **Laventair-EMEA/H/C/003754/WS0979/0013** MAH: Glaxo Group Ltd, Lead Rapporteur: Nithyanandan Nagercoil Opinion adopted on 13.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0986 **Anoro-EMEA/H/C/002751/WS0986/0010** **Laventair-EMEA/H/C/003754/WS0986/0011** **Relvar Ellipta-EMEA/H/C/002673/WS0986/0024** **Revinty Ellipta-EMEA/H/C/002745/WS0986/0019** MAH: Glaxo Group Ltd, Lead Rapporteur: Nithyanandan Nagercoil Opinion adopted on 29.09.2016.	Positive Opinion adopted by consensus on 29.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0994 **Clopidogrel Zentiva-EMEA/H/C/000975/WS0994/0054** **Iscover-EMEA/H/C/000175/WS0994/0127** **Plavix-EMEA/H/C/000174/WS0994/0123** MAH: Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes Opinion adopted on 22.09.2016.	Positive Opinion adopted by consensus on 22.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0997/G **Silodyx-EMEA/H/C/001209/WS0997/0026/G** **Urorec-EMEA/H/C/001092/WS0997/0028/G** MAH: Recordati Ireland Ltd, Lead Rapporteur: Nithyanandan Nagercoil Opinion adopted on 29.09.2016.	Positive Opinion adopted by consensus on 29.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS0999/G **Silodyx-EMEA/H/C/001209/WS0999/0025/G** **Urorec-EMEA/H/C/001092/WS0999/0027/G** MAH: Recordati Ireland Ltd, Lead Rapporteur: Nithyanandan Nagercoil Opinion adopted on 29.09.2016.	Positive Opinion adopted by consensus on 29.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1008 **Harvoni-EMEA/H/C/003850/WS1008/0034** **Sovaldi-EMEA/H/C/002798/WS1008/0032** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Filip Josephson Opinion adopted on 06.10.2016.	Positive Opinion adopted by consensus on 06.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1018 **Helixate NexGen-EMEA/H/C/000276/WS1018/0179** **KOGENATE Bayer-EMEA/H/C/000275/WS1018/0186** MAH: Bayer Pharma AG, Duplicate, Duplicate of KOGENATE Bayer, Lead Rapporteur: Jan Mueller-Berghaus	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS1025 **Relvar Ellipta-EMEA/H/C/002673/WS1025/0026** **Revinty Ellipta-EMEA/H/C/002745/WS1025/0022** MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, “To update section 4.4 of the SmPC for FF/VI (Relvar/Revinty) 184/22 mcg strength following the conclusion of the Article 31 Referral (Procedure number: EMEA/H/A-31/1415) regarding pneumonia risk for `Inhaled corticosteroids containing medicinal products indicated in the treatment of chronic obstructive pulmonary disease' (PRAC recommendation March 2016; Commission Decision 29th June 2016) during which section 4.4 of the SmPC for FF/VI 92/22 mcg (Relvar/Revinty) was updated.” Opinion adopted on 13.10.2016.	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1032 **Abseamed-EMEA/H/C/000727/WS1032/0058** **Binocrit-EMEA/H/C/000725/WS1032/0059** **Epoetin alfa**	Positive Opinion adopted by consensus on 13.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Hexal-EMEA/H/C/000726/WS1032/0057 MAH: Hexal AG, Duplicate, Duplicate of Binocrit, Lead Rapporteur: Pierre Demolis, “To update the product Information to align it with the originator Eprex: sections 2, 4.2, 4.4, 5.1 and 5.2 of the SmPC have been updated as a consequence. The PI has been also updated accordingly. To update of the Instruction For Use (IFU) to include the additional statement (in blue) as minor change: “Instructions on how to inject yourself (for patients with symptomatic anaemia caused by kidney disease, for patients receiving chemotherapy or adult patients scheduled for orthopaedic surgery only).” To align the PI to the latest QRD template version 10. Minor typo and format corrections and an update of the Greek, French and Romanian local representatives for Binocrit only were included.” Opinion adopted on 13.10.2016.	

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

ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0135 MAH: Pfizer Limited, Rapporteur: Hanne Lomholt Larsen Withdrawal request submitted on 07.10.2016.	The MAH withdrew the procedure on 07.10.2016.
WS1038 **Epclusa-EMEA/H/C/004210/WS1038/0004** **Harvoni-EMEA/H/C/003850/WS1038/0037** **Sovaldi-EMEA/H/C/002798/WS1038/0035** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Filip Josephson Withdrawal request submitted on 13.10.2016.	The MAH withdrew the procedure on 13.10.2016.

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

Zinforo (EMEA/H/C/002252/II/0029), (ceftaroline fosamil), MAH: AstraZeneca AB, Rapporteur: Greg Markey, Procedure Manager: Rocio Gonzalo Ruiz, EPL: Radu Botgros, "Update of sections 4.2, 4.4 and 5.1 to amend the S.aureus breakpoints (Susceptible and Resistant). Consequently the package leaflet is amended." Request for Supplementary Information adopted on 21.07.2016.	The Committee adopted a revised timetable for Request for Supplementary information.

