28 November 2018
EMA/CHMP/821741/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Minutes of the meeting on 15-18 October 2018

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified as included in the list of participants and restrictions. See (current) October 2018 CHMP minutes for the list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session held 15-18 October 2018 (to be published post November 2018 CHMP meeting).

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

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

The CHMP noted a new alternate member Marcin Kolakowski from Poland.

1.2. Adoption of agenda

CHMP agenda for 15-18 October 2018

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 17-20 September 2018.

The CHMP adopted the CHMP minutes for 17-20 September 2018. The Minutes of the October 2018 CHMP ORGAM meeting held on 8 October 2018, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. Bevespi Aerosphere - glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004245

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

Scope: Oral explanation

Action: Oral explanation to be held on 16 October 2018 at time 09:00

Fixed combination application (Article 10b of Directive No 2001/83/EC)

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

The CHMP agreed that no oral explanation is needed this time.

See 3.1

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

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

Scope: Possible oral explanation

Action: Possible oral explanation to be held on 16 October 2018 at time 11:00

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

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

The CHMP agreed that no oral explanation is needed this time.

See 3.1

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Caprelsa - vandetanib - EMEA/H/C/002315/II/0028

Genzyme Europe BV

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: Oral explanation to be held on 16 October 2018 at time 16:00

Action: For adoption
Request for Supplementary Information adopted on 26.04.2018, 14.12.2017.

The CHMP agreed that no oral explanation is needed this time.

See 9.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Bevespi Aerosphere - glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004245

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

Scope: Opinion

Action: For adoption

Fixed combination application (Article 10b of Directive No 2001/83/EC)

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

See 2.1

The CHMP agreed that no oral explanation is needed this time.

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

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (27 positive out of 31 votes) together with the CHMP assessment report and translation timetable.

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

The divergent position (Martina Weise, Johann Lodewijk Hillege, Jan Mueller-Berghaus, Alexandre Moreau) was appended to the opinion.

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

The summary of opinion was circulated for information.

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

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

Scope: Possible oral explanation

Action: Possible oral explanation to be held on 16 October 2018 at time 11:00

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

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

The CHMP agreed that no oral explanation is needed this time.

See 2.1

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

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (30 positive out of 33 votes) together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that dengue tetravalent vaccine (live, attenuated) is a new active substance, as claimed by the applicant.

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

The divergent position (Bart van der Schueren, Koenraad Norga, Bruno Sepodes) was appended to the opinion.

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

The summary of opinion was circulated for information.

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

Seqirus Netherlands B.V.; prophylaxis of influenza in adults and children from 9 years of age

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 22.03.2018.

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

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

timetable.

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 9 October 2018.

The summary of opinion was circulated for information.

3.1.4. Namuscla - mexiletine hcl - Orphan - EMEA/H/C/004584

Lupin Europe GmbH; Treatment of non-dystrophic myotonic disorders

Scope: Opinion

Action: For adoption

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

Oral explanation held on 18.09.2018. List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

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

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

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

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

The CHMP noted the letter of recommendations dated 17 October 2018.

The summary of opinion was circulated for information.

3.1.5. Ogivri - trastuzumab - EMEA/H/C/004916

MYLAN S.A.S; treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)

Scope: Opinion

Action: For adoption

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

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

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

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

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

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

The summary of opinion was circulated for information.

3.1.6. TAKHZYRO - lanadelumab - Orphan - EMEA/H/C/004806

Accelerated assessment

Shire Pharmaceuticals Ireland Limited; treatment of angioedema attacks, prevention of angioedema attacks

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 18.09.2018. List of Questions adopted on 26.06.2018.

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

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

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

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

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

The summary of opinion was circulated for information.

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

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

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

Scope: List of outstanding issues, List of questions to SAG

Action: For adoption

List of Questions adopted on 09.11.2017.

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

The Committee adopted a list of outstanding issues.

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

The CHMP agreed to consult the SAG HIV/Viral Diseases and adopted a list of questions to this group.

3.2.2. zanamivir - EMEA/H/C/004102

treatment of influenza A or B virus infection

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 26.04.2018.

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

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

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

3.2.3. lorlatinib - EMEA/H/C/004646

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

Scope: List of outstanding issues, request by the applicant for extension to the clock stop to respond to the list of outstanding issues

Action: For adoption

List of Questions adopted on 31.05.2018.

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

The Committee adopted a list of outstanding issues.

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

3.2.4. lusutrombopag - EMEA/H/C/004720

treatment of thrombocytopenia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 31.05.2018.

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

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

3.2.5. botulinum toxin type a - EMEA/H/C/004587

temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 09.11.2017.

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

The Committee adopted a list of outstanding issues.

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

3.2.6. treosulfan - Orphan - EMEA/H/C/004751

medac Gesellschaft fur klinische Spezialpraparate mbH; conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 31.05.2018.

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

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

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

3.3.1. angiotensin II - EMEA/H/C/004930

treatment of hypotension in adults with distributive or vasodilatory shock who remain hypotensive despite fluid and vasopressor therapy

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.2. enasidenib - Orphan - EMEA/H/C/004324

Celgene Europe Limited; treatment of acute myeloid leukaemia (AML)

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.3. L-lysine hydrochloride / L-arginine hydrochloride - EMEA/H/C/004541

reduction of renal radiation exposure during Peptide-Receptor Radionuclide Therapy (PRRT) with lutetium (177Lu) oxodotreotide

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.4. posaconazole - EMEA/H/C/005028

treatment of fungal infections in adults

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.5. rituximab - EMEA/H/C/004807

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

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application

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

3.3.6. tobramycin - EMEA/H/C/005086

management of chronic pulmonary infection due to Pseudomonas aeruginosa in patients aged 6 years and older with cystic fibrosis (CF)

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

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

3.4.1. viable T-cells - Orphan - ATMP - EMEA/H/C/002397

Kiadis Pharma Netherlands B.V.; adjunctive treatment in haematopoietic stem cell transplantation (HSCT) for a malignant disease

Scope: Request by the applicant for an extension to the clock stop to respond to the List of Outstanding Issues adopted on 20.09.2018

Action: For adoption

List of Outstanding Issues adopted on 20.09.2018, 25.05.2018. List of Questions adopted on 08.09.2017.

The CHMP agreed to the request for an extension to the clock stop to respond to the List of Outstanding Issues adopted on 14.09.2018 with a specific timetable as adopted by CAT at its October meeting.

3.4.2. sotagliflozin - EMEA/H/C/004889

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

Scope: List of questions to the Ad Hoc Expert Group

Action: For adoption

List of Questions adopted on 26.07.2018.

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

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

No items

3.6. Initial applications in the decision-making phase

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

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

Scope: Final similarity assessment report.

Action: For information

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

Opinion adopted 26.07.2018. List of Outstanding Issues adopted on 28.06.2018, 31.05.2018, 22.03.2018. List of Questions adopted on 14.12.2017.

The CHMP noted the final similarity assessment report.

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Vihuma - simoctocog alfa - EMEA/H/C/004459/X/0006/G

Octapharma AB

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

Scope: “Extension application to add new strengths of 2500 IU, 3000 IU and 4000 IU, powder and solvent for solution for injection.
The above line extension is grouped with the following variations:
- C.I.4 - to update sections 4.2, 4.8 and 5.1 of the SmPC to reflect available data from Previously Untreated Patients (PUP) from GENA-05 (interim report) study
- C.I.11.b - to update the Risk Management Plan (version 10) to align the content in a single harmonised worldwide version for simocotocg alfa (rFVIII).
- C.I.1.b - to update the Product Information with the wording agreed in the Art. 31 referral (EMEA/H/A-31/1448).”

Action: For adoption

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

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

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

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

No items

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

No items

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

No items

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

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

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

Roche Registration GmbH

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

Scope: “Extension of Indication to include routine prophylaxis of bleeding episodes in patients with hemophilia A without factor VIII inhibitors, for Hemlibra. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated with efficacy and safety information of the pivotal trials:
- Study BH30071 (HAVEN 3) - an ongoing, multicenter, open-label, randomized Phase III clinical study evaluating the efficacy, safety and PK of emicizumab prophylaxis at doses of 1.5 mg/kg/week (QW) and 3 mg/kg/every 2 weeks (Q2W) versus no prophylaxis in adults and adolescent patients (age of 12 or above) with haemophilia A without inhibitors against factor VIII (FVIII).
- Study BO39182 (HAVEN 4) - an ongoing multicenter, open-label, non-randomized Phase III study evaluating the efficacy, safety and PK of emicizumab given as the dose of 6 mg/kg/every 4 weeks (Q4W) in adults and adolescent patients (age of 12 or above) with hemophilia A with or without FVIII inhibitors.
- Study BH29992 (HAVEN 2) - a multicenter, open-label, non-randomized Phase III study evaluating the efficacy, safety and PK of emicizumab at the QW dose in pediatric patients (<12 years old or 12-17 years old and <40kg) with hemophilia A with FVIII inhibitors.
The Package Leaflet and the Risk Management Plan (v.2.0) is updated in accordance.

In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor corrections and clarity to sections 4.4, 4.5 and 4.6 of the SmPC."

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

Action: For adoption

Request for Supplementary Information adopted on 26.07.2018.

Letter from third party

The Committee discussed the issues identified in this application.

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

The CHMP noted the letter from third party and assessment to this.

5.1.2. Imnovid - pomalidomide - Orphan - EMEA/H/C/002682/II/0031/G

Celgene Europe BV

Rapporteur: Robert James Hemmings, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Patrick Batty

Scope: "Extension of indication to include treatment with Imnovid in combination with bortezomib and dexamethasone of adult patients with multiple myeloma who have received at least one prior treatment regimen including lenalidomide; as a result, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.
As a consequence the MAH submitted a request to add 14-capsule pack sizes for the 1 mg, 2 mg, 3 mg and 4 mg Imnovid strengths to support the proposed posology and pomalidomide dose modification. The SmPC, Labelling and Package leaflet are updated in accordance.
Update of section 5.1 of the SmPC in order to update the information on pomalidomide mechanism of action based on literature data."

Action: For adoption

The Committee discussed the issues identified in this application. The Committee discussed the clinical data with specific focus on the observed effect on progression free survival and the potential translation in overall survival and in this context an additional 1 year marketing protection request.

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

5.1.3. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0069

Vertex Pharmaceuticals (Europe) Ltd.

Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "Extension of Indication to include treatment of cystic fibrosis in children age 12 to less than 24 months who have one of the currently approved gating mutations in the CFTR

gene for Kalydeco 50 mg & 75 mg Granules; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. Relevant consequential changes are made to the Kalydeco 150 mg film-coated tablet Product Information. The Package Leaflet is updated in accordance.
The RMP version 8.1 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 20.09.2018, 28.06.2018.

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

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

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

The summary of opinion was circulated for information.

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

Merck Sharp & Dohme B.V.

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

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

Action: For adoption

Request for Supplementary Information adopted on 26.07.2018.

The Committee discussed the issues identified in this application. The members discussed the available clinical data and whether it is considered sufficient to conclude on the extension of indication request.

The CHMP adopted a positive opinion by majority (22 positive out of 32 votes) together with the CHMP Assessment Report and translation timetable.

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

The divergent position *(*Bart van der Schueren, Jorge Camarero Jimenez, Jayne Crowe, Johann Lodewijk Hillege, Katarina Vucic, Koenraad Norga, Kristina Dunder, Outi Maki-Ikola*,* Robert James Hemmings, Sol Ruiz) was appended to the opinion.

The summary of opinion was circulated for information.

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

Merck Sharp & Dohme B.V.

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

Scope: "Extension of Indication to include 1st line treatment of locally advanced or metastatic non-small cell lung cancer tumours expressing PD-L1 with a ≥ 1% tumour proportion score (TPS), based on data from study KEYNOTE-042; an international, randomized, open-label Phase 3 study investigating KEYTRUDA monotherapy compared to standard of care platinum-based chemotherapy in patients with locally advanced or metastatic PD-L1 positive (TPS ≥ 1%) NSCLC, and on supportive data from the final planned analysis of KEYNOTE-024; a Phase 3 randomized open-label study of KEYTRUDA monotherapy compared to platinum-based chemotherapy in metastatic NSCLC with PD-L1 TPS ≥50%. As a result, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated. An updated RMP version 18.1 was provided as part of the application."

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to the available clinical data and whether the efficacy has been sufficiently demonstrated in the sought patient population.

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

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

Novo Nordisk A/S

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

Scope: "Extension of Indication to include patients with Glanzmann's thrombasthenia with past or present refractoriness to platelet transfusions, or where platelets are not readily available, based on a prospective observational registry and literature references. As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in section 4.8 of the SmPC and in Package Leaflet. The updated RMP version 7.1 has been agreed within this procedure."

Action: For adoption

Request for Supplementary Information adopted on 26.07.2018.

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

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

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

The summary of opinion was circulated for information.

5.1.7. Praluent - alirocumab - EMEA/H/C/003882/II/0042

sanofi-aventis groupe

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include the prevention of cardiovascular events in patients with established atherosclerotic cardiovascular disease for Praluent based on the final study report of EFC11570; as a consequence, sections, 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and RMP v4, have been updated accordingly."

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

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to the wording of the indication and in relation to the additional 1 year marketing protection request.

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

5.1.8. Rapiscan - regadenoson - EMEA/H/C/001176/II/0027

GE Healthcare AS

Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty

Scope: "Extension of Indication to include use in the measurement of fractional flow reserve (FFR) during invasive coronary angiography (ICA) in patients presenting a coronary artery stenosis for Rapiscan based on study 060912001: Comparison of Regadenoson (RAPISCAN) and Central Intravenous Adenosine for Measurement of Fractional Flow Reserve and data from published literature. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated RMP version 10.0 was provided as part of this extension of indication."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018.

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

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

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

AstraZeneca AB

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

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

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018.

The Committee discussed the issues identified in this application. The main issue discussed was on the proposed indication wording, in particular in the context of an appropriate subpopulation and the risk of diabetic ketoacidosis.

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

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

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

No items

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

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

Amgen Europe B.V.Scope: “Extension of Indication to include the treatment of adults with minimal residual disease (MRD) positive B-cell precursor acute lymphoblastic leukaemia (ALL) for BLINCYTO;
as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, and to update the safety information. The Labelling is updated in accordance.
RMP version 4.0 is included in this submission.”

List of questions to the SAG

Action: For adoption

Opinion adopted on 26.07.2018. An oral explanation was held on 24.07.2018.

The CHMP adopted a list of questions to the SAG-Oncology.

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

Bristol-Myers Squibb Pharma EEIG

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

List of questions to the SAG.

Action: For adoption

Opinion adopted on 26.07.2018. An oral Explanation was held on 25.07.2018.

The CHMP adopted a list of questions to the SAG-Oncology.

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. fenfluramine hcl - Orphan - H0003933

Zogenix International Ltd; treatment of seizures associated with Dravet syndrome.