B.5.11. Worksharing variations according to Article 20 of Commission Regulation (EC) No 1234/2008 (listing intended submissions of type II variations for CAPs and NAPS with the outcome regarding the Lead Rapporteur)

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

- plitidepsin - EMEA/H/C/004354, Orphan Applicant: Pharma Mar, S.A., treatment of multiple myeloma	
- avelumab - EMEA/H/C/004338, Orphan Applicant: Merck Serono Europe Limited, treatment of Merkel cell carcinoma (MCC)	
- glibenclamide - EMEA/H/C/004379, Orphan Applicant: Pharma Services, treatment of neonatal diabetes	Accelerated review
- trastuzumab - EMEA/H/C/002575 , treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)	
- insulin glargine - EMEA/H/C/004280 , treatment of diabetes mellitus	
- nusinersen - EMEA/H/C/004312 , for the treatment of Spinal Muscular Atrophy (SMA).	Accelerated review
- beclometasone dipropionate anhydrous / formoterol / glycopyrronium bromide - EMEA/H/C/004257 , for the symptomatic treatment and reduction of exacerbations in adult patients with chronic obstructive pulmonary disease (COPD) with airflow limitation and who are at risk of exacerbation	
- simoctocog alfa - EMEA/H/C/004459	

, Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII
deficiency).
Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency)

- niraparib tosylate monohydrate - EMEA/H/C/004249

, Maintenance treatment of adult patients with platinum-sensitive recurrent high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer

- buprenorphine / naloxone - EMEA/H/C/004407

, treatment for opioid drug dependence

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

Benlysta - belimumab - EMEA/H/C/002015/X/0046/G

MAH: Glaxo Group Ltd, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel
Liminga“Line extension application for a new route of administration (subcutaneous use), new formulation (solution for injection) and new strengh of 200 mg.”

Exjade - deferasirox - EMEA/H/C/000670/X/0054, Orphan

MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, , “Extension application for a new pharmaceutical form (Exjade 90, 180 and 360 mg granules).”

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

- abaloparatide - EMEA/H/C/004157

treatment of osteoporosis
List of Questions adopted on 01.04.2016.

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

treatment of haemophilia A,
List of Questions adopted on 21.07.2016.

- fluciclovine (18F) - EMEA/H/C/004197

diagnostic agent for PET of adult men with suspected recurrence of prostate cancer,

List of Questions adopted on 28.04.2016.

Esbriet - pirfenidone - EMEA/H/C/002154/X/0035/G, Orphan

MAH: Roche Registration Limited, Rapporteur: Greg Markey, Co-Rapporteur: David Lyons, PRAC Rapporteur: Julie Williams,"Extension application to introduce a new pharmaceutical form associated with 3 new strengths (267mg, 534mg and 801mg film-coated tablets).

List of Questions adopted on 15.09.2016.

Ilaris - canakinumab - EMEA/H/C/001109/X/0045/G

MAH: Novartis Europharm Ltd, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Brigitte Keller-Stanislawski"Grouped application comprising an extension application covering an additional formulation (150 mg/ml solution for injection) and a type II variation (C.I.6.a) to add a new indication.

The proposed new indication is based on the results of the pivotal phase 3 study CACZ885N2301 and covers the treatment of adults and children of 2 years of age and older with one of the following Periodic Fever Syndromes:

- Tumour Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS);
- Hyperimmunoglobulin D Syndrome (HIDS) / Mevalonate Kinase Deficiency (MKD);
- Familial Mediterranean Fever (FMF) in patients in whom colchicine is contraindicated, is not tolerated, or does not provide an adequate response.

As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are proposed to be updated and the Package Leaflet is proposed to be updated accordingly. In addition, the annexes have been aligned with the latest QRD template v.10. A revised RMP version 11 was provided as part of the application."

List of Questions adopted on 15.09.2016.

- ivabradine - EMEA/H/C/004241

treatment of angina pectoris,

List of Questions adopted on 01.04.2016.

- pemetrexed - EMEA/H/C/004488

treatment of malignant pleural mesothelioma and non-small cell lung cancer ,

List of Questions adopted on 21.07.2016.

- vosaroxin - EMEA/H/C/004118, Orphan
Applicant: Sunesis Europe Ltd, treatment acute myeloid leukaemia,
List of Questions adopted on 28.04.2016.

- padeliporfin - EMEA/H/C/004182
, treatment of prostate cancer,
List of Questions adopted on 26.05.2016.

- tofacitinib - EMEA/H/C/004214
treatment of active rheumatoid arthritis,
List of Questions adopted on 21.07.2016.

- human IgG1 monoclonal antibody specific for human interleukin-1 alpha - EMEA/H/C/004388
treatment of metastatic colorectal cancer,
List of Questions adopted on 21.07.2016.

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

Glybera - alipogene tiparvovec - EMEA/H/C/002145/S/0057, Orphan, ATMP
MAH: uniQure biopharma B.V., Rapporteur: Christiane Niederlaender, PRAC Rapporteur: Julie Williams

Ilaris - canakinumab - EMEA/H/C/001109/S/0047
MAH: Novartis Europharm Ltd, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Orphacol - cholic acid - EMEA/H/C/001250/S/0016, Orphan
MAH: LABORATOIRES CTRS - BOULOGNE BILLANCOURT, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Rafe Suvarna

Raxone - idebenone - EMEA/H/C/003834/S/0005, Orphan
MAH: Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Carmela Macchiarulo

Vedrop - tocofersolan - EMEA/H/C/000920/S/0019
MAH: Orphan Europe S.A.R.L., Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams

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

Bosulif - bosutinib -
EMEA/H/C/002373/R/0023, Orphan
MAH: Pfizer Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber

Fycompa - perampanel -
EMEA/H/C/002434/R/0035
MAH: Eisai Europe Ltd., Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams

Jentadueto - linagliptin / metformin -
EMEA/H/C/002279/R/0036
MAH: Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst

Kalydeco - ivacaftor -
EMEA/H/C/002494/R/0052, Orphan
MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas

Siklos - hydroxycarbamide -
EMEA/H/C/000689/R/0030, Orphan
MAH: Addmedica, Rapporteur: Koenraad Norga, Co-Rapporteur: Dimitrios Kouvelas, PRAC Rapporteur: Jean-Michel Dogné

Zyclara - imiquimod -
EMEA/H/C/002387/R/0012
MAH: Meda AB, Rapporteur: Nithyanandan Nagercoil

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

Gazyvaro - obinutuzumab -
EMEA/H/C/002799/II/0016, Orphan
MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Julie Williams, “Extension of Indication to include a new indication for Gazyvaro in combination with chemotherapy, followed by Gazyvaro maintenance therapy in patients achieving a response, for the treatment of patients with previously untreated advanced follicular lymphoma.

As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and the RMP are updated in accordance. In addition, the due date for provision of the final clinical study report of study BO21223/GALLIUM listed in the Gazyvaro RMP as Category 3 has been updated. Furthermore, the PI is brought in line with the missing information of QRD template version 9.1 regarding annex II C. In addition, clarification or editorial changes to the SmPC are proposed for accuracy and clarity." Request for 1 year of market protection for a new indication (Article 10(5) of Directive 2001/83/EC)	
Harvoni - sofosbuvir / ledipasvir - EMEA/H/C/003850/II/0039 MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Margarida Guimarães, "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."	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0014 MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus, "Extension of Indication to include the treatment of classical Hodgkin Lymphoma (cHL) in adults who have refractory disease, or who have relapsed after greater than 3 prior lines of therapy, based on the results from study KEYNOTE-087, an open-label Phase II trial of pembrolizumab in subjects with relapsed or refractory cHL and study KEYNOTE-013, a Phase Ib multi-cohort trial of pembrolizumab in subjects with hematologic malignancies. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated and the Package Leaflet is updated accordingly. An updated RMP version 5.0 was provided as part of the application."	
Orencia - abatacept - EMEA/H/C/000701/II/0105	

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, “Extension of Indication to include a new indication for Orencia: treatment of psoriatic arthritis in adults.
As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are proposed to be updated. The Package Leaflet is updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.
A revised RMP was included in this submission (version 21).”

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Ixiaro - japanese encephalitis vaccine (inactivated, adsorbed) - EMEA/H/C/000963/II/0083
MAH: Valneva Austria GmbH, Rapporteur: Jan Mueller-Berghaus

Opdivo - nivolumab - EMEA/H/C/003985/II/0022/G
MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez

Praluent - alirocumab - EMEA/H/C/003882/II/0014/G
MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege

Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0147/G
MAH: Pfizer Limited, Rapporteur: Kristina Dunder

Prezista - darunavir - EMEA/H/C/000707/II/0083/G
MAH: Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0110
MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus,

Repatha - evolocumab - EMEA/H/C/003766/II/0012
MAH: Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege

Savene - dexrazoxane - EMEA/H/C/000682/II/0031, Orphan

MAH: Clinigen Healthcare Ltd, Rapporteur: Pierre Demolis

Simponi - golimumab - EMEA/H/C/000992/II/0071/G
MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder

Soliris - eculizumab - EMEA/H/C/000791/II/0088/G, Orphan
MAH: Alexion Europe SAS, Rapporteur: Aranzazu Sancho-Lopez

Soliris - eculizumab - EMEA/H/C/000791/II/0089, Orphan
MAH: Alexion Europe SAS, Rapporteur: Aranzazu Sancho-Lopez

WS1003
HyQvia-EMEA/H/C/002491/WS1003/0031
Kiovig-EMEA/H/C/000628/WS1003/0075
MAH: Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus

WS1061/G
Humalog-EMEA/H/C/000088/WS1061/0151/G
Liprolog-EMEA/H/C/000393/WS1061/0115/G
MAH: Eli Lilly Nederland B.V., Lead Rapporteur: Robert James Hemmings

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

Arzerra - ofatumumab - EMEA/H/C/001131/II/0048, Orphan
MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, “Submission of final clinical study of the study OMB115991: 'A Phase II, Multi-Centre Study Investigating the Safety and Efficacy of Ofatumumab Plus Bendamustine in Patients with Untreated or Relapsed CLL'. With the present submission, no changes to the product information are proposed.”

Fycompa - perampanel - EMEA/H/C/002434/II/0034/G
MAH: Eisai Europe Ltd., Rapporteur: Robert James Hemmings“Update of sections 4.5 and 5.1 of the SmPC in order to add information on the conversion of patients to Fycompa monotherapy (E2007-G000-504, hereby Study 504) and to include the effect of withdrawal of concomitant

enzyme-inducing antiepileptic drugs (EIAEDs) on plasma concentrations of perampanel (A supportive analysis, CPMS-E2007-0013R). In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10."	
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"	
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."	
Ivemend - fosaprepitant - EMEA/H/C/000743/II/0034/G MAH: Merck Sharp & Dohme Limited, Rapporteur: Filip Josephson"C.I.4 - Update of sections 5.1 and 5.2 of the SmPC in order to include pharmacodynamic and pharmacokinetic data relevant to the paediatric population. C.I.4 - Update of sections 5.3 of the SmPC in order to include non-clinical data relevant to the paediatric population. The Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0."	
Levemir - insulin detemir - EMEA/H/C/000528/II/0082 MAH: Novo Nordisk A/S, Rapporteur: Hanne Lomholt Larsen, "Update of sections 4.4 of the SmPC with additional information regarding avoidance of accidental mix-ups and medication errors. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 9.1 and 10.0 and to correct a mistake in the recommendation for use of the first of the two	

titration algorithms in section 4.2 of the SmPC."