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

Action: For adoption

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

8.1.2. cilastatin sodium, imipenem monohydrate, relebactam - H0004808

indicated for the treatment of bacterial infections due to gram-negative microorganisms in patients 18 years of age and older with limited treatment options.

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

Action: For adoption

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

8.1.3. potassium bicarbonate, potassium citrate monohydrate - Orphan - H0004460

Advicenne Pharma S.A., treatment of distal Renal Tubular Acidosis (dRTA)

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

Action: For adoption

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

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

Action: For information

The CHMP noted the list of applications received.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 6 recommendations for eligibility to PRIME: All 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. Caprelsa - vandetanib - EMEA/H/C/002315/II/0028

Genzyme Europe BV

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: "Update of sections 4.1, 4.4 and 5.1 of the SmPC in order to delete the information regarding Rearranged during Transfection (RET) mutation. The application addresses SOB 001 and the MAH proposes to revert from conditional marketing authorisation to standard marketing authorisation. Annex II and Package Leaflet are updated accordingly. The RMP version 12.2 has also been submitted.
In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10."

Action: For adoption
Request for Supplementary Information adopted on 26.04.2018, 14.12.2017.

See 2.3

The Committee discussed the issues identified in this application. The members were reminded that the product received a conditional approval in 2012 with a specific obligation to submit the final clinical study report of study D4200C00104. In the current procedure, the MAH provided updated results of study D4200C00104. The members agreed that the provided data was still insufficient to conclude on the benefit/risk in the RET negative population and therefore the specific obligation was not considered fulfilled. The Committee noted the foreseen timeline for study D4200C00104 , which was considered too long. The members agreed to request further information from the MAH and to cancel the oral explanation at this stage.

The CHMP agreed that no oral explanation is needed this time.

The Committee adopted a 3rd request for supplementary information.

The CHMP agreed to the request for an clock stop to respond to the request for supplementary information with a specific timetable.

9.1.2. Evoltra - clofarabine - EMEA/H/C/000613/S/0059

Genzyme Europe BV

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: Opinion

Action: For discussion

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 CHMP recommended that the remaining specific obligation (SOB) is considered fulfilled based on data submitted in this procedure and the Product Information should therefore be revised to remove this SOB from Annex II.E and to add the new specific obligation requesting yearly updates on efficacy and safety.

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

The summary of opinion was circulated for information.

9.1.3. IONSYS - fentanyl - EMEA/H/C/002715

MAH: Incline Therapeutics Europe Ltd, treatment of acute moderate to severe post-operative pain
Rapporteur: Greg Markey, Co-Rapporteur: Outi Mäki-Ikola,
Scope: Letter from the applicant dated 4 September 2018 informing EMA about the withdrawal of the marketing authorisation on commercial reasons

Action: For information

The CHMP noted the withdrawal of marketing authorisation.

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

Merck Sharp & Dohme Limited

Rapporteur: Greg Markey

Scope: PRAC Recommendation/Opinion

Action: For discussion

The CHMP noted the PRAC recommendation.

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.

9.1.5. VELCADE - bortezomib - EMEA/H/C/000539/II/0088

Janssen-Cilag International NV

Rapporteur: Daniela Melchiorri

Scope: "Update of sections 4.2 and 5.1 of the SmPC in order to add a new dosing schedule for VELCADE (bortezomib) in combination with melphalan and prednisone (VMP) for the treatment of patients with newly diagnosed multiple myeloma who are not eligible for high-dose chemotherapy with hematopoetic stem cell transplant. The proposed new dosing schedule is supported by analyses comparing the current approved VcMP schedule (from 26866138MMY3002 [VISTA] study) with pooled modified less intensive ("once-weekly") VcMP schedules (from 54767414MMY3007 [ALCYONE], GIMENA MM-03-05 [GIMENA]). Additional supportive efficacy and safety data come from GEM2005MAS65 [PETHEMA]. The PL (section 3) is amended accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the PL."

Letter by the MAH dated 16.10.2018 informing the EMA about the withdrawal of the variation application

Action: For information

Request for Supplementary Information adopted on 26.07.2018, 22.03.2018.

The CHMP noted the withdrawal of the variation application.

10. Referral procedures

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

No items

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

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

MAHs: various

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

Scope: Update on procedure

Action: For discussion

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

The CHMP was updated on the procedure and the next steps and noted the specific timetable.

CHMP LoOI/CHMP opinion: November 2018 CHMP

10.2.2. Norethisterone and Ethinylestradiol – EMEA/H/A-5(3)/1470

MAH various

Rapporteur: Paula Boudewina van Hennik, Co-rapporteur: Kristina Dunder

Scope: List of outstanding Issues/Opinion

Action: For adoption

Request from UK for a CHMP opinion on a recently published study using the zebrafish model for studying the developmental effect of norethisterone acetate and ethinylestradiol and any potential clinical implications on the human foetus

The CHMP was updated on the report from the SWP.

The CHMP adopted an opinion by consensus, recommending the following:

If appropriately qualified, a well-performed ZET may contribute to the evaluation of the teratogenic potential of a compound as part of an integrated testing strategy. A proper qualification of a ZET has not yet been performed and it is premature to conclude on its suitability to predict potential teratogenic effects of norethisterone and ethinylestradiol in human pregnancy. The results of such a study still needs to be evaluated together with all available *in vivo* non-clinical and human data, including exposure data, as part of an integrated risk assessment approach.

The data evaluated as part of this procedure indicates effects on survival and development of the zebrafish embryo following direct exposure of a mixture of NA and EE in a ratio of 500:1 at high concentrations. However, the reliability of the performed studies could not be fully evaluated due to methodological limitations. The available data is not considered sufficient for establishing a direct teratogenic effect of the NA:EE mixture or of the individual components.

The results of the ZET study are consistent with the results of studies in non-human mammalian species. There is no clear and consistent non-clinical evidence that a combination of NA and EE causes foetal malformations in non-reproductive tissue. The results of the ZET are not considered by the CHMP to give rise to any new concerns.

The CHMP took into account the responses of the Safety Working Party, regarding the zebrafish model in the preclinical setting, the robustness of the study, and the potential clinical implications.

The CHMP adopted the assessment report.

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

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

No items

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

10.4.1. Paclitaxel Hetero - EMEA/H/A-29(4)/1256

Hetero Europe S.L.

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

Scope: Opinion

Action: For adoption

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

The Committee discussed the available data and whether the bioequivalence between Paclitaxel Hetero and the EU reference medicinal product had been established.

The CHMP adopted a negative opinion by consensus, recommending that the application does not satisfy the criteria for authorisation. Therefore, the CHMP recommended that the marketing authorisations for the medicinal products concerned should be refused.

The CHMP adopted the assessment report.

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

The CHMP agreed to the public health communication.

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

MAH: Actavis Group PTC EHF

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

Scope: Opinion

Action: For adoption

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

The CHMP discussed the bioequivalence between Perlinring with the reference product for 21 and 28 days.

The CHMP adopted an opinion by majority (18 out of 33 votes), recommending that the marketing authorisation(s) should be granted.

Based on evaluation of the currently available data, the CHMP considered that bioequivalence to the reference medicinal product has been shown for the authorised duration of treatment (3 weeks). In addition, there is enough evidence to expect that Perlinring continues to be effective for an additional 4th week, as is the case for Nuvaring.

The CHMP therefore concluded that the benefits of Perlinring outweigh its risks and recommended that the marketing authorisation be granted in all concerned Member States.

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

The divergent position (Agnes Gyurasics, Alexandre Moreau, Andrea Laslop, Bart van der Schueren, Concepcion Prieto Yerro, Daniela Melchiorri, Ewa Balkowiec Iskra, Jacqueline Genoux-Hames, Jan Mueller-Berghaus, Johann Lodewijk Hillege, Koenraad Norga, Martina Weise, Mila Vlaskovska, Rajko Kenda, Simona Badoi) was appended to the opinion.

The CHMP agreed to the public health communication.

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

MAH: Temmler Pharma GmbH

Rapporteur: Greg Markey, Co-Rapporteur: Martina Weise

Scope: Appointment of rapporteurs, Draft timetable

Action: For adoption

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

The CHMP appointed Greg Markey as Rapporteur (interest level 1) and Martina Weise as Co-Rapporteur (interest level 2).

The CHMP agreed to a short procedure (no list of questions at this stage) with a specific timetable.

Notification: 28.09.2018

Start of procedure (CHMP): 18.10.2018

Rapporteur/co-rapporteur assessment report circulated to CHMP: 02.11.2018

CHMP comments: 06.11.2018

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 08.11.2018

CHMP opinion / CHMP list of questions: November 2018 CHMP

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

MAHs: various

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Martina Weise

Scope: Updated timetable was adopted via written procedure on 2 October 2018

Action: For information

The CHMP noted the adopted timetable.

Submission of responses: 11.10.2018

Re-start of the procedure: 18.10.2018

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 31.10.2018

Comments: 05.11.2018

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 08.11.2018

CHMP Opinion: November 2018 CHMP

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

No items

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

10.6.1. Bacterial lysates-containing based medicinal products for respiratory conditions - EMEA/H/A-31/1465

MAH various

Rapporteur: Daniela Melchiorri, Co-rapporteur: Jan Mueller-Berghaus

Scope: List of outstanding Issues

Action: For adoption

Review of the benefit-risk balance following notification by AIFA in Italy on 22 May 2018 of a referral under Article 31 of Directive 2001/83/EC.

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

Submission of responses: 10.01.2019

Re-start of the procedure: 31.01.2019

Rapporteur/co-rapporteur joint assessment report(s) circulated to CHMP: 08.02.2019

SAG meeting: exact date to be confirmed

Comments: 15.02.2019

Updated Rapporteur/co-rapporteur joint assessment reports circulated to CHMP: 21.02.2019

CHMP LoOI/CHMP opinion: February 2019 CHMP

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

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

MAHs: various

Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

Scope: List of outstanding Issues/SAG Report from meeting held 10 October 2018

Updated list of experts to the SAG CVS was adopted via written procedure on 8 October 2018.

Action: For adoption

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

The CHMP noted the report from the SAG meeting held on 10 October 2018.

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

Submission of responses: 09.11.2018

Re-start of the procedure: 15.11.2018

Rapporteur / co-rapporteur joint assessment report circulated to CHMP: 30.11.2018

CHMP Comments: 05.12.2018

Updated rapporteur / co-rapporteur joint assessment report circulated to CHMP: 07.12.2018

CHMP opinion: December 2018 CHMP

10.6.3. Gadolinium-containing contrast agents (GdCA): Gadobenate dimeglumine; gadobutrol; gadodiamide; gadopentetic acid dimeglumine, gadoteric acid (intra articular formulation); gadoteric acid (intrvenous and intravascular formulations); gadoteridol; gadoxetic acid disodium (NAP)

Lead Rapporteur: Patrick Batty,

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

Action: For adoption

The CHMP adopted the annual cumulative reviews.

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

MAHs: various

Rapporteur: Martina Weise

Scope: CHMP LoQ to EDQM and OMCLs was adopted via written procedure on 05.10.2018

Action: For information

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

The CHMP noted the list of questions to EDQM and OMCLs adopted via written procedure on 05.10.2018.

Post-meeting note: The CHMP adopted the revised LoQ to SWP via written procedure on 26.10.2018.

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

The CHMP noted the ENS.

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

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

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Election of new CHMP vice-chairperson

Further to the election of Harald Enzmann as new CHMP Chairperson, the election of a new Vice-Chairperson took place at the October 2018 CHMP meeting.

Action: For adoption

The CHMP elected Bruno Sepodes as new CHMP Vice-Chair for a 3-year mandate, starting on 15 October 2018.

14.1.2. EMA-FDA analysis on marketing authorisations

Action: For discussion

The CHMP noted the comparison of EMA and FDA Decisions for New Drug Marketing Applications.

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

Follow up from SRLM

Action: For discussion

The CHMP noted the questions and responses of the discussion on biosimilars.

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 01-04 October 2018

Action: For information

The CHMP noted the summary of recommendations and advice.

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

Action: For adoption

The CHMP adopted the EURD list.

List of questions from PRAC to Safety Working Party (SWP) on dolutegravir

Action: For adoption

The CHMP adopted the list of questions to the SWP.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 10-12 October 2018
Action: For information

The CHMP noted the minutes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 24-27 September 2018

Action: For information

The CHMP noted the report.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at October 2018 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 18-21 September 2018

Action: For information

The CHMP noted the report.

Joint CHMP-PDCO session

Action: For discussion

The Joint CHMP-PDCO session was held.

FINAL reflection paper on the use of extrapolation in the development of medicines for paediatrics

CHMP: Rob Hemmings

Action: For adoption

Follow-up from October ORGAM

The CHMP adopted the reflection paper.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 09-11 October 2018

Action: For information

The CHMP noted the report.

14.2.6. Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 15-17 October 2018

Action: For information

The CHMP noted the report.

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

14.3.1. Quality Working Party (QWP)

Chair: Keith Pugh/Blanka Hirschlerova

Small Volume Q&A (EMA/CHMP/QWP/672418/2018)

Rapporteur Diana van Riet (via TC)

Action: For adoption

The CHMP adopted the Q&A.

Enteral feeding tubes Q&A (EMA/CHMP/QWP/710828/2018)

Rapporteur Abigail Moran (via TC)

Action: For adoption

The CHMP adopted the Q&A.

Guideline of quality and equivalence of topical products (EMA/678311/2018)

Presented by Sean Jones

Action: For adoption for public consultation

Follow-up from October ORGAM

The CHMP adopted the guideline for public consultation.

Quality data requirements to demonstrate suitability of multidose containers for preservative free eye drops (EMA/CHMP/QWP/677572/2018)

Presented by Blanka Hirschlerova

Action: For adoption

Follow-up from October ORGAM

The CHMP adopted the quality data requirements.

Guideline on Active Substance Master File Procedure – corrections to the GL

Presented by Blanka Hirschlerova

Action: For adoption

Follow-up from October ORGAM

The CHMP adopted the guideline.

QWP letter to EDQM (Ph Eur chapter 2.2.46)

Presented by Blanka Hirschlerova

Action: For adoption

The CHMP adopted the letter to EDQM.

14.3.2. Scientific Advice Working Party (SAWP)

Chair: Robert Hemmings

Report from the SAWP meeting held on 01-04 October 2018. Table of conclusions

Action: For information

The CHMP noted the report.

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

14.3.3. Geriatric Expert Group (GEG)

Chair: Katarina Vučić

Outcome of geriatric pilot on 10 products

Action: For discussion

The CHMP noted the outcome of the geriatric pilot on 10 products assessed during MA procedures and proposals for further actions. The CHMP agreed on the need for further actions and to raise awareness on the need for more geriatric data.

14.3.4. Safety Working Party (SWP)

Summary report of EMA workshop on non-animal approaches in support of medicinal product development – challenges and opportunities for use of micro-physiological systems held on 5 October 2017 (EMA/CHMP/SWP/250438/2018)

Action: For adoption

The CHMP adopted the summary report.

Election of SWP Chair

Action: For adoption

The CHMP re-elected Jan Willem van der Laan as SWP chair.

14.3.5. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 26 September 2018.

Action: For adoption

The CHMP adopted the NRG table of decisions.

14.3.6. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP October 2018 meeting to CHMP for adoption:

- 9 reports on products in scientific advice and protocol assistance
- 6 reports on products in pre-authorisation procedures
- 3 reports on products in plasma master file

Action: For adoption

The CHMP adopted the BWP reports.

Questions and answers on Bovine Spongiform Encephalopathies (BSE) and vaccines (EMA/CHMP/BWP/192228/2017)

Action: For adoption

The CHMP adopted the Q&A.

Overview of comments received on 'Questions and Answers on Bovine Spongiform Encephalopathies (BSE) and vaccines' (EMEA/CHMP/BWP/637549/2018)

Action: For information

Follow-up from October ORGAM

The CHMP noted the overview of comments.

Questions and answers on the Haemagglutination Inhibition (HI) test for qualification of influenza vaccine (inactivated) seed preparations (EMA/CHMP/BWP/426390/2017)

Action: For adoption

- Overview of comments received on “Questions and answers on the Haemagglutination Inhibition (HI) test for qualification of influenza vaccine (inactivated) seed preparations” (EMEA/CHMP/BWP/652969/2018)

Action: For information

Follow-up from October ORGAM

The CHMP adopted the Q&A and noted the overview of comments.

Guideline on quality aspects included in the product information for vaccines for human use (EMEA/CHMP/BWP/133540/2017)

Action: For adoption

- Overview of comments received on 'Guideline on quality aspects included in the product information for vaccines for human use' (EMEA/CHMP/BWP/668918/2018)

Action: For information

Follow-up from October ORGAM

The CHMP adopted the guideline and noted the overview of comments.

Revision of the CHMP position statement on Creutzfeldt-Jakob disease and plasma-derived and urine-derived medicinal products (EMA/CHMP/BWP/303353/2010 Rev 1)

Action: For adoption for public consultation

Follow-up from October ORGAM

The CHMP adopted the revision for public consultation.

14.3.7. Vaccines Working Party (VWP)

Chair: Mair Powell/Svein Rune Andersen

Final joint guideline with IDWP on the clinical evaluation of medicinal products indicated for the prophylaxis or treatment of respiratory syncytial virus (RSV) disease.

Action: For adoption

Follow-up from October ORGAM

The CHMP adopted the final joint guideline.

14.3.8. Cardiovascular Working Party (CVSWP)

Chair: Kristina Dunder/Alar Irs

Paediatric addendum to CHMP guidelines on the clinical investigations of medicinal products for the prevention and treatment of thromboembolic disease (EMA/CHMP/763438/2017)

Action: For adoption for public consultation

Follow-up from October ORGAM

The CHMP adopted the addendum for public consultation.

Concept Paper on the revision of the Guideline on clinical investigation of medicinal products for the treatment of peripheral arterial occlusive disease (CPMP/EWP/714/98 rev.1) (EMA/CHMP/78339/2018)

Action: For adoption for public consultation

Follow-up from October ORGAM

The CHMP adopted the concept paper for public consultation.

14.3.9. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Henrike Potthast

Guideline on equivalence studies for the demonstration of therapeutic equivalence for locally acting products in the gastrointestinal tract (CPMP/EWP/239/95 Rev. 1)

Rapporteur: Alfredo Garcia-Arieta

Action: For adoption

- Overview of comments received on 'Guideline on equivalence studies for the demonstration of therapeutic equivalence for products that are locally applied, locally acting in the gastrointestinal tract (EMA/CPMP/EWP/239/95 Rev.1)

Action: For information

Follow-up from October ORGAM

The CHMP adopted the guideline and noted the overview of comments.

14.3.10. Excipients Drafting Group

Chair: Dominique Masset

Nomination of new member Fokaline Vroom to replace Diana van Riet–Nales

Action: For information

The CHMP noted Fokaline Vroom as new member.

14.3.11. Joint CVMP/CHMP ad-hoc expert group on the application of the 3Rs (replacement, reduction and refinement) in the regulatory testing of medicinal products (J 3RsWG)

Chair: Ellen-Margrethe Vestergaard, Co-Chair: Susanne Brendler-Schwaab

Reflection paper providing an overview of the current regulatory testing requirements for medicinal products for human use and opportunities for implementation of the 3Rs (EMA/CHMP/CVMP/3Rs/742466/2015)

Action: For adoption

The CHMP adopted the reflection paper.

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

No items

15. Any other business

15.1. AOB topic

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 15 – 18 October 2018 meeting

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Harald Enzmann	Chair	Germany	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Bart Van der Schueren	Member	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Katarina Vučić	Member	Croatia	No interests declared	
Emilia Mavrokordatou	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Mark Ainsworth	Alternate	Denmark	No participation in final deliberations and voting on:	5.1.6. NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0104
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Joseph Emmerich	Alternate	France	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Maria Orfanou	Alternate	Greece	No interests declared	
Agnes Gyurasics	Member	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	
Peter Kiely	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Natalja Karpova	Alternate	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No participation in final deliberations and voting on:	5.1.1. Hemlibra - emicizumab - EMEA/H/C/004406/II/0002
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Svein Rune Andersen	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No restrictions applicable to this meeting	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Bruno Sepodes	Vice-Chair	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Simona Badoi	Member	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	
Rajko Kenda	Member	Slovenia	No restrictions applicable to this meeting	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Jorge Camarero Jiménez	Alternate	Spain	No participation in final deliberations and voting on:	5.1.1. Hemlibra - emicizumab - EMEA/H/C/004406/II/0002
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Greg Markey	Member	United Kingdom	No interests declared	
Nithyanandan Nagercoil	Alternate	United Kingdom	No restrictions applicable to this meeting	
Robert James Hemmings	Co-opted member	United Kingdom	No interests declared	
Koenraad Norga	Co-opted member	Belgium	No participation in final deliberations and voting on:	3.2.2. zanamivir - EMEA/H/C/004102;
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Blanka Hirschlerova	Co-opted member	Czech Republic	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Ingrid Schellens	Expert - in person*	Netherlands	No interests declared	
Agustin Portela Moreira	Expert - in person*	Spain	No interests declared	
Jutta Dedorath	Expert - in person*	Germany	No interests declared	
Janet Koenig	Expert - in person*	Germany	No interests declared	
Andrew Exley	Expert - in person*	United Kingdom	No interests declared	
Jasbinder Sumal	Expert - in person*	United Kingdom	No interests declared	
Francisco DeMatos Afonso Pereira	Expert - in person*	United Kingdom	No interests declared	
Claire Hearnden	Expert - in person*	United Kingdom	No interests declared	
Marianne Orholm	Expert - via telephone*	Denmark	No interests declared	
Mette Linnert Jensen	Expert - via telephone*	Denmark	No interests declared	
Franz Kleber	SAG chair	Germany	No interests declared	
Vassilis Violakis	Expert - via telephone*	Greece	No interests declared	
Nicole Visser	Expert - via telephone*	Netherlands	No interests declared	
Diana van Riet-Nales	Expert - via telephone*	Netherlands	No interests declared	
Christian Syverten	Expert - via telephone*	Norway	No interests declared	
Gro Dalseng Haakonsen	Expert - via telephone*	Norway	No interests declared	
Susan Cole	Expert - via telephone*	United Kingdom	No restrictions applicable to this meeting	
Abigail Moran	Expert - via telephone*	United Kingdom	No interests declared	
Julian Paesler	Expert - via Adobe*	Germany	No interests declared	
Susanna Hausmann	Expert - via Adobe*	Germany	No interests declared	
Nele Berthels	Expert - via Adobe*	Belgium	No interests declared	
A representative from the European Commission attended the meeting Meeting run with the help of EMA staff				

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

17. Explanatory notes

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

Oral explanations *(section 2)*

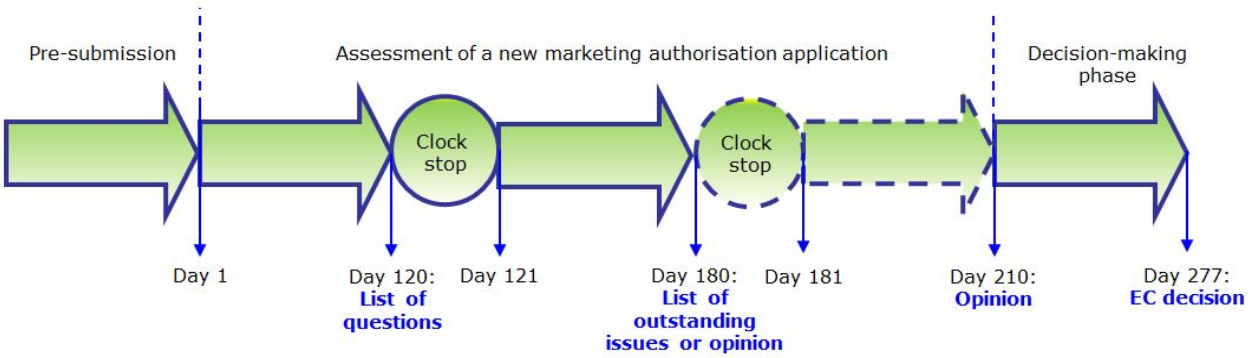
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

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

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

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

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

28 November 2018
EMA/CHMP/834762/2018

Annex to CHMP 15-18 October 2018 Minutes

Pre submission and post authorisation issues

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Send a question via our website www.ema.europa.eu/contact

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

A.2. APPOINTMENT OF RAPPORTEUR / CO-RAPPORTEUR FULL APPLICATIONS

Final Outcome of Rapporteurship allocation for October 2018: **For adoption**	Adopted.

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

Information related to pre-submission of initial applications cannot be released at the present time as these contain commercially confidential information.

B. POST-AUTHORISATION PROCEDURES OUTCOMES

Annual re-assessment outcomes

B.1.1. Annual reassessment for products authorised under exceptional circumstances

Evoltra - clofarabine - EMEA/H/C/000613/S/0059 Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni	Positive Opinion adopted by consensus together with the CHMP assessment report. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Entyvio - vedolizumab - EMEA/H/C/002782/R/0032 Takeda Pharma A/S, Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Adam Przybylkowski Request for Supplementary Information adopted on 20.09.2018.	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Thymanax - agomelatine - EMEA/H/C/000916/R/0040 Servier (Ireland) Industries Ltd., Duplicate, Duplicate of Valdoxan, Rapporteur: Svein Rune	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of

Andersen, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Karen Pernille Harg Request for Supplementary Information adopted on 20.09.2018.	the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Valdoxan - agomelatine - EMEA/H/C/000915/R/0042 Les Laboratoires Servier, Rapporteur: Svein Rune Andersen, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Karen Pernille Harg Request for Supplementary Information adopted on 20.09.2018.	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Granupas - para-aminosalicylic acid - EMEA/H/C/002709/R/0026, Orphan Eurocept International B.V., Rapporteur: Greg Markey, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - EMEA/H/C/002450/R/0021, Orphan, ATMP Chiesi Farmaceutici S.p.A., Rapporteur: Egbert Flory, PRAC Rapporteur: Julie Williams Request for Supplementary Information adopted on 12.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Jardiance - empagliflozin - EMEA/H/C/002677/R/0040 Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Eva A. Segovia Request for Supplementary Information adopted on 18.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Mepact - mifamurtide - EMEA/H/C/000802/R/0047, Orphan Takeda France SAS, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted	Request for Supplementary Information adopted with a specific timetable.

on 18.10.2018.	
Pregabalin Pfizer - pregabalin - EMEA/H/C/003880/R/0025 Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Liana Gross-Martirosyan	Positive Opinion adopted by consensus together with the CHMP assessment report ‹and translation timetable›. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Ulunar Breezhaler - indacaterol / glycopyrronium - EMEA/H/C/003875/R/0028 Novartis Europharm Limited, Rapporteur: Mark Ainsworth, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Anette Kirstine Stark Request for Supplementary Information adopted on 18.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Vimizim - elosulfase alfa - EMEA/H/C/002779/R/0024, Orphan BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Patrick Batty Request for Supplementary Information adopted on 20.09.2018.	Positive Opinion adopted by consensus together with the CHMP assessment report ‹and translation timetable›. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/R/0039 Janssen-Cilag International NV, Rapporteur: Martina Weise, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Menno van der Elst	Positive Opinion adopted by consensus together with the CHMP assessment report ‹and translation timetable›. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

B.2.3. Renewals of Conditional Marketing Authorisations

Caprelsa - vandetanib - EMEA/H/C/002315/R/0032 Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni Request for Supplementary Information adopted	Request for Supplementary Information adopted with a specific timetable.

on 18.10.2018.	
OCALIVA - obeticholic acid - EMEA/H/C/004093/R/0009, Orphan Intercept Pharma Ltd, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 20.09.2018.	Positive Opinion adopted by consensus together with the CHMP assessment report ‹and translation timetable›. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection PRAC recommendations on signals adopted at the PRAC meeting held on 01-04 October 2018 PRAC:	
Signal of dysglycaemia: Direct Acting Antivirals **Daklinza – DACLATASVIR – EMEA/H/C/003768** Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, Co-Rapporteur: Robert James Hemmings **Epclusa – SOFOSBUVIR/VELPATASVIR - EMEA/H/C/004210** Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs **Harvoni – LEDIPASVIR/SOFOSBUVIR - EMEA/H/C/003850** Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, Co-Rapporteur: Joseph Emmerich **Sovaldi – SOFOSBUVIR - EMEA/H/C/002798** Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs **Vosevi – SOFOSBUVIR/VELPATASVIR/** **VOXILAPREVIR - EMEA/H/C/004350** Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, Co-Rapporteur: Greg Markey **Zepatier – ELBASVIR/GRAZOPREVIR - EMEA/H/C/004126** Rapporteur: Greg Markey, Co-Rapporteur:	Adopted.