NovoMix - insulin aspart -
EMEA/H/C/000308/II/0087
MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, , "Update of section 4.4 of the SmPC to include a warning on the risk of medication errors. The package leaflet 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."

Orkambi - lumacaftor / ivacaftor -
EMEA/H/C/003954/II/0014
MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil, "Update of section 5.3 of the SmPC in order to revise the ivacaftor animal:human exposure ratio. The Package Leaflet is updated accordingly."

Otezla - apremilast -
EMEA/H/C/003746/II/0011
MAH: Celgene Europe Limited, Rapporteur: Patrick Salmon, "Submission of study report CC-10004-PSOR-010; a Phase 3b, multicenter, randomized, placebo-controlled, double-blind, double-dummy, study of the efficacy and safety of apremilast (CC-10004), etanercept, and placebo, in subjects with moderate to severe plaque psoriasis. The submission of this clinical study report fulfils PAM EMEA/H/C/003746/MEA/003."

Pradaxa - dabigatran etexilate -
EMEA/H/C/000829/II/0097
MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen, "Submission of final study report of study 1160.173 "A prospective, open label study to evaluate the pharmacokinetics of dabigatran in non-valvular atrial fibrillation (NVAF) patients with severely impaired renal function on dabigatran etexilate 75 mg BID therapy"."

Rapamune - sirolimus -
EMEA/H/C/000273/II/0163/G
MAH: Pfizer Limited, Rapporteur: Kristina Dunder"Update of section 4.4 of the SmPC to update the current warning on angioedema to include a possible dose-dependent effect between sirolimus and angioedema based on post-marketing data. Update of section 4.8 of the

SmPC to include neuroendocrine carcinoma of the skin and malignant carcinoma as new ADRs and to includesquamous cell carcinoma of the skin and basal cell carcinoma as part of the ADR 'skin cancer' based on post-marketing data. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to combine the 0.5 mg, 1 mg and 2 mg tablets SmPC, to fully detail all components of the Rapamune printing ink in section 6.1 of the SmPC and in the Package Leaflet, to align the wording in section 4 of the Package Leaflet with section 4.8 of the SmPC regarding Clostridium difficile, to update the list of local representatives for the Czech republic, Norway and Sweden in the Package Leaflet and to bring the PI in line with the latest QRD template version 10."	
Revestive - teduglutide - EMEA/H/C/002345/II/0032, Orphan MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Sinan B. Sarac, "Update of sections 4.3, 4.4, and 4.8 of the SmPC in order to update the safety information in line with updated CCDS following review of the MAH's safety database. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in section 5.1 of the SmPC."	
Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0025 MAH: AbbVie Ltd., Rapporteur: Filip Josephson, "Update of sections 4.3 and 4.5 of the SmPC to add three additional contraindication medications with dronedarone, lurasidone and ranolazine. The Package Leaflet is updated accordingly."	
Vimpat - lacosamide - EMEA/H/C/000863/II/0066/G MAH: UCB Pharma S.A., Rapporteur: Filip JosephsonUpdate of section 4.2 of the SmPC in order to update the safety information regarding the use of lacosamide in patients with hepatic impairment, section 4.8 to add a new adverse drug reaction (hepatic enzyme increased (> 2x ULN)) and section 4.9 regarding lacosamide overdose based on postmarketing reports. 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 and to make minor editorial change in the SmPC."

Zydelig - idelalisib -
EMEA/H/C/003843/II/0029
MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, "Submission of the final study report for the clinical study 101-07 "A Phase I Study To Investigate the Safety and Clinical Activity of Idelalisib in Combination with Chemotherapeutic Agents, Immunomodulatory Agents and Anti-CD-20 mAb in Subjects with Relapsed or Refractory Indolent B-cell Non-Hodgkin Lymphoma, Mantle Celle Lymphoma or Chronic Lymphocytic Leukemia", in order to fulfil of the Post Approval Measure (PAM) MEA 009 for Zydelig."

WS1019
Clopidogrel
Zentiva-EMEA/H/C/000975/WS1019/0055
Clopidogrel/Acetylsalicylic acid
Zentiva-EMEA/H/C/001144/WS1019/0047
DuoPlavin-EMEA/H/C/001143/WS1019/0046
Iscover-EMEA/H/C/000175/WS1019/0128
Plavix-EMEA/H/C/000174/WS1019/0124
MAH: Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC in order to add Kounis syndrome as a new ADR. The Package Leaflet is updated accordingly. In addition the Worksharing applicant (WSA) took the opportunity to make minor amendments to Annex II for Clopidogrel Zentiva, Iscover and Plavix, to update the contact details of the Italian, Hungarian and Lithuanian local representatives in the Package Leaflet for Clopidogrel Zentiva, Iscover and Plavix, to combine the two strengths SmPCs for all the products involved in this Worksharing application, to combine the two strengths Package Leaflet for DuoPlavin and Clopidogrel/Acetylsalicylic acid Zentiva. Furthermore, the PI is brought in line with the latest QRD template version 10."