Johann Lodewijk Hillege **Exviera – DASABUVIR - EMEA/H/C/003837** AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege **Maviret – GLECAPREVIR/PIBRENTASVIR - EMEA/H/C/004430** AbbVie Deutschland GmbH & Co. KG, Rapporteur: Joseph Emmerich, Co-Rapporteur: Filip Josephson **Viekirax – OMBITASVIR/PARITAPREVIR/RITONAVIR - EMEA/H/C/003839** Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege PRAC recommendation on a variation**: For adoption**	
Signal of suicidality with hormonal contraceptives following a recent publication: Hormonal Contraceptives **EVRA - ETHINYLESTRADIOL/NORELGESTROMIN – EMEA/H/C/000410** Janssen-Cilag International NV, Rapporteur: Paula B. van Hennik, Co-Rapporteur: Concepcion Prieto Yerro **ZOELY - NOMEGESTROL ACETATE/ESTRADIOL – EMEA/H/C/001213** Teva B.V., Rapporteur: Joseph Emmerich, Co-Rapporteur: Agnes Gyurasics PRAC recommendation on a variation**: For adoption**	Adopted.
Signal of dyslipidaemia **AUBAGIO -Teriflunomide – EMEA/H/C/002514** sanofi-aventis groupe, Rapporteur: Martina Weise, Co-Rapporteur: Johann Lodewijk Hillege PRAC recommendation on a variation**: For adoption**	Adopted
Signal on evaluation of preliminary data from an observational study on birth outcomes in human immunodeficiency virus (HIV)-infected women	Adopted

Dolutegravir; abacavir sulfate, dolutegravir sodium, lamivudine; rilpivirine – **TIVICAY – DOLUTEGRAVIR - EMEA/H/C/002753** ViiV Healthcare B.V., Rapporteur: Filip Josephson, Co-Rapporteur: Joseph Emmerich **TRIUMEQ – DOLUTEGRAVIR/ABACAVIR/LAMIVUDINE - EMEA/H/C/002754** ViiV Healthcare UK Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege **JULUCA - DOLUTEGRAVIR/RILPIVIRINE – EMEA/H/C/004427** ViiV Healthcare UK Limited, Rapporteur: Martina Weise, Co-Rapporteur: Johann Lodewijk Hillege PRAC recommendation on a variation**: For adoption**	
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its October 2018 meeting:	
EMEA/H/C/PSUSA/00002330/201802 (pemetrexed) CAPS: **Alimta** (EMEA/H/C/000564) (pemetrexed), Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau **Armisarte** (EMEA/H/C/004109) (pemetrexed), Actavis Group PTC ehf, Rapporteur: Alar Irs NAPS: **NAPs** - EU , PRAC Rapporteur: Ghania Chamouni, “05-Feb-2015 - 04-Feb-2018”	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following change(s): Update of section 4.8 of the SmPC to include that Hyperpigmentation has been reported with a common frequency and to include that infectious and non-infectious disorders of the dermis, the hypodermis and/or the subcutaneous tissue (e.g. acute bacterial dermo-hypodermitis, pseudocellulitis and dermatitis) have been reported with an unknown frequency. The Package leaflet is updated accordingly.
EMEA/H/C/PSUSA/00003127/201802 (voriconazole) CAPS: **Vfend** (EMEA/H/C/000387) (voriconazole), Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the

NAPS: **VORICONAZOL ARISTO** - ARISTO PHARMA IBERIA, S.L., ARISTO PHARMA GMBH (ART 57) **VORICONAZOLE ARISTO** - ARISTO PHARMA GMBH (ART 57) , PRAC Rapporteur: Liana Gross-Martirosyan, "01-Mar-2017 to 28-Feb-2018"	terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following change(s): Update of sections 4.4 and 4.8 of the SmPC to add drug reaction with eosinophilia and systemic symptoms (DRESS) with a frequency rare and to add a warning on drug reaction with eosinophilia and systemic symptoms (DRESS). Annex IIIA was updated to correct the EU number from I (Roman numeral) to 1 (Arabic number) across all formulations. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010317/201803 (naloxegol) CAPS: **Moventig** (EMEA/H/C/002810) (naloxegol), Kyowa Kirin Holdings B.V., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Rhea Fitzgerald, "September 2017 to 15 March 2018"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.5 of the SmPC to add a warning against use of naloxegol with other opioid antagonists. 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/00010338/201803 (apremilast) CAPS: **Otezla** (EMEA/H/C/003746) (apremilast), Celgene Europe BV, Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, "21 March 2017 - 20 March 2018"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update section 4.8 of the SmPC to add the adverse drug reactions angioedema with a frequency unknown and urticaria with an uncommon frequency. 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/00010403/201803 (pembrolizumab) CAPS: **Keytruda** (EMEA/H/C/003820) (pembrolizumab), Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Menno van der Elst, "04/09/2017 - 03/03/2018"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC to add Vogt-Koyanagi-Harada syndrome and pure red cell aplasia as new ADRs with the frequency rare and to add "including exacerbation" to the already included ADR myasthenia gravis. The Package Leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
Ivabradine – CORLENTOR (CAP), IVABRADINE ANPHARM (CAP), PROCORALAN (CAP); NAP - EMEA/H/C-N/PSR/S/0019 Anpharm Przedsiebiorstwo Farmaceutyczne (Ivabradine Anpharm), Les Laboratoires Servier (Corlentor, Procolaran), various PRAC Rapporteur: Menno van der Elst Scope: Results for a drug utilisation study (DUS) conducted in several European Economic Area (EEA) countries aimed at describing the characteristics of ivabradine users, as well as describing the patterns of use of ivabradine and adherence to the existing risk minimisation measures **Action:** Adoption of recommendation	Adopted.

B.4. EPARs / WPARs

Alunbrig - brigatinib - EMEA/H/C/004248 Takeda Pharma A/S, treatment of anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Apealea - paclitaxel - EMEA/H/C/004154 Oasmia Pharmaceutical AB, treatment of ovarian cancer, Known active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.

Buvidal - buprenorphine - EMEA/H/C/004651 Camurus AB, treatment of opioid dependence within a framework of medical, social and psychological treatment, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746 Merck Sharp & Dohme B.V., treatment of adults infected with HIV-1 without past or present evidence of viral resistance to doravirine, lamivudine, or tenofovir, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Emgality - galcanezumab - EMEA/H/C/004648 Eli Lilly Nederland B.V., prophylaxis of migraine, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Exondys - eteplirsen - EMEA/H/C/004355, Orphan AVI Biopharma International Ltd, treatment of Duchenne muscular dystrophy, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Fulphila - pegfilgrastim - EMEA/H/C/004915 MYLAN S.A.S, treatment of neutropenia, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Jivi - damoctocog alfa pegol - EMEA/H/C/004054, Orphan Bayer AG, Treatment and prophylaxis of haemophilia A, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Luxturna - voretigene neparvovec - EMEA/H/C/004451, Orphan, ATMP Spark Therapeutics Ireland Ltd, treatment of patients with vision loss due to Leber congenital amaurosis or retinitis pigmentosa inherited retinal dystrophy, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Pelmeg - pegfilgrastim - EMEA/H/C/004700 Cinfa Biotech S.L., treatment of neutropenia, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.

Pifeltro - doravirine - EMEA/H/C/004747 Merck Sharp & Dohme B.V., treatment of adults infected with HIV-1 without past or present evidence of viral resistance to treatment of adults infected with HIV-1 without past or present evidence of viral resistance to doravirine, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
POTELIGEO - mogamulizumab - EMEA/H/C/004232, Orphan Kyowa Kirin Holdings B.V., treatment of cutaneous T-cell lymphoma, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Symkevi - tezacaftor / ivacaftor - Orphan - EMEA/H/C/004682 Vertex Pharmaceuticals (Europe) Ltd.; treatment of cystic fibrosis, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Vabomere - meropenem / vaborbactam - EMEA/H/C/004669 Rempex London Ltd, treatment of urinary tract infection (cUTI), including pyelonephritis, intra-abdominal infection (cIAI), hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP)including ventilator associated pneumonia (VAP), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Ziextenzo - pegfilgrastim - EMEA/H/C/004802 Sandoz GmbH, treatment of neutropenia, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Ceprotin - human protein C - EMEA/H/C/000334/II/0106/G Baxter AG, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 18.10.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ceprotin - human protein C - EMEA/H/C/000334/II/0107/G	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP

Baxter AG, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 18.10.2018.	Members were in agreement with the CHMP recommendation.
Entecavir Accord - entecavir - EMEA/H/C/004458/II/0001 Accord Healthcare Limited, Generic, Generic of Baraclude, Rapporteur: Ewa Balkowiec Iskra Opinion adopted on 18.10.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0107 Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 18.10.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Flixabi - infliximab - EMEA/H/C/004020/II/0031 Samsung Bioepis UK Limited, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 27.09.2018.	Request for Supplementary Information adopted with a specific timetable.
Fuzeon - enfuvirtide - EMEA/H/C/000514/II/0051/G Roche Registration GmbH, Rapporteur: Kristina Dunder Opinion adopted on 27.09.2018. Request for Supplementary Information adopted on 26.07.2018.	Positive Opinion adopted by consensus on 27.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
HBVAXPRO - hepatitis B vaccine (rDNA) - EMEA/H/C/000373/II/0064 MSD Vaccins, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 11.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0025/G Sanofi Belgium, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth Opinion adopted on 18.10.2018. Request for Supplementary Information adopted on 13.09.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Levemir - insulin detemir - EMEA/H/C/000528/II/0089 Novo Nordisk A/S, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 27.09.2018.	Request for Supplementary Information adopted with a specific timetable.
NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0026/G Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus	Request for Supplementary Information adopted with a specific timetable.

Request for Supplementary Information adopted on 27.09.2018, 19.07.2018.	
Orencia - abatacept - EMEA/H/C/000701/II/0120/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola Opinion adopted on 27.09.2018.	Positive Opinion adopted by consensus on 27.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Orphacol - cholic acid - EMEA/H/C/001250/II/0025, Orphan Laboratoires CTRS, Rapporteur: Robert James Hemmings Request for Supplementary Information adopted on 11.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0024 CSL Behring GmbH, Rapporteur: Kristina Dunder Opinion adopted on 04.10.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0099/G Genzyme Europe BV, Rapporteur: Peter Kiely Opinion adopted on 11.10.2018.	Positive Opinion adopted by consensus on 11.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vimpat - lacosamide - EMEA/H/C/000863/II/0074/G UCB Pharma S.A., Rapporteur: Filip Josephson Opinion adopted on 11.10.2018.	Positive Opinion adopted by consensus on 11.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xofigo - radium-223 - EMEA/H/C/002653/II/0034 Bayer AG, Rapporteur: Harald Enzmann Request for Supplementary Information adopted on 18.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Yargesa - miglustat - EMEA/H/C/004016/II/0004 JensonR+ Limited, Generic, Generic of Zavesca, Rapporteur: Milena Stain Opinion adopted on 04.10.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1393/G **Hexacima-EMEA/H/C/002702/WS1393/0080/G** **Hexaxim-EMEA/H/W/002495/WS1393/0085/G** **Hexyon-EMEA/H/C/002796/WS1393/0084/G** Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted	Request for Supplementary Information adopted with a specific timetable.

on 11.10.2018, 19.07.2018.	
WS1404 **Nuwiq-EMEA/H/C/002813/WS1404/0022** **Vihuma-EMEA/H/C/004459/WS1404/0004** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 18.10.2018. Request for Supplementary Information adopted on 13.09.2018, 05.07.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1438/G **Hexacima-EMEA/H/C/002702/WS1438/0083/G** **Hexaxim-EMEA/H/W/002495/WS1438/0088/G** **Hexyon-EMEA/H/C/002796/WS1438/0087/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 04.10.2018.	Request for Supplementary Information adopted with a specific timetable.
WS1462 **Rixathon-EMEA/H/C/003903/WS1462/0014** **Riximyo-EMEA/H/C/004729/WS1462/0014** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 11.10.2018.	Request for Supplementary Information adopted with a specific timetable.

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

Adenuric - febuxostat - EMEA/H/C/000777/II/0051 Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, “Update of section 5.1 of the SmPC in order to include the results of the clinical safety study CARES (TMX-67_301), to compare the cardiovascular outcomes of febuxostat and allopurinol in subjects with gout and cardiovascular comorbidities; this is a Multicenter, Randomized, Active-Control, Phase 3B Study. In addition, the Marketing authorisation holder (MAH) took the opportunity to provide a consolidated Module 2.7.6 in order to list all the synopsis of individual studies in a unique tabular	Request for Supplementary Information adopted with a specific timetable.

format." Request for Supplementary Information adopted on 04.10.2018.	
Brineura - cerliponase alfa - EMEA/H/C/004065/II/0007, Orphan BioMarin International Limited, Rapporteur: Martina Weise, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update the safety information of Brineura in relation to device-related complications and meningitis, and to include meningitis as a possible adverse reaction, based on data collected from clinical trials and post-marketing experience. The package leaflet is updated accordingly." Request for Supplementary Information adopted on 04.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Brineura - cerliponase alfa - EMEA/H/C/004065/II/0011, Orphan BioMarin International Limited, Rapporteur: Martina Weise, "Update of section 4.4 of the SmPC to include a warning in relation to the access device use life following a review of the global safety database for all device-related events. The PL is updated accordingly." Request for Supplementary Information adopted on 18.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Cayston - aztreonam - EMEA/H/C/000996/II/0073, Orphan Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study GX US 205-0128, listed as a category 3 study in the RMP. This is a prospective, observational, 5 year registry study carried out to monitor the susceptibility to aztreonam of Pseudomonas aeruginosa isolates from patients with Cystic Fibrosis in the US. The population eligible for the registry included paediatric subjects, and the final study population included approximately 26% of subjects of less than 18 years of age." Opinion adopted on 18.10.2018. Request for Supplementary Information adopted on 19.07.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cetrotide - cetrorelix - EMEA/H/C/000233/II/0068 Merck Europe B.V., Rapporteur: Martina Weise, "Update of section 4.2 of the SmPC based on literature review to add an alternative option for the treatment initiation to start once the leading	Request for Supplementary Information adopted with a specific timetable.

follicle(s) reach a size that could lead to premature LH (Luteinizing Hormone) surge and ovulation. The Package Leaflet (PL) is updated in accordance. Correction in section 3 of the PL to regarding the timing of ovulation induction. In addition, the Marketing authorisation holder (MAH) took the opportunity to delete the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.0." Request for Supplementary Information adopted on 18.10.2018.	
Darzalex - daratumumab - EMEA/H/C/004077/II/0019, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "Update of sections 4.2, 4.8 and 5.2 of the SmPC in order to include the possibility for a split first dose for the treatment of patients with multiple myeloma, based on the Phase 1b open-label, nonrandomized, multicenter Study 54767414MMY1001. The package leaflet is updated accordingly." Request for Supplementary Information adopted on 18.10.2018.	Request for Supplementary Information adopted with a specific timetable.
IBRANCE - palbociclib - EMEA/H/C/003853/II/0011 Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC to update the clinical efficacy data from pivotal Phase 3 Study A5481008 (PALOMA-2), a study of IBRANCE in combination with letrozoleto, to include the results from recent analyses of the study with a data cutoff date of 31 May 2017. In addition, the MAH took the oportunity to update section 4.2 to include that when coadministered with an aromatase inhibitor, the later should be administered according to the dose schedule reported in the Summary of Product Characteristics." Request for Supplementary Information adopted on 27.09.2018, 26.07.2018, 17.05.2018.	Request for Supplementary Information adopted with a specific timetable.
Isentress - raltegravir - EMEA/H/C/000860/II/0073 Merck Sharp & Dohme B.V., Rapporteur: Greg Markey, "Update of sections 4.6 and 5.3 of the SmPC, upon request by PRAC following the assessment of the latest PSUR	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. See 9.1.