WS1020
Clopidogrel/Acetylsalicylic acid
Zentiva-EMEA/H/C/001144/WS1020/0046
DuoPlavin-EMEA/H/C/001143/WS1020/0045
MAH: Sanofi Clir SNC, Lead Rapporteur: Bruno

Sepodes, “Update of sections 4.4 and 4.5 of the SmPC in order to add a new drug-drug interaction between nicorandil and NSAIDs including acetylsalicylic acid (ASA) and lysine-acetylsalicylate (LAS) and its increased risk for severe complications including gastrointestinal ulceration, perforation and haemorrhage. The Package Leaflet is updated accordingly. In addition the Worksharing applicant (WSA) took the opportunity to make a minor correction in Annex II (typographical change).”	
WS1034 **Descovy-EMEA/H/C/004094/WS1034/0007** **Genvoya-EMEA/H/C/004042/WS1034/0021** **Odefsey-EMEA/H/C/004156/WS1034/0005** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, “Update of section 4.5 of the SmPC with new pharmacology date from the final Study GS-US-311-1790.”	
WS1045 **Entresto-EMEA/H/C/004062/WS1045/0008** **Neparvis-EMEA/H/C/004343/WS1045/0006** MAH: Novartis Europharm Ltd, Lead Rapporteur: Johann Lodewijk Hillege, “Submission of study no. 1570187: Effect of LBQ657 on cloned hERG potassium channels expressed in human embryonic kidney cells. No changes to PI has been proposed.”	

B.6.10. CHMP-PRAC assessed procedures

Aluvia - lopinavir / ritonavir - EMEA/H/W/000764/II/0100 MAH: AbbVie Ltd., Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard, “Update of sections 4.2 and 5.1 of the SmPC in order to update information following analysis of the published 48-week study results for “A Kaletra ONCE daily randomised Trial of the pharmacokinetics, safety and efficacy of twice-daily versus once-daily lopinavir/ritonavir tablets dosed by weight as part of combination antiretroviral therapy in HIV-1–infected	

children"(PENTA 18/KONCERT) in fulfilment of a Post Authorisation Measure MEA (Additional PhV activity in the Risk Management Plan). In addition, the SOH takes the opportunity to remove the Missing Information safety concern of Limited Information of the Kaletra 100 mg/25 mg film-coated tablets in the paediatric population as part of the submitted RMP version 8."	
Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0085 MAH: GSK Biologicals SA, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné, "Submission of Study EPI-HPV-069, a meta-analysis assessing the risk of three autoimmune diseases following vaccination with Cervarix: autoimmune thyroiditis (AIT), Guillain-Barre Syndrome (GBS) and Inflammatory Bowel Disease (IBD). The EPI-HPV-069 study is a post-licensure commitment to the EMA (PASS register number EUPAS13332). As part of this submission, an updated RMP (version 18) is provided, including changes related to the EPI-HPV-069 meta-analysis submitted and minor updates related to other studies."	
Epclusa - sofosbuvir / velpatasvir - EMEA/H/C/004210/II/0003 MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Margarida Guimarães, "Update of sections 4.4, 4.5 and 5.1 of the SmPC in order to reflect on emerging clinical data from study GS-US-342-1202 investigating efficacy andsafety in subjects with chronic hepatitis C virus (HCV) and human immunodeficiency virus (HIV)-1 coinfection. In addition, minor administrative changes are implemented throughout the Product Information."	
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 and update in the due date for the prospective observational cohort study of Flixabi in AS (Ankylosing Spondylitis) and CD (Crohn's Disease) patients."

Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0061
MAH: MedImmune LLC, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.3 and 4.8 of the SmPC to reflect that Fluenz Tetra is contraindicated only in children with severe hypersensitivity to eggs (instead of all children with egg allergy), and to update the safety information (update of the number of children and adolescents in the safety database). The PIL is amended accordingly.
The RMP is updated to implement administrative changes to the high level description on Enhanced Safety Surveillance, and to change the milestones for study MA-VA-MEDI3250-1116."

Imbruvica - ibrutinib - EMEA/H/C/003791/II/0029, Orphan
MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams, "Update of sections 4.5 of the SmPC to remove the statement that an interaction between products increasing stomach pH and ibrutinib have not been studied and section 5.2 to include the findings from study CLL1005. The Package Leaflet is not impacted by these changes.
In addition, the RMP is updated to version 6.3 to reflect this new safety information."

Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0027/G
MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver"C.I.4 (Type II): Submission of the final study report for the study TDM4997g/BO25734 (TH3RESA tudy) to address the safety concerns in Left Ventricular Dysfunction and Safety in

Elderly patients. The RMP and Annex II.D are updated. C.I.11.z (Type IB): To update the RMP following the submission of the third annual report of study H4621g. The MAH takes the opportunity to implement the following administrative changes to the RMP: - Inclusion of standard post-authorization data based on PSUR number 4 (reporting period from 22 February 2015 to 21 February 2016). - Change of Herceptin picture in the Kadcyla Educational Material to align the picture with the recently approved version of the Herceptin vial label and carton.”	
Kaletra - lopinavir / ritonavir - EMEA/H/C/000368/II/0160 MAH: AbbVie Ltd., Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard, “Update of sections 4.2 and 5.1 of the SmPC in order to update information following analysis of the published 48-week study results for “A Kaletra ONCE daily randomised Trial of the pharmacokinetics, safety and efficacy of twice-daily versus once-daily lopinavir/ritonavir tablets dosed by weight as part of combination antiretroviral therapy in HIV-1–infected children”(PENTA 18/KONCERT) in fulfilment of a Post Authorisation Measure MEA (Additional PhV activity in the Risk Management Plan). In addition, the MAH takes the opportunity to remove the Missing Information safety concern of Limited Information of the Kaletra 100 mg/25 mg film-coated tablets in the paediatric population as part of the submitted RMP version 8.”	
Lyxumia - lixisenatide - EMEA/H/C/002445/II/0020 MAH: Sanofi-Aventis Groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, “Submission of the final clinical study report for study EFC12382, a randomized double-blind, placebo-controlled, 2 arm parallel group, multicentre study with a 24-week treatment period to assess the efficacy and safety of lixisenatide in patients with T2DM insufficiently controlled with basal insulin or without metformin, in order to fulfil MEA 004. In addition the MAH took the opportunity to update the RMP (version 4.0) accordingly.”	
Plegridy - peginterferon beta-1a -	

EMEA/H/C/002827/II/0031/G

MAH: Biogen Idec Ltd, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams“II: C.I.4 Update of section 4.8 of the SmPC with data on exposure and section 5.1 of the SmPC with information on maintenance of long-term efficacy based on clinical study data (study ATTAIN)
II: C.I.4 Update of section 4.8 of the SmPC in order to add information concerning the onset and duration of flu-like symptoms based on clinical study data (study ALLOW). The Package Leaflet is updated accordingly.”

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.”

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."

Reyataz - atazanavir / atazanavir sulfate - EMEA/H/C/000494/II/0105/G

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard"Scope C.I.4
Update of section 4.6 of the SmPC in order to update the safety information on lactation to indicate that atazanavir has been detected in human milk. The Package Leaflet and the RMP are updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.
Scope C.I.11.b
This type II variation aims to update the RMP in order to add "IRIS" and "angioedema" to Important Identified Risks and to update the epidemiology/exposure sections. The MAH also took the opportunity to make some reformatting changes to align the RMP with the current approved EMA template."

Tagrisso - osimertinib - EMEA/H/C/004124/II/0009/G

MAH: AstraZeneca AB, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Sabine Straus"Update of SmPC sections 4.2, 4.4, 4.8, 5.1 and 5.2 based on the results from study D5160C00003 (AURA3) and the updated CSRs for studies D5160C00001 (AURAex) and D5160C00002 (AURA2). The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make editorial changes in the SmPC and Package Leaflet.
The application included an updated RMP version 6.0.
The provision of the CSR from study AURA3 addresses the Specific Obligation for Tagrisso and hence the MAH requests the conversion from a Conditional Marketing
Authorisation to a Marketing Authorisation not subject to Specific Obligations."

Tasigna - nilotinib - EMEA/H/C/000798/II/0087, Orphan

MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver,

“Submission of the final CSR from the clinical drug-drug interaction study CAMN107A2132. An updated RMP version 17 was included as part of the application.”	
Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0035 MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, “To update section 4.8 (Undesirable effects) of the SmPC under the sub-heading 'Tabulated summary of adverse reactions', to include 'liver function abnormalities' as an adverse event, observed in the post-marketing setting, and under the sub-heading 'Hepatic transaminases' to clarify events not observed in placebo-controlled studies. The package leaflet has been updated accordingly (section 4 under heading 'Possible side effects'). The MAH has also taken the opportunity to make minor administrative changes in the package leaflet and to review and update the status timelines of clinical and nonclinical study reports in the Risk Management Plan (v8).”	
Torisel - temsirolimus - EMEA/H/C/000799/II/0064, Orphan MAH: Pfizer Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, “Update of section 4.5 of the SmPC in order to add drug-drug interaction information based upon the PK analysis of Study 3066K1-148-US and supportive literature. The Package Leaflet is updated accordingly.”	
Zelboraf - vemurafenib - EMEA/H/C/002409/II/0037 MAH: Roche Registration Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, “Update of section 4.5 of the SmPC in order to include information on Drug-drug interaction with rifampicin. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the RMP and to request modification of MEA 011 part 2 “Study GO29475: Two-part steady-state interaction study with and rifampin (3YP3A4 inducer). Furthermore the MAH is requesting change of due dates for category 3 final study reports for studies GO29475 (MEA011), MO25515 (MEA006) and GP28492 (MEA010). The MAH is also including request for deletion	

from the RMP of the study “Phase I dose-escalation with efficacy tail extension study of vemurafenib in pediatric patients with surgically incurable and unresectable Stage IIIC or Stage IV melanoma harboring BRAFV600 mutations (MEA 005)” to reflect the Paediatric Product Specific Waiver for treatment of melanoma as agreed with the PDCO on 24 April 2016.”

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: 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.”