(PSUSA/00010373/201703), to include revised safety information about pregnancy and risk of malformative or foetal toxicity (LEG). The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representative in Belgium in the Package Leaflet." Opinion adopted on 18.10.2018. Request for Supplementary Information adopted on 26.07.2018, 12.04.2018.	
Ivemend - fosaprepitant - EMEA/H/C/000743/II/0040 Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of sections 4.4 of the SmPC in order to update the safety information related to Infusion Site Reactions (ISR) based on reports of post-marketing experience resulting the cumulative search of the company global safety data base for serious adverse events (interventional, spontaneous, literature and non-interventional study reports) which led to a safety labelling change notification issued by the FDA on the 23rd January2018; the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include edits in the SmPC previously and in the Package Leaflet." Request for Supplementary Information adopted on 11.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Kuvan - sapropterin - EMEA/H/C/000943/II/0060, Orphan BioMarin International Limited, Rapporteur: Peter Kiely, "Update of the section 4.8 of the Summary of Product Characteristics (SmPC) to add oesophagitis as a new adverse drug reaction with a frequency unknown. The Package Leaflet (PL) is updated accordingly and editorial changes are made in section 4 of the PL." Opinion adopted on 11.10.2018.	Positive Opinion adopted by consensus on 11.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kuvan - sapropterin - EMEA/H/C/000943/II/0061, Orphan BioMarin International Limited, Rapporteur: Peter Kiely, "Update of section 5.2 of the Summary of Product Characteristics (SmPC) for Kuvan in order to update the information related to the interaction with digoxin (P-gp) when administered concomitanly based on pharmacokinetic study in healthy volunteers." Request for Supplementary Information adopted	Request for Supplementary Information adopted with a specific timetable.

on 18.10.2018.	
Latuda - lurasidone - EMEA/H/C/002713/II/0021 Aziende Chimiche Riunite Angelini Francesco S.p.A., Rapporteur: Filip Josephson, "Update of sections 5.1 of the SmPC to add new paediatric data available in children and adolescent patients (10-17 years of age) with bipolar I disorder, upon request by CHMP following the assessment of the paediatric study D1050326 submitted according to Art. 46 procedure (no. EMEA/H/C/002713/P46/008). In addition, section 4.2 of the SmPC has been updated to cross refer to section 5.1." Opinion adopted on 18.10.2018. Request for Supplementary Information adopted on 20.09.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029/II/0003/G AstraZeneca AB, Rapporteur: Romaldas Mačiulaitis, "1) type II (C.I.4): Update of sections 4.8 and 5.1 of the SmPC in order to update the information based on final results from study ZS-005 (category 3 PASS study in the RMP). This is an open-label, multicentre, multi-dose, prospective maintenance study to investigate the long-term safety and efficacy of Lokelma (sodium zirconium cyclosilicate) in subjects with hyperkalaemia. 2) type II (C.I.4): Update of section 4.5 of the SmPC in order to add information regarding the use with drugs that have the potential for drug-drug interaction based on an increase in gastric PH. The Package Leaflet has been updated accordingly." Request for Supplementary Information adopted on 04.10.2018, 28.06.2018.	Request for Supplementary Information adopted with a specific timetable.
Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0035 GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, "Submission of the final report from study MALARIA-071. This is a phase IIA, open-label, controlled, single-centre, single-country study, to evaluate efficacy, safety, reactogenicity and immunogenicity of GSK Biologicals' candidate malaria vaccine in healthy	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

malaria-naïve adults." Opinion adopted on 04.10.2018.	
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0083 Pfizer Europe MA EEIG, Rapporteur: Greg Markey, "Update of section 4.4 of the SmPC in order to include a safety warning of the risk for invasive disease caused by Meningococcal polysaccharide serogroups A, C, W-135 and Y because of the use of Nimenrix with concomitant treatment of eculizumab." Request for Supplementary Information adopted on 18.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0084 Pfizer Europe MA EEIG, Rapporteur: Greg Markey, "Update of section 4.2 of the SmPC in order to update the posology information in infants, following the final results from study MenACWY-TT-087 (Study 087); this is a phase IIIb, controlled, randomised, open study aimed to demonstrate the immunogenicity and safety of Nimenrix in healthy infants, given on a 3+1 primary and booster (2, 4, 6 and 15-18 months of age), a 1+1 primary and booster (6 and 15-18 months of age) or as a single dose at 15-18 months of age. The Package Leaflet is updated accordingly. The MAH took the opportunity to include editorial changes in sections 4.4 and 4.8 of the SmPC." Request for Supplementary Information adopted on 18.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Ozempic - semaglutide - EMEA/H/C/004174/II/0001 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the final results from the SUSTAIN 7 trial (NN9535-4216), a 40-week open-label trial comparing the safety and efficacy of 0.5 mg of Ozempic to 0.75 mg of dulaglutide and 1 mg of Ozempic to 1.5 mg of dulaglutide in patients on metformin with type-2 diabetes." Opinion adopted on 18.10.2018. Request for Supplementary Information adopted on 13.09.2018, 26.07.2018, 25.05.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
RAVICTI - glycerol phenylbutyrate -	Positive Opinion adopted by consensus on

EMEA/H/C/003822/II/0023, Orphan Horizon Pharma Ireland Limited, Rapporteur: Greg Markey, "Update of section 5.1 of the Summary of Product Characteristics (SmPC) in order to update the efficacy and safety information based on study HPN-100-011, a non randomised, open-label safety extension study on the long term use of HPN-100 in Urea Cycle Disorders. In addition, QRD changes are made in Annex IIIA related to the addition of section 17 and 18 and in line with the QRD template version 10.0" Opinion adopted on 18.10.2018.	18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0046 Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, "Update of the PI to align with the company's Core Safety Data Sheet: · Update of information related to liver function tests, thrombotic and thromboembolic complications, MDS in the section 4.4; · Update of DDI and food interaction information in the sections 4.5 and 5.2; · Update of the section 4.8 by: inclusion and removal of ADRs, changes in some ADRs frequencies following pooling of safety data; · Reorganisation of the section 5.1 in relation to severe aplastic anaemia; · Update of the section 5.3 with information related to Juvenile animal studies. The MAH took the opportunity to make some editorial changes throughout the PI. The Package leaflet is updated accordingly." Request for Supplementary Information adopted on 11.10.2018, 03.05.2018.	Request for Supplementary Information adopted with a specific timetable.
Rubraca - rucaparib - EMEA/H/C/004272/II/0002, Orphan Clovis Oncology UK Limited, Rapporteur: Jorge Camarero Jiménez, "Submission of the final study report (QS-CLV-010) on the exploratory population pharmacokinetic analysis of rucaparib undertaken to test additional semi-mechanistic absorption and distribution models." Request for Supplementary Information adopted on 18.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Stelara - ustekinumab - EMEA/H/C/000958/II/0066 Janssen-Cilag International NV, Rapporteur: Greg Markey, "Update of section 4.8 of the SmPC	Request for Supplementary Information adopted with a specific timetable.

to add allergic alveolitis and eosinophilic pneumonia as rare adverse reaction. The PL is updated accordingly."	
Stribild - elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil - EMEA/H/C/002574/II/0097 Gilead Sciences Ireland UC, Rapporteur: Robert James Hemmings, "Submission of the final report from study GS-US-236-0112, a phase 2/3, open-label study of the pharmacokinetics, safety and antiviral activity of the elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate single tablet regimen (STR) in HIV-1 infected antiretroviral treatment-naive adolescents. This submission fulfils the post-authorisation measures MEA 019 and P46 020." Request for Supplementary Information adopted on 11.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Sutent - sunitinib - EMEA/H/C/000687/II/0070 Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include paediatric study results (from studies A6181196 and ACNS1021) performed in compliance with a paediatric investigation plan (PIP)." Request for Supplementary Information adopted on 27.09.2018.	Request for Supplementary Information adopted with a specific timetable.
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0054/G Biogen Idec Ltd, Rapporteur: Martina Weise, "Type II grouped variation (3xC.I.13) for the submission of results of the below listed studies in order to fulfil LEG 004: 1. RSCH-2018-30: In vitro transcriptional profiling feasibility pilot study to determine the mechanism of action for lymphopenia in dimethyl fumarate-treated patients. 2. DMF-109MS301: Ex vivo transcriptional profiling study to assess the transcriptional changes induced by DMF in whole blood in 109MS301 and 109MS302 cohorts. 3. NLD-BGT-15-10945 (kinetic study): Characterisation of the immune-modulatory effects of Tecfidera in multiple sclerosis patients: exploration of drug mechanism and methodological feasibility." Request for Supplementary Information adopted	Request for Supplementary Information adopted with a specific timetable.

on 18.10.2018.	
VELCADE - bortezomib - EMEA/H/C/000539/II/0088 Janssen-Cilag International NV, Rapporteur: Daniela Melchiorri, “Update of sections 4.2 and 5.1 of the SmPC in order to add a new dosing schedule for VELCADE (bortezomib) in combination with melphalan and prednisone (VMP) for the treatment of patients with newly diagnosed multiple myeloma who are not eligible for high-dose chemotherapy with hematopoetic stem cell transplant. The proposed new dosing schedule is supported by analyses comparing the current approved VcMP schedule (from 26866138MMY3002 [VISTA] study) with pooled modified less intensive ("once-weekly") VcMP schedules (from 54767414MMY3007 [ALCYONE], GIMENA MM-03-05 [GIMENA]). Additional supportive efficacy and safety data come from GEM2005MAS65 [PETHEMA]. The PL (section 3) is amended accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the PL.” Request for Supplementary Information adopted on 26.07.2018, 22.03.2018.	The MAH withdrew the procedure on 16.10.2018.
Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0048 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, “Submission of the final report from study M13-101 listed as a category 3 study in the RMP. This is an open-label study to examine the safety, antiviral activity and pharmacokinetics of Direct-Acting Antiviral Agent (paritaprevir/ritonavir/ombitasvir) treatment in combination with Peginterferon α-2a and Ribavirin (PegIFN/RBV) in Chronic Hepatitis C Virus (HCV) infected patients who had experienced virologic failure while participating in a previous MAH combination study.” Opinion adopted on 18.10.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xadago - safinamide - EMEA/H/C/002396/II/0027 Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.4 and 4.5 of the SmPC in order to implement information regarding interaction of safinamide and rosuvastatin, following results from study	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

CRO-PK-17-318. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Ireland in the Package Leaflet and to include editorial changes in the English, German and Spanish product information." Opinion adopted on 18.10.2018. Request for Supplementary Information adopted on 13.09.2018.	
WS1371 **Rasilez-EMEA/H/C/000780/WS1371/0119** **Rasilez** **HCT-EMEA/H/C/000964/WS1371/0086** Noden Pharma DAC, Lead Rapporteur: Daniela Melchiorri, "Update of sections 4.4, 4.8 and 5.1 of the SmPC of Rasilez and Rasilez/HCTZ SmPC in order to reflect the results from paediatric study CSPP100A2365E2 (a multicenter, 52 to 104 week extension study to evaluate the long term growth and development of pediatric hypertensive patients 6–17 years of age treated previously with aliskiren) provided as per the requirement of article 46. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement minor amendments in sections 4.2, 4.3, 4.5 and 4.7, 5.2 of Rasilez SmPC and package leaflet in alignment with Rasilez/HCTZ product information, as well as an editorial change in Annex II. Moreover, section 4.2 of the Rasilez/HCTZ SmPC has been updated to cross refer to sections 4.8, 5.1, and 5.2 in alignment with Rasilez SmPC." Opinion adopted on 18.10.2018. Request for Supplementary Information adopted on 20.09.2018, 31.05.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1392 **ProQuad-EMEA/H/C/000622/WS1392/0125** MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC of ProQuad and Varivax in order to reflect that complications of varicella from vaccine strain including herpes zoster and disseminated diseases such as aseptic meningitis and encephalitis have been reported in immunocompromised or immunocompetent individuals. The package leaflet is updated accordingly. In addition, the MAH took the	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

opportunity to make some editorial changes in the product information and to update the list of local representatives in the package leaflet." Opinion adopted on 18.10.2018. Request for Supplementary Information adopted on 13.09.2018, 05.07.2018.	
WS1401 **Genvoya-EMEA/H/C/004042/WS1401/0047** **Stribild-EMEA/H/C/002574/WS1401/0094** **Tybost-EMEA/H/C/002572/WS1401/0044** Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings, "Update of section 4.6 the SmPC for Tybost, Stribild and Genvoya based on pharmacokinetics data in pregnancy from IMPAACT study P1026s (ClinicalTrials.gov ID NCT00042289); this is an ongoing, nonrandomized, open-label, parallel-group, multi-centre phase 4 prospective study of antiretroviral (ARV) pharmacokinetics (PK) and safety in HIV-1 infected pregnant women that includes an arm for EVG/COBI. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 11.10.2018, 12.07.2018.	Request for Supplementary Information adopted with a specific timetable.
WS1454 **Zypadhera-EMEA/H/C/000890/WS1454/0035** **Zyprexa-EMEA/H/C/000115/WS1454/0127** **Zyprexa Velotab-EMEA/H/C/000287/WS1454/0095** Eli Lilly Nederland B.V., Duplicate, Duplicate of Olansek (SRD), Lead Rapporteur: Outi Mäki-Ikola, "Update section 4.8 of the SmPC to add stuttering as adverse drug reaction based on data from clinical trials and spontaneous reporting. PL is updated accordingly. In addition, the MAH took this opportunity to revised wording of section 5.2 for smokers to improve clarity." Request for Supplementary Information adopted on 18.10.2018.	Request for Supplementary Information adopted with a specific timetable.
WS1472 **Exviera-EMEA/H/C/003837/WS1472/0040** **Viekirax-EMEA/H/C/003839/WS1472/004**	Request for Supplementary Information adopted with a specific timetable.

9 AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, “Submission of the final report from study M12-999 listed as a category 3 study in the RMP. This is an open-label, phase 2 study to evaluate the safety and efficacy of the combination of of ombitasvir/paritaprevir/ritonavir with or without dasabuvir and with or without ribavirin (RBV) in adult liver or renal transplant recipients with Hepatitis C Virus (HCV) GT1 or GT4 infection (CORAL I).” Request for Supplementary Information adopted on 18.10.2018.	
WS1473 **Exviera-EMEA/H/C/003837/WS1473/0041** **Viekirax-EMEA/H/C/003839/WS1473/0050** AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, “Submission of the final report from study M14-004 listed as a category 3 study in the RMP. This is a multipart, open-label study to evaluate the safety and efficacy of ombitasvir/paritaprevir/ritonavir with or without dasabuvir coadministered with and without ribavirin in adults with Genotype 1 or 4 Chronic Hepatitis C Virus infection and Human Immunodeficiency Virus, Type 1 co-infection (TURQUOISE-I).” Request for Supplementary Information adopted on 18.10.2018.	Request for Supplementary Information adopted with a specific timetable.
WS1474/G **Prezista-EMEA/H/C/000707/WS1474/0098/G** **Rezolsta-EMEA/H/C/002819/WS1474/0027/G** **Symtuza-EMEA/H/C/004391/WS1474/0011/G** Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege, “Update of section 4.3 of the SmPC of Prezista, Rezolsta and Symtuza to contra-indicate the concomitant use with dabigatran, as well as to update section 4.5 of the SmPC of Prezista, Rezolsta and Symtuza on the interaction with edoxaban and dabigatran. Update of section 4.5 of the SmPC of Prezista, Rezolsta and Symtuza on the interaction with Hepatitis C virus direct-acting antivirals: glecaprevir/pibrentasvir.”	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 18.10.2018.	

B.5.3. CHMP-PRAC assessed procedures

Avastin - bevacizumab - EMEA/H/C/000582/II/0106/G Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "1) Type II Variation (C.I.4): Update of section 5.1 of the SmPC to reflect final overall survival data from the long-term follow-up study JO25567 in order to fulfil ANX 085 for study JO29424. 2) Type IB Variation (C.I.11.z): Change in the deadline for the fulfilment of ANX 086 from Q4 2018 to Q2 2019. Annex II.D and the RMP (ver 29.0) have been updated accordingly. The RMP is submitted according to template Rev 2 and consolidates the approved versions (27.1 & 28.1)." Request for Supplementary Information adopted on 18.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Caprelsa - vandetanib - EMEA/H/C/002315/II/0028 Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of sections 4.1, 4.4 and 5.1 of the SmPC in order to delete the information regarding Rearranged during Transfection (RET) mutation. The application addresses SOB 001 and the MAH proposes to revert from conditional marketing authorisation to standard marketing authorisation. Annex II and Package Leaflet are updated accordingly. The RMP version 12.2 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 18.10.2018, 26.04.2018, 14.12.2017.	Request for Supplementary Information adopted with a specific timetable.
Dacogen - decitabine - EMEA/H/C/002221/II/0033, Orphan Janssen-Cilag International N.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of section sections 4.2, 4.8, 5.1 and 5.2 of the SmPC to reflect the results from paediatric study DACOGENAML2004 titled 'Phase 1-2 Safety and Efficacy Study of DACOGEN in sequential administration with	Request for Supplementary Information adopted with a specific timetable.

Cytarabine in children with relapsed or refractory acute myeloid leukemia', provided as per the requirement of article 46. The RMP version 3.1 (in line with the revision 2 of the RMP template) has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.4 of the SmPC to align the safety warning related to sodium excipient with the Annex to the revised European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use'. The Package Leaflet is updated in accordance. Moreover, the contact details of the local representative in Slovenia have been updated in the Package Leaflet." Request for Supplementary Information adopted on 18.10.2018, 26.07.2018, 31.05.2018.	
ELOCTA - efmoroctocog alfa - EMEA/H/C/003964/II/0026 Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Julie Williams, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to add a statement for a once-weekly prophylaxis dose and to update the safety information based on the final results from study 8HA01EXT listed as a category 3 study in the RMP; this is a interventional study that evaluated the long-term safety (particularly immunogenicity) and efficacy of ELOCTA in the prevention and treatment of bleeding episodes and for perioperative management. This variation is a follow-up of P46/005 submitted on 16.04.18 RMP version 2.1 was submitted and followed revision 2 of the template." Request for Supplementary Information adopted on 18.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Entyvio - vedolizumab - EMEA/H/C/002782/II/0034 Takeda Pharma A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Adam Przybylkowski, "Update of section 5.1 of the SmPC in order to provide the final efficacy results up to week 348 regarding clinical study c13008, listed as a category 3 study in the RMP. This is a Phase 3, Open-label Study to Determine the Long-term Safety and Efficacy of Vedolizumab in subjects with Ulcerative Colitis and Crohn's Disease. The RMP version 4 has also been submitted." Request for Supplementary Information adopted	Request for Supplementary Information adopted with a specific timetable.

on 04.10.2018.	
Erbitux - cetuximab - EMEA/H/C/000558/II/0082 Merck KGaA, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "C.I.4) To update sections 4.4 and 4.8. of the SmPC regarding the existing warning on Interstitial lung disease (ILD), by specifying potentially fatal ILD outcome, patients with contributory factors at risk of fatal events and need for close monitoring of these patients. RMP version 19.0 has been submitted in relation to the above changes and also to include changes recommended in latest PSUSA. MAH also took the opportunity to update Annex II-D to delete an obsolete sentence which refers to an RMP to be submitted in 2014." Opinion adopted on 18.10.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
IMVANEX - modified vaccinia ankara virus - EMEA/H/C/002596/II/0035 Bavarian Nordic A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "Update of sections 4.4., 4.8 and 5.1 of the SmPC in order to update the safety information and to add urticaria as an adverse reaction following the final results from study POX-MVA-037 (phase II, randomized, open-label, multicenter trial designed to evaluate the safety and immunogenicity of IMVANEX (MVA-BN smallpox vaccine) when increasing the dose or the number of injections compared with the standard 2-dose regimen in a population of adult, vaccinia naive, immunocompromised subjects with human immunodeficiency virus (HIV) infection) listed as a category 3 study in the RMP (described as post authorisation MEA 007); The RMP version 7.1 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10." Request for Supplementary Information adopted on 04.10.2018.	Request for Supplementary Information adopted with a specific timetable.
IMVANEX - modified vaccinia ankara virus - EMEA/H/C/002596/II/0036 Bavarian Nordic A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update the safety information and to provide confirmation in terms of immunogenicity based on the results from study (POX-MVA-006) (a randomized, open-label phase III non-inferiority	Request for Supplementary Information adopted with a specific timetable.

trial to compare indicators of efficacy for smallpox vaccine to the US licensed replicating smallpox vaccine in 18-42 year old healthy vaccinia-naïve subjects) listed as an obligation in the Annex II (ANX 004); the Package Leaflet is updated accordingly. The RMP version 7.2 has also been submitted." Request for Supplementary Information adopted on 04.10.2018. Clockstop extension of , responses expected 15.01.2019. Adopted.	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0058 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Menno van der Elst, "Update of section 4.4 of the SmPC, to include in the existing warning regarding immune-related adverse reactions the fact that these reactions may be fatal in patients treated with pembrolizumab, as well as minor consequential amendments to increase consistency. The Package Leaflet is being updated accordingly, and for consistency with the already existing statement in the SmPC section 4.4, the Package Leaflet is also being updated to include the fact that immune-related adverse reactions can occur after discontinuation of pembrolizumab treatment. An updated RMP version 20.0 was agreed during the procedure." Opinion adopted on 04.10.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0068 Roche Registration GmbH, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "Submission of the final report from study BH21260 listed as a category 3 study in the RMP (MEA008.5). This is a randomized, controlled, open-label, multicenter, parallel-group study to assess all-cause mortality and cardiovascular morbidity in patients with chronic kidney disease on dialysis and those not on renal replacement therapy under treatment with Mircera® or reference ESAs. The RMP (version 12.0) is updated accordingly and transitioned to the new EU RMP template in line with the revised Good Pharmacovigilance Practice (GVP) Module V (Revision 2) guideline." Request for Supplementary Information adopted	Request for Supplementary Information adopted with a specific timetable.

on 04.10.2018.	
Oncaspar - pegaspargase - EMEA/H/C/003789/II/0016/G Baxalta Innovations GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty, "Update of sections 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC based on the final results from studies DFCI 11-001 and AALL07P4 listed as category 3 studies in the Risk Management Plan: Study DFCI 11-001 is a Phase 2, open-label, randomized, multicenter study to determine the safety and feasibility of administering an investigational asparaginase product (asparaginase formulation) compared with Oncaspar in subjects aged 1 to <22 years with newly diagnosed Acute Lymphoblastic Leukaemia (ALL) and lymphoblastic lymphoma. Study AALL07P4 is a multicenter, open label, randomized, active-controlled, parallel design clinical pilot study conducted to evaluate the pharmacokinetics, pharmacodynamics, safety, immunogenicity and efficacy of an investigational asparaginase product in comparison with Oncaspar in patients aged 1 to <31 years newly diagnosed with high risk B-precursor ALL. The Package Leaflet has been updated accordingly. The RMP version 3.0 has also been submitted." Opinion adopted on 04.10.2018. Request for Supplementary Information adopted on 06.09.2018, 17.05.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Onivyde - irinotecan hydrochloride trihydrate - EMEA/H/C/004125/II/0008, Orphan Baxalta Innovations GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: David Olsen, "Update of sections 1, 2, 4.2, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC in order to reflect the expression of strength based on irinotecan anhydrous free-base. The Labelling and Package Leaflet are updated accordingly. In addition the MAH took the opportunity to introduce minor editorial changes. The updated RMP version 2.1 has also been submitted." Request for Supplementary Information adopted on 18.10.2018, 20.09.2018.	Request for Supplementary Information adopted with a specific timetable.
Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0046	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP

Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams, “Update of sections 4.4 and 4.8 of the SmPC in order to add new warning and safety information about anaphylaxis. RMP version 3.3 was also approved.” Opinion adopted on 04.10.2018. Request for Supplementary Information adopted on 06.09.2018.	Members were in agreement with the CHMP recommendation.
Remicade - infliximab - EMEA/H/C/000240/II/0214 Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Update of the RMP (v 17.0) and Annex II-D of the Product Information to remove the Educational material for health care professionals. In addition, the MAH is taking the opportunity to update the package leaflet with some missing warnings and ADRs already reflected in the SmPC, as requested by CHMP, and to introduce some minor QRD related changes.” Opinion adopted on 18.10.2018. Request for Supplementary Information adopted on 20.09.2018, 26.07.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Reyataz - atazanavir / atazanavir sulfate - EMEA/H/C/000494/II/0117 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, “Submission of the final reports from studies AI424397 (PRINCE I) and AI424451 (PRINCE II) listed as a category 3 studies in the RMP. These studies were phase IIIb, prospective, single arm, open-label, international, multicentre studies to evaluate the safety, efficacy and pharmacokinetics of atazanavir powder boosted with ritonavir and administered with an optimised NRTI background therapy, in HIV infected paediatric patients. The RMP version 15.0 has also been submitted to reflect on the final data from these two paediatric studies. In addition, the MAH took the opportunity to introduce the new RMP template Rev. 2.” Request for Supplementary Information adopted on 04.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0027 Merck Sharp & Dohme B.V., Rapporteur: Bruno	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Sepodes, PRAC Rapporteur: Maria del Pilar Rayon, “Submission of the final results from Bayer study 16099, a prospective, randomised, open-label, active-controlled, multicentre study to evaluate the efficacy and safety of tedlizolid in Japanese patients with MRSA infections (skin and soft tissue infection [SSTI] and SSTI-related bacteraemia) listed as a Post-Authorisation Efficacy Study (PAES) in the RMP. The MAH obligations with regard to this PAES are considered fulfilled. The updated RMP version 5.0, implementing Revision 2 of the RMP template, is adopted.” Opinion adopted on 04.10.2018. Request for Supplementary Information adopted on 14.06.2018.	recommendation.
Vimpat - lacosamide - EMEA/H/C/000863/II/0073/G UCB Pharma S.A., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, “Update of sections 4.4, 4.5 and 4.8 of the SmPC in order to include new safety information on cardiac arrhythmias based on safety signal assessment report (SSAR). Update of section 4.8 of the SmPC to update the frequency of some adverse events (AEs) based on data obtained from the updated safety pool analysis (Pool DBC-1). The Package Leaflet is updated accordingly. The RMP version 13 has also been submitted.” Request for Supplementary Information adopted on 04.10.2018.	Request for Supplementary Information adopted with a specific timetable.
Xolair - omalizumab - EMEA/H/C/000606/II/0092 Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, “Update of sections 4.2, 4.4, 4.6 and 6.6 of the Xolair solution for injection in pre-filled syringe SmPC to allow home use of omalizumab for severe allergic asthma and chronic spontaneous urticaria. This is based on four case series reporting the clinical experience with self-administration of omalizumab. Consequential updates are applied to the SmPC for powder and solvent for solution for injection. Artwork for the outer box, the blister and the syringe label for Xolair solution for injection in pre-filled syringe have been updated to ensure that patients/lay caregiver can more easily distinguish the 2 strengths of Xolair pre-filled syringe. The Package Leaflet and Labelling are	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

updated accordingly. The RMP has been updated to version 13.0." Opinion adopted on 18.10.2018.	

B.5.4. PRAC assessed procedures

PRAC Led **Aclasta - zoledronic acid - EMEA/H/C/000595/II/0069** Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final 5-year report from study (ZOL446H2422) listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study using health registries to compare safety of Aclasta against oral bisphosphonates and untreated population controls." Opinion adopted on 04.10.2018. Request for Supplementary Information adopted on 11.01.2018, 06.07.2017.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0148** Amgen Europe B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Update of annex IID to implement information on education material proposal to address the incorrect self-administration of Aranesp via the SureClick pre-filled pen and associated dosing errors. The RMP (version 9.1) is updated accordingly and aligned to the latest revision 2." Request for Supplementary Information adopted on 04.10.2018.	Request for Supplementary Information adopted with a specific timetable.
PRAC Led **Betmiga - mirabegron - EMEA/H/C/002388/II/0030** Astellas Pharma Europe B.V., Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Submission of the final report of the Drug Utilization Study of mirabegron using real-word healthcare databases from the NL, UK and FI (study 178-PV-002), as agreed via MEA 009.2." Request for Supplementary Information adopted	Request for Supplementary Information adopted with a specific timetable.

on 04.10.2018.	
PRAC Led **Bosulif - bosutinib - EMEA/H/C/002373/II/0030** Pfizer Europe MA EEIG, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "Submission of an updated RMP (finally agreed version 4.4) in line with changes requested by the CHMP following variation II/25/G in fulfilment of REC 014; in addition, the MAH took the opportunity to extend the due date of the Specific Obligation (SOB) study of the conditional marketing authorisation. Annex II has been updated accordingly." Opinion adopted on 18.10.2018. Request for Supplementary Information adopted on 26.07.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/II/0063** Omrix Biopharmaceuticals N. V., PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "C.I.11: Submission of an updated RMP version 14.2 in order to transition to RMP version 2, updated exposure data, updates following PRAC request in accordance to PSUSA/00010297 (removal of lack of efficacy as identified risk), reclassification and/or removal of risk from the safety specification." Request for Supplementary Information adopted on 04.10.2018.	Request for Supplementary Information adopted with a specific timetable.
PRAC Led **Farydak - panobinostat - EMEA/H/C/003725/II/0013, Orphan** Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Submission of an updated RMP version 5.0 in order to remove the commitment to conduct a non-interventional PASS study (LBH589D2408) of panobinostat use in relapsed or relapsed/refractory multiple myeloma patients who have received at least two prior regimens including bortezomib and an immunomodulatory agent in a real-world setting according to the current EU prescribing information and document adherence to dosing regimen (including the	Request for Supplementary Information adopted with a specific timetable.

dosing card, blister pack) by describing clinical characteristics, frequency and severity of the medication error events; listed as a category 3 study in the RMP." Request for Supplementary Information adopted on 04.10.2018.	
PRAC Led **ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0147** Pfizer Europe MA EEIG, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final report from study B1831007 (previously referred to as Study 3082B2-4435-WW) listed as a category 3 study in the RMP. This is a post authorization safety surveillance registry in previously untreated patients with severe hemophilia A in usual care settings, in order to fulfil the post-approval commitment MEA 115." Opinion adopted on 04.10.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Repatha - evolocumab - EMEA/H/C/003766/II/0028** Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Tuomo Lapveteläinen, "Submission of an updated RMP version 5.0 in order to provide the final results of study 20120332 (GAUSS-3, part C), listed as a category 3 study in the RMP. This is a 3-part, phase 3, multicenter, randomized, double-blind, ezetimibe-controlled, parallel-group study. Part C was a 2-year, open-label extension that evaluated the long-term safety and efficacy of evolocumab in hypercholesterolemic subjects unable to tolerate an effective dose of a statin. The MAH has consequentially proposed to remove missing information of use in patients with severe hepatic impairment (Child-Pugh class C) and use in patients with hepatitis C." Request for Supplementary Information adopted on 04.10.2018.	Request for Supplementary Information adopted with a specific timetable.
PRAC Led **Thalidomide Celgene - thalidomide - EMEA/H/C/000823/II/0056, Orphan** Celgene Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni,	Request for Supplementary Information adopted with a specific timetable.