B.6.11. PRAC assessed procedures

PRAC Led
Eperzan - albiglutide -
EMEA/H/C/002735/II/0028/G
MAH: GlaxoSmithKline Trading Services, PRAC Rapporteur: Julie Williams, “II: C.I.11.b - Submission of a revised RMP in order to introduce the additional risk minimisation measures addressing the important potential risk of medication errors. Annex II of the Product Information is updated accordingly.
II: C.I.11.b – Update of the RMP to add a new category 3 study as an additional pharmacovigilance activity - Study 204879: A Randomized, Open-label, Active-Controlled, Parallel-Group, Exploratory Study on the Effects of Repeated Doses of Albiglutide compared to Exenatide on Gastric Myoelectrical Activity and Gastric Emptying in Subjects with Type 2 Diabetes Mellitus
II: C.I.11.b - Update of the RMP to add a new

category 3 study as an additional pharmacovigilance activity – Study 201840 - An Exploratory Randomized, 2-Part, Single-blind, 2-Period Crossover Study Comparing the Effect of Albiglutide with Exenatide on Regional Brain Activity Related to Nausea in Healthy Volunteers II: C.I.11.b – Update of the RMP to add a new category 3 study as an additional pharmacovigilance activity – Cross-sectional survey to assess the effectiveness of the proposed additional educational materials using Patient Connect”	
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 from a phase 3 study, E7389-A001-303 (ACCRU) to an observational study, E7389-M044-504 (IRENE). The submission of the corresponding study report to the EMA / PRAC remains unchanged and is planned during 2019.”	
PRAC Led **Inflectra - infliximab -** **EMEA/H/C/002778/II/0047** MAH: Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna, , “Update of the RMP (v 7.0) to merge the RMPs for Remsima and Inflectra.”	
PRAC Led **Lyxumia - lixisenatide -** **EMEA/H/C/002445/II/0019** MAH: Sanofi-Aventis Groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, , “Submission of the final clinical study report for a non-interventional PASS: a retrospective database study of GLP-1 receptor agonists and risk of acute pancreatitis, pancreatic cancer and thyroid cancer in particular medullary thyroid cancer, a category 3 study in order to fulfil MEA 007.2”	
PRAC Led	

Rapiscan - regadenoson -
EMEA/H/C/001176/II/0023
MAH: Rapidscan Pharma Solutions EU Ltd., Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, , “Submission of study report 01-1-401 to assess the safety profile of Rapiscan (regadenoson) in patients with liver impairment and to observe common adverse events reported in the post marketing setting.”

PRAC Led
Remsima - infliximab -
EMEA/H/C/002576/II/0039
MAH: Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna, , “Update of the RMP (v 7.0) to merge the RMPs for Remsima and Inflectra.”

PRAC Led
Thymanax - agomelatine -
EMEA/H/C/000916/II/0031
MAH: Servier (Ireland) Industries Ltd., Duplicate, Duplicate of Valdoxan, Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Kristin Thorseng Kvande, , “Submission of the final study report for study CLE-20098-095: ‘HLA alleles as genetic risk factors for elevation of aminotransferase levels in patients treated with agomelatine’. The product information and RMP are not impacted by this change.”

PRAC Led
Thyrogen - thyrotropin alfa -
EMEA/H/C/000220/II/0088
MAH: Genzyme Europe BV, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner, , “To transfer the RMP to the latest RMP template. As a consequence, gastrointestinal symptoms, constitutional symptoms, and injection site reactions have been downgraded to identified risks, not categorized as important and therefore have been deleted. In addition, “perceived lower TSH elevation after thyrotropin alfa administration” does not correspond to a safety risk for the patients treated with Thyrogen and was also deleted from the list of important potential risks.
Finally, study results and completion date of T4 study have been included and as a consequence, "Use of Thyrogen for remnant ablation in patients originally diagnosed with T4N0-1M0-1 thyroid cancer" was removed from the missing

information section.
RMP version 9.0 is being submitted."

PRAC Led
Valdoxan - agomelatine -
EMEA/H/C/000915/II/0033
MAH: Les Laboratoires Servier, Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Kristin Thorseng Kvande, , "Submission of the final study report for study CLE-20098-095: 'HLA alleles as genetic risk factors for elevation of aminotransferase levels in patients treated with agomelatine'.
The product information and RMP are not impacted by this change."

PRAC Led
Zypadhera - olanzapine -
EMEA/H/C/000890/II/0032
MAH: Eli Lilly Nederland B.V., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, , "Submission of the final study report of the PASS: Post-Injection Syndrome in Patients with Schizophrenia Receiving
Olanzapine Long-Acting Injection.
The Risk Management Plan (version 12) has been revised to reflect the results of the study."

PRAC Led
WS1028
Relvar
Ellipta-EMEA/H/C/002673/WS1028/0027
Revinty
Ellipta-EMEA/H/C/002745/WS1028/0023
MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, , "Submission of study HZA107112 (A randomised, double-blind, two-way crossover study to investigate the effect of inhaled fluticasone furoate on short-term lower-leg growth in paediatric subjects with asthma), a post-authorization safety study (PASS) (Category 3) within the EU-RMP to investigate the important potential risk of growth retardation in children.
This study was conducted as part of the Paediatric Investigational Plan (EMEA-000431-PIP01-08).
In addition, the due date for study 205052 is amended in the RMP version 8.2 submitted."