PRAC-CHMP liaison: Alexandre Moreau, “Update of the RMP version 19 in line with the updated Guideline on Good Pharmacovigilance Practices (GVP) Module V to propose the reclassification and/or renaming of known safety concerns associated with the use of thalidomide. Consequently, Annex IID, SmPC section 4.4 and 4.6 and PL have been updated accordingly.” Request for Supplementary Information adopted on 04.10.2018.	
PRAC Led **Votrient - pazopanib - EMEA/H/C/001141/II/0049** Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, “Submission of the final report from the non-interventional post-authorisation safety study PZP034AKR02 to monitor the safety and effectiveness of Votrient in Korea. This study is listed as a category 3 study in the RMP.” Opinion adopted on 04.10.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Votrient - pazopanib - EMEA/H/C/001141/II/0050** Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, “Submission of the final report from the observational study PZP034A2401 ‘A prospective observational study of real world treatment patterns and treatment outcomes in patients with advanced or metastatic renal cell carcinoma receiving pazopanib. This study is listed as a category 3 study in the RMP.” Opinion adopted on 04.10.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1364** **Lyrica-EMEA/H/C/000546/WS1364/0092** **Pregabalin** **Pfizer-EMEA/H/C/003880/WS1364/0021** Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP version 12.0 in order to include the changes proposed by EMEA/H/C/PSUSA/00002511/201701, updating the safety specifications and risk minimisation measures. The pharmacovigilance plan has also	Request for Supplementary Information adopted with a specific timetable.

been updated. The draft protocol for non-interventional non-imposed PASS (A0081359) titled “A population-based cohort study of Pregabalin to characterize pregnancy outcomes” has been submitted. The MAH has taken the opportunity to include minor updates and to align the RMP to template revision 2.” Request for Supplementary Information adopted on 04.10.2018, 17.05.2018.	
PRAC Led **WS1441** **Descovy-EMEA/H/C/004094/WS1441/0034** **Genvoya-EMEA/H/C/004042/WS1441/0051** **Odefsey-EMEA/H/C/004156/WS1441/0035** **Vemlidy-EMEA/H/C/004169/WS1441/0016** Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, “Submission of an updated RMP version 3.1 for Vemlidy, Descovy and Odefsey, as well as version 3.3 for Genvoya according to GVP Module V (revision 2) in order to revise the safety concerns in alignment with the approved RMP for Biktarvy. In addition, the MAH took the opportunity to update category 3 studies and the address of the MAH.” Opinion adopted on 04.10.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.5. CHMP-CAT assessed procedures

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

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

WS1387 **Infanrix hexa-EMEA/H/C/000296/WS1387/0242** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 18.10.2018. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 19.07.2018.	
WS1394 **Hexacima-EMEA/H/C/002702/WS1394/0082** **Hexaxim-EMEA/H/W/002495/WS1394/0087** **Hexyon-EMEA/H/C/002796/WS1394/0086** Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 27.09.2018.	Positive Opinion adopted by consensus on 27.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1421 **Infanrix hexa-EMEA/H/C/000296/WS1421/0244** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 04.10.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1430 **Descovy-EMEA/H/C/004094/WS1430/0033** **Genvoya-EMEA/H/C/004042/WS1430/0049** **Odefsey-EMEA/H/C/004156/WS1430/0034** **Vemlidy-EMEA/H/C/004169/WS1430/0014** Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings Opinion adopted on 04.10.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1435/G **Infanrix hexa-EMEA/H/C/000296/WS1435/0245/G** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 18.10.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1442 **Infanrix hexa-EMEA/H/C/000296/WS1442/0246** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 18.10.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1445 **Kisplyx-EMEA/H/C/004224/WS1445/0017** **Lenvima-EMEA/H/C/003727/WS1445/002**	Request for Supplementary Information adopted with a specific timetable.

0 Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 11.10.2018.	
WS1446 **Kisplyx-EMEA/H/C/004224/WS1446/0016** **Lenvima-EMEA/H/C/003727/WS1446/0019** Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren Opinion adopted on 04.10.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1447 **Atripla-EMEA/H/C/000797/WS1447/0132** **Eviplera-EMEA/H/C/002312/WS1447/0093** **Stribild-EMEA/H/C/002574/WS1447/0096** **Truvada-EMEA/H/C/000594/WS1447/0150** **Viread-EMEA/H/C/000419/WS1447/0192** Gilead Sciences Ireland UC, Lead Rapporteur: Greg Markey Opinion adopted on 04.10.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1457/G **Fertavid-EMEA/H/C/001042/WS1457/0040/G** **Puregon-EMEA/H/C/000086/WS1457/0098/G** Merck Sharp & Dohme B.V., Informed Consent of Puregon, Lead Rapporteur: Nithyanandan Nagercoil Request for Supplementary Information adopted on 11.10.2018.	Request for Supplementary Information adopted with a specific timetable.
WS1458 **Cervarix-EMEA/H/C/000721/WS1458/0097** **Fendrix-EMEA/H/C/000550/WS1458/0065** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 18.10.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1465/G **Abseamed-EMEA/H/C/000727/WS1465/0075/G** **Binocrit-EMEA/H/C/000725/WS1465/0075/G** **Epoetin alfa Hexal-EMEA/H/C/000726/WS1465/0074/**	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

G Sandoz GmbH, Lead Rapporteur: Alexandre Moreau Opinion adopted on 04.10.2018.	
WS1470 **Abseamed-EMEA/H/C/000727/WS1470/0076** **Binocrit-EMEA/H/C/000725/WS1470/0076** **Epoetin alfa** **Hexal-EMEA/H/C/000726/WS1470/0075** Medice Arzneimittel Pütter GmbH & Co. KG, Duplicate, Duplicate of Epoetin alfa Hexal, Lead Rapporteur: Alexandre Moreau Opinion adopted on 04.10.2018.	Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Mosquirix-EMEA/H/W/002300/WS1434/0034 **Shingrix-EMEA/H/C/004336/WS1434/0008** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 27.09.2018.	Positive Opinion adopted by consensus on 27.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Mosquirix-EMEA/H/W/002300/WS1450/0037 **Shingrix-EMEA/H/C/004336/WS1450/0010** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Jan Mueller-Berghaus, Opinion adopted on 18.10.2018.	Positive Opinion adopted by consensus on 18.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0141/G Merck Europe B.V., Rapporteur: Nithyanandan Nagercoil Withdrawal request submitted on 10.10.2018.	The MAH withdrew the procedure on 10.10.2018.
Imraldi - adalimumab - EMEA/H/C/004279/II/0016/G Samsung Bioepis UK Limited (SBUK), Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga Withdrawal request submitted on 16.10.2018.	The MAH withdrew the procedure on 16.10.2018.

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

bortezomib - EMEA/H/C/005074 treatment of multiple myeloma, Generic, Generic of VELCADE	
clopidogrel / acetylsalicylic acid - EMEA/H/C/004996 indicated for the secondary prevention of atherothrombotic indicated for the secondary prevention of atherothrombotic events, Generic, Generic of DuoPlavin	
dolutegravir / lamivudine - EMEA/H/C/004909 treatment of Human Immunodeficiency Virus type 1 (HIV-1)	
fostamatinib - EMEA/H/C/005012 indicated for the treatment of thrombocytopenia	
autologous cd34+ cell enriched population that contains hematopoietic stem cells transduced with lentiglobin bb305 lentiviral vector encoding the beta-a-t87q-globin gene - EMEA/H/C/003691, Orphan, ATMP bluebird bio GmbH, treatment of transfusion-dependent β-thalassaemia (TDT)	**Accelerated review**
clofarabine - EMEA/H/C/005039 treatment of acute lymphoblastic leukaemia, Generic, Generic of Evoltra	
siponimod - EMEA/H/C/004712 , treatment of secondary progressive multiple sclerosis (SPMS),	
omadacycline tosylate - EMEA/H/C/004715 , treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI) in adults.	
netarsudil - EMEA/H/C/004583 , indicated for the reduction of elevated intraocular pressure (IOP) in adults with open-angle glaucoma or ocular hypertension.	

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

Nucala - mepolizumab - EMEA/H/C/003860/X/0018
GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Extension application to introduce a new pharmaceutical form, solution for injection (in pre-filled syringe or in pre-filled pen).”

Pemetrexed Fresenius Kabi - pemetrexed - EMEA/H/C/003895/X/0009
Fresenius Kabi Deutschland GmbH, Generic, Generic of Alimta, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ghania Chamouni, “Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion) associated with new strength 25 mg/ml.”

Tecentriq - atezolizumab - EMEA/H/C/004143/X/0017
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Extension application to add a new strength of 840 mg (60 mg/ml) for Tecentriq concentrate for solution for infusion in a vial and a new indication (metastatic triple-negative breast cancer (TNBC)). The new indication applies only to the 840mg strength.” Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

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

avacopan - EMEA/H/C/004487, Orphan
ChemoCentryx Ltd, induction of response in adult patients with granulomatosis with polyangiitis (Wegener’s) (GPA) or microscopic polyangiitis (MPA)
List of Questions adopted on 26.04.2018.

febuxostat - EMEA/H/C/004773
, treatment of hyperuricaemia, Generic, Generic of Adenuric
List of Questions adopted on 20.09.2018.

pegfilgrastim - EMEA/H/C/004556
, reduction in the duration of neutropenia and the

incidence of febrile neutropenia
List of Questions adopted on 22.03.2018.

Orencia - abatacept - EMEA/H/C/000701/X/0117/G

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Extension application to add 2 new strengths of 50 mg and 87.5 mg for solution for injection in a pre-filled syringe with needle guard, for subcutaneous (SC) administration, grouped with a type II variation (C.I.6.a) to include paediatric use of polyarticular Juvenile Idiopathic Arthritis (2 years and above) for solution for injection (50 mg, 87.5 mg and 125 mg).
The above-described changes are grouped
List of Questions adopted on 26.07.2018.

pegvaliase - EMEA/H/C/004744, Orphan

BioMarin International Limited, treatment of adults with phenylketonuria (PKU) who have inadequate blood phenylalanine control
List of Questions adopted on 26.07.2018.

Simponi - golimumab - EMEA/H/C/000992/X/0083/G

Janssen Biologics B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to add a new strength of 100 mg/ml solution for injection for paediatric use.
C.I.6.a - Extension of indication to include paediatric patients from the age of 2 years and older for the treatment of polyarticular juvenile idiopathic arthritis (pJIA) with Simponi 100 mg/ml solution for injection. As a consequence, sections 4.1, 4.2, 5.1 and section 4.1 of the 50mg strength have been updated accordingly.
C.I.11.z - To update the RMP to version 18.0 to delete the following safety concerns: vasculitis, psoriasis (new onset or worsening of pre-existing), and sarcoidosis/sarcoid like reaction. This change has been agreed by the CHMP in the outcome of variation Type II/068.
C.I.11.z - To update the RMP to version 18.0 to change the due date of the category 3 study MK-8259-050. This change has been agreed by the CHMP in the outcome of MEA033.
In addition, the marketing authorisation holder took the opportunity to:
- update the Product Information in line with the

latest QRD template (version 10);
- implement the recommendations stated in the revised Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' with regards to the excipient Sorbitol (E420);
- add a statement in Section 4.4 of the SmPC to record the name and the batch number of the administered product, in line with Good Pharmacovigilance Practice (GVP) Module PII: Biological medicinal products."
List of Questions adopted on 20.09.2018.