PRAC Led
WS1063

Exviera-EMEA/H/C/003837/WS1063/0022
Viekirax-EMEA/H/C/003839/WS1063/0027

MAH: AbbVie Ltd., Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Dolores Montero Corominas, , "To update the RMP for Exviera and Viekirax with the following chnages:
1. The addition of information on cases of hepatic decompensation observed in patients with Child-Pugh B hepatic impairment, and the revision of the SmPC to change the dose recommendation of these patients to "not recommended", as well as the addition of statements recommending the monitoring of hepatic function in these patients as approved on 25 January 2016 ((Ref: EMEA/H/C/WS/0873).
2. Addition of a reference to nine drug-drug interaction studies as approved on 28 April 2016 (Ref: EMEA/H/C/WS0896/G).
3. Reference to the completion of rat 2 year carcinogenicity studies on dasabuvir (Exviera) and ombitasvir (Viekirax) as approved on 24 September 2015 (Ref: EMEA/H/C/003837/II/0006 and EMEA/H/C/003839/II/0004).
4. Update of section 4.2 of SmPC for Virkirax to recommend a decrease in treatment duration of 12 weeks in GT4 cirrhotic patients, with a consequential change to sections 4.4 and 5.1 as approved on 18 August 2016 (Ref: EMEA/H/C/003839/II/0022/G).
5. Removal of the nonclinical PAMS 1-3 in the initial RMP, (Ref: EMEA/H/C/03837/MEA/003, EMEA/H/C/038397/MEA/002, EMEA/H/C/03839/MEA/003)."

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

WS0989
M-M-RVAXPRO-EMEA/H/C/000604/WS0989/0077
ProQuad-EMEA/H/C/000622/WS0989/0111

MAH: Sanofi Pasteur MSD SNC, Lead Rapporteur: Jan Mueller-Berghaus

WS1007 **Ambirix-EMEA/H/C/000426/WS1007/0081** **Fendrix-EMEA/H/C/000550/WS1007/0056** **Infanrix hexa-EMEA/H/C/000296/WS1007/0209** **Twinrix Adult-EMEA/H/C/000112/WS1007/0115** **Twinrix Paediatric-EMEA/H/C/000129/WS1007/0116** MAH: GlaxoSmithKline Biologicals, Lead Rapporteur: Bart Van der Schueren	
WS1016/G **Aclasta-EMEA/H/C/000595/WS1016/0067/G** **Zometa-EMEA/H/C/000336/WS1016/0076/G** MAH: Novartis Europharm Ltd, Lead Rapporteur: Sinan B. Sarac	
WS1052 **Entresto-EMEA/H/C/004062/WS1052/0009** **Neparvis-EMEA/H/C/004343/WS1052/0007** MAH: Novartis Europharm Ltd, Lead Rapporteur: Johann Lodewijk Hillege	
WS1054 **Humalog-EMEA/H/C/000088/WS1054/0149** **Liprolog-EMEA/H/C/000393/WS1054/0113** MAH: Eli Lilly Nederland B.V., Lead Rapporteur: Robert James Hemmings“To update sections 1, 2.2, 4.2, 4.4, 5.1, 6.6 of the SmPC with minor amendments, e.g. to change “u/ml” to “units/ml”. The package leaflet and labelling were updated accordingly and minor editorial changes were also included in annex II. In addition a newly formatted user manual for insulin lispro KwikPen 100 units/ml was introduced. The new format aims to present the information related to the operating the pen in a simpler manner and to reduce the repetition of information as compared to the previous version.”	

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

B.7.1. Line listing for Variation Type I and Variation Type II (MMD only) post authorisation procedures from the beginning of the year.

B.7.2. Line listing overview of all applications under the centralised procedure (MMD only). line listing - products - authorised, under evaluation, suspended.xls

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 10-13 October 2016 CHMP plenary:

1.	ATMP; Hematopoietic reconstitution of patients who are medically indicated for allogeneic hematopoietic stem cell transplantation	The CHMP denied eligibility to PRIME and adopted the critical summary report.
2.	Treatment of patients with advanced or metastatic ALK-positive NSCLC resistant or refractory to one or more prior ALK inhibitor therapies	The CHMP denied eligibility to PRIME and adopted the critical summary report.
3.	In combination with a hypomethylating agent (HMA) for the frontline treatment of patients with acute myeloid leukaemia (AML) who are not candidates for intensive induction therapy	The CHMP denied eligibility to PRIME and adopted the critical summary report.
4.	Treatment of paroxysmal nocturnal haemoglobinuria	The CHMP denied eligibility to PRIME and adopted the critical summary report.
5.	Allogeneic Epstein-Barr virus-specific cytotoxic T lymphocytes (ATA129)ATMP; Treatment of patients with Epstein-Barr Virus-associated Post Transplant Lymphoproliferative Disorder in the allogeneic hematopoietic cell transplant setting who have failed on rituximab.	The CHMP granted eligibility to PRIME and adopted the critical summary report.
6.	Treatment of Type 1 Diabetes with Residual Beta Cell Function	The CHMP denied eligibility to PRIME and adopted the critical summary report.
7.	MBX-8025; Treatment of Primary Biliary Cholangitis (PBC)	The CHMP granted eligibility to PRIME and adopted the critical summary report.
8.	A4250; Treatment of Progressive Familial Intrahepatic Cholestasis (PFIC).	The CHMP granted eligibility to *PRIME at the proof of principle stage* and adopted the critical summary report.
9.	Relief of pain and improvement of joint function in osteoarthritis of the knee	The CHMP denied eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in September 2016 for November 2016 CHMP adoption of outcomes

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