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

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/0035
Pfizer Europe MA EEIG, Rapporteur: Harald Enzmann, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Martin Huber

Deltyba - delamanid -
EMEA/H/C/002552/R/0033, Orphan
Otsuka Novel Products GmbH, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

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

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

ATryn - antithrombin alfa -
EMEA/H/C/000587/II/0036
Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Alexandre Moreau

Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) -
EMEA/H/C/002333/II/0069
GSK Vaccines S.r.l, Rapporteur: Kristina Dunder

Darzalex - daratumumab -
EMEA/H/C/004077/II/0023, Orphan
Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac

Entyvio - vedolizumab -
EMEA/H/C/002782/II/0036/G
Takeda Pharma A/S, Rapporteur: Greg Markey

Fulvestrant Mylan - fulvestrant -
EMEA/H/C/004649/II/0005
Mylan S.A.S, Generic, Generic of Faslodex,
Rapporteur: Natalja Karpova

Humira - adalimumab -
EMEA/H/C/000481/II/0184/G
AbbVie Deutschland GmbH & Co. KG,
Rapporteur: Kristina Dunder

Imfinzi - durvalumab -
EMEA/H/C/004771/II/0001
AstraZeneca AB, Rapporteur: Sinan B. Sarac

InductOs - dibotermin alfa -
EMEA/H/C/000408/II/0093
Medtronic BioPharma B.V., Rapporteur: Johann
Lodewijk Hillege

KANJINTI - trastuzumab -
EMEA/H/C/004361/II/0006/G
Amgen Europe B.V., BREDA, Rapporteur: Jan
Mueller-Berghaus

Kevzara - sarilumab -
EMEA/H/C/004254/II/0010/G
sanofi-aventis groupe, Rapporteur: Jan
Mueller-Berghaus

Metalyse - tenecteplase -
EMEA/H/C/000306/II/0057
Boehringer Ingelheim International GmbH,
Rapporteur: Harald Enzmann

MVASI - bevacizumab -
EMEA/H/C/004728/II/0005/G
Amgen Europe B.V., Duplicate, Duplicate of
KYOMARC, Rapporteur: Svein Rune Andersen

Natpar - parathyroid hormone -
EMEA/H/C/003861/II/0015, Orphan
Shire Pharmaceuticals Ireland Limited,
Rapporteur: Bart Van der Schueren

Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine -
EMEA/H/C/002226/II/0086/G
Pfizer Europe MA EEIG, Rapporteur: Greg Markey

Obizur - susoctocog alfa -
EMEA/H/C/002792/II/0022/G
Baxalta Innovations GmbH, Rapporteur:

Nithyanandan Nagercoil

Ocrevus - ocrelizumab -
EMEA/H/C/004043/II/0007
Roche Registration GmbH, Rapporteur: Mark Ainsworth

Omidria - phenylephrine / ketorolac -
EMEA/H/C/003702/II/0008/G
Omeros London Limited, Rapporteur: Jayne Crowe

Pheburane - sodium phenylbutyrate -
EMEA/H/C/002500/II/0019
Lucane Pharma, Rapporteur: Jayne Crowe

Remsima - infliximab -
EMEA/H/C/002576/II/0060/G
Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey

Stelara - ustekinumab -
EMEA/H/C/000958/II/0070/G
Janssen-Cilag International NV, Rapporteur: Greg Markey

Vizarsin - sildenafil -
EMEA/H/C/001076/II/0029
KRKA, d.d., Novo mesto, Generic, Generic of Viagra, Rapporteur: Alexandre Moreau

Zinplava - bezlotoxumab -
EMEA/H/C/004136/II/0013
Merck Sharp & Dohme B.V., Rapporteur: Jan Mueller-Berghaus

WS1478
Saxenda-EMEA/H/C/003780/WS1478/0019
Victoza-EMEA/H/C/001026/WS1478/0048
Xultophy-EMEA/H/C/002647/WS1478/0027
Novo Nordisk A/S, Lead Rapporteur: Johann Lodewijk Hillege

WS1479/G
Halimatoz-EMEA/H/C/004866/WS1479/0001/G
Hefiya-EMEA/H/C/004865/WS1479/0001/G
Hyrimoz-EMEA/H/C/004320/WS1479/0001/G
Sandoz GmbH, Lead Rapporteur: Milena Stain, Lead PRAC Rapporteur: Ulla Wändel Liminga

WS1480
Rixathon-EMEA/H/C/003903/WS1480/0015
Riximyo-EMEA/H/C/004729/WS1480/0015
Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus

WS1499
Fluenz Tetra-EMEA/H/C/002617/WS1499/0085
Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/WS1499/0018
AstraZeneca AB, Lead Rapporteur: Jan Mueller-Berghaus

WS1502
Fertavid-EMEA/H/C/001042/WS1502/0042
Puregon-EMEA/H/C/000086/WS1502/0100
Merck Sharp & Dohme B.V., Lead Rapporteur: Nithyanandan Nagercoil

WS1503/G
Prezista-EMEA/H/C/000707/WS1503/0100/G
Rezolsta-EMEA/H/C/002819/WS1503/0029/G
Symtuza-EMEA/H/C/004391/WS1503/0013/G
Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege

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

Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0021, Orphan
Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Update of sections 4.8 and 5.1 of the SmPC to include new clinical efficacy and safety data on long-term treatment with Alprolix. The submission includes integrated evaluation of data from the extension study (9HB01EXT (BYOND) which was submitted in a previous P46 procedure) and the pivotal parent studies. The PIL is updated accordingly. In addition, the MAH took the opportunity to update the product information to comply with the latest

version of the “Excipients in the labelling and package leaflet of medicinal products for human use"guideline. The list of local representatives has been updated and other minor editorial changes have been included in the PIL.”

AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0020

sanofi-aventis groupe, Rapporteur: Martina Weise, “Submission of the final report from study LTS 6050. This is a phase 3 long term interventional study to document the safety of two doses of teriflunomide (7 and 14 mg) in patients with multiple sclerosis with relapses.”

Epivir - lamivudine - EMEA/H/C/000107/II/0108

ViiV Healthcare UK Limited, Rapporteur: Joseph Emmerich, “Update of section 4.2 of the SmPC in order to correct the posology of paediatric patients at least 3 months of age and weighting less than 25 kg with renal impairment.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the PI in relation to sodium and propylene glycol content in line with QRD. The package leaflet is updated in accordance.”

Ferriprox - deferiprone - EMEA/H/C/000236/II/0128

Apotex Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, “Update section 4.4 of the SmPC and the patient/carer reminder card in order to update and change the recommended frequency of ANC monitoring throughout Ferriprox treatment from a weekly basis to every week for the first six months of Ferriprox therapy, once every two weeks after six months of Ferriprox therapy, and to monthly after one year of therapy. The package leaflet has been updated accordingly. The RMP version 13.2 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update minor linguistic amendments in the HU and MT product information.”

Halaven - eribulin - EMEA/H/C/002084/II/0047

Eisai GmbH, Rapporteur: Filip Josephson, “Update of section 4.8 of the SmPC in order to add Hypocalcaemia as new adverse reaction with

frequency 'common' as a result of a cumulative review on the matter requested during EMEA/H/C/PSUSA/00001254/201711 procedure (LEG 021). The Package Leaflet is updated accordingly."	
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0042/G Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Submission of an updated RMP version 8 in order to remove MotHER pharmacovigilance activities [MEA 011] from the European Union Risk Management Plan (EU RMP) and use the Global Enhanced Pharmacovigilance (PV) Pregnancy Program to fulfil the commitment (c.1.11.b) and to change the due date of final results for the provision of the final study report for BO27938 (KATHERINE), a category 3 study in the RMP (c.1.11.z). A randomized, multicenter, open label Phase III study to evaluate the efficacy and safety of Trastuzumab emtansine versus trastuzumab as adjuvant therapy for patients with Her2-positive primary breast cancer who have residual tumor present pathologically in the breast or axillary lymph nodes following preoperative therapy to address the following safety concerns: Left ventricular dysfunction, safety in elderly patients, immunogenicity (Anti-therapeutic Antibodies [ATAs] In addition, the MAH takes the opportunity to update the RMP in line with the version 2.0 or new GVP Module V. and include an update of Kadcyla Educational Material to reflect changes in the Prescribing information following the renewal of the marketing authorisation."	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0062 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Update of sections 4.2 and 5.1 of the SmPC to add an alternative dosing regimen of 400 mg every 6 weeks (Q6W) for all approved indications and indications currently under review in addition to the currently approved 200 mg every Q3W, based on modeling and simulation analysis. No new clinical or pre-clinical studies are being submitted as part of the current application. The Package Leaflet (section 3) is	

updated accordingly."

Lartruvo - olaratumab - EMEA/H/C/004216/II/0012, Orphan
Eli Lilly Nederland B.V., Rapporteur: Jorge Camarero Jiménez, "Submission of the final report from Study 15B-EW-JGDI (JGDI) - An Open-Label Study to Evaluate the Pharmacokinetics of Doxorubicin Following the Concomitant Intravenous Administration of Olaratumab (IMC-3G3) to Patients with Advanced Soft Tissue Sarcoma."

Latuda - lurasidone - EMEA/H/C/002713/II/0022
Aziende Chimiche Riunite Angelini Francesco S.p.A., Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to update the safety information following literature review regarding drug interaction between a strong CYP3A4 inhibitor (i.e.posaconazole) and lurasidone."

Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0038
GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, "Submission of the final report from study Malaria-063; this is a phase III randomized, open, controlled study to evaluate the long term immune response to the hepatitis B antigen of the RTS,S/AS01E candidate vaccine, when administered as primary vaccination integrated into an Expanded Program on Immunization (EPI) regimen to infants living in sub-Saharan Africa."

Ongentys - opicapone - EMEA/H/C/002790/II/0015
Bial - Portela & Cª, S.A., Rapporteur: Greg Markey, "Submission of the analytical data results on M10 in patients treated once daily for more than 6 months using a validated analytical method. This variation fulfills the commitment made in REC 002."

OPDIVO - nivolumab - EMEA/H/C/003985/II/0057
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, "Update of section 5.1 of the SmPC in order to include descriptive efficacy data available from study CA209374 (A

Phase 3b/4 Safety Trial of Nivolumab (BMS-936558) in Subjects With Advanced or Metastatic Renal Cell Carcinoma)."

Resolor - prucalopride - EMEA/H/C/001012/II/0046

Shire Pharmaceuticals Ireland Limited, Rapporteur: Greg Markey, "Update of section 4.8 of the SmPC in order to add migraine and vertigo as uncommon adverse events, based on a reanalysis of the integrated safety information of 16 double-blind, placebo-controlled studies.

In addition, the Marketing authorisation holder (MAH) made editorial revision proposals for sections 4.4, 4.6 and 5.2 for alignment with Company Core Data Sheet version 12 and QRD templated wording.

The MAH also took the opportunity to propose minor editorial changes to Package Leaflet and sections 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC."

Tyverb - lapatinib - EMEA/H/C/000795/II/0057

Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update the safety information on pregnancy and breast-feeding following review of the company Core Data Sheet (CDS).The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Estonia and Lithuania in the Package Leaflet. Moreover, the MAH took the opportunity to make minor editorial changes/clarification in labelling for bottle presentations."

Vosevi - sofosbuvir / velpatasvir / voxilaprevir - EMEA/H/C/004350/II/0018

Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC based on final results from study GS-US-367-4181. This is an open-label study to evaluate the safety and efficacy of sofosbuvir/velpatasvir/voxilaprevir fixed-dose combination for 12 weeks in subjects who participated in a prior Gilead-sponsored HCV treatment study."

Zykadia - ceritinib - EMEA/H/C/003819/II/0027

Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, “C.I.13: Submission of the final Biomarker annual update report from phase II studies (A2201 and Study A2203) in order to fulfil the following Post-Marketing Measure identified by the CHMP: To submit a yearly update of the biomarker program for ceritinib.”

WS1468
Mekinist-EMEA/H/C/002643/WS1468/0030
Tafinlar-EMEA/H/C/002604/WS1468/0034
Novartis Europharm Limited, Lead Rapporteur: Paula Boudewina van Hennik, “Update of sections 4.4 and 5.1 of the SmPC in order to reflect study results from study BRF117277, a Phase II, Open-Label, Multicentre Study of Dabrafenib plus Trametinib in Subjects with BRAF Mutation-Positive Melanoma that has Metastasized to the Brain (COMBI-MB).”

WS1488
Segluromet-EMEA/H/C/004314/WS1488/0004
Steglatro-EMEA/H/C/004315/WS1488/0004
Steglujan-EMEA/H/C/004313/WS1488/0006
Merck Sharp & Dohme B.V., Lead Rapporteur: Kristina Dunder, “Submission of the final CSR for Study P007/1017 - a Phase 3, randomized, double-blind, placebo-controlled, 26-week multicenter study with a 78-week extension to evaluate the efficacy and safety of ertugliflozin in subjects with type 2 Diabetes Mellitus and inadequate glycaemic control on metformin monotherapy - together with the final summarized data of all adjudicated confirmed fractures from the broad pool and pooled 2-year safety data from the 7 completed Phase 3 studies, including both 2-year studies P007/1017 and P002/1013.”

WS1495
Lyrica-EMEA/H/C/000546/WS1495/0096
Pregabalin
Pfizer-EMEA/H/C/003880/WS1495/0026
Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.8 and 5.1 of the SmPC in order to reflect information from study A0081042 A Double-Blind,

Placebo-Controlled, Parallel-Group, Multicenter Study of the Efficacy and Safety of Pregabalin as Adjunctive Therapy in Children 1 Month through less than 4 Years of Age with Partial Onset Seizures. This submission relates to paediatric studies submitted according to Article 46 of the paediatric regulation (EC) No 1901/2006."

WS1506/G
Nuwiq-EMEA/H/C/002813/WS1506/0026/G
Vihuma-EMEA/H/C/004459/WS1506/0009/G
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2, 4.8 and 5.1 of the SmPC based on clinical data from studies GENA-21 and GENA-13. The Package Leaflet is updated accordingly."

B.6.10. CHMP-PRAC assessed procedures

Darzalex - daratumumab - EMEA/H/C/004077/II/0020, Orphan
Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Submission of study report of trial SMM2001 - A randomised Phase 2 trial to evaluate 3 daratumumab dose schedules in smouldering multiple myeloma. Consequently, the RMP is updated (version 4.1) in order to remove QTc prolongation as an Important Potential Risk from the RMP."

Darzalex - daratumumab - EMEA/H/C/004077/II/0021, Orphan
Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of section 5.2 of the SmPC to remove the following a sentence from the Immunogenicity subsection regarding the assay detecting anti daratumumab antibodies. WIth this submission the MAH considers MEA-005 to be fulfilled. The RMP is updated accordingly."

Entyvio - vedolizumab - EMEA/H/C/002782/II/0035
Takeda Pharma A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Adam Przybylkowski, "Update of sections 4.2, 4.4, 4.6, 5.1 and 5.3 of the SmPC in order to update the safety information following review of Company Core Data Sheet

and literature review. Update of sections 4.6 and 5.3. is proposed with regards to the information on lactation, based on findings from non-Takeda, recently published data. In addition, the MAH proposed clarifications to other sections of the SmPC. The Package Leaflet is updated accordingly. The MAH also took the opportunity to correct typographical errors, spelling mistakes and other minor updates to the local languages Product Information."	
MabThera - rituximab - EMEA/H/C/000165/II/0157 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Update of Annex II section D of the product information, resulting from the obligation fulfilment for the rituximab subcutaneous formulation at a dose of 1400 mg by the submission of the final clinical study report for study BO22334 (SABRINA, category 1) including reports on long-term safety in relation to body surface area (BSA) (as a measure for exposure variation) and to gender. SABRINA is a two-stage Phase III, international, multi-centre, randomized, controlled, open-label study investigating the pharmacokinetics (PK), efficacy and safety of rituximab SC in combination with cyclophosphamide, doxorubicin, vincristine, prednisolone (CHOP) chemotherapy or cyclophosphamide, vincristine, prednisolone (CVP) chemotherapy versus rituximab IV in combination with CHOP or CVP chemotherapy followed by maintenance treatment with either rituximab SC or rituximab IV.) Furthermore, the RMP version 19.0 has also been updated accordingly to reflect the removal this commitment. In addition, the Marketing authorisation holder (MAH) took the opportunity to include other changes to the RMP including the fulfilment of the previous information on concluded commitments such as the prolonged B-cell depletion and immunogenicity associated with the subcutaneous formulation."	
MabThera - rituximab - EMEA/H/C/000165/II/0158 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Update of Annex II section D of the product information, resulting from the obligation fulfilment for the	

rituximab subcutaneous formulation at a dose of 1400 mg by the submission of the final clinical study report for study BO25341 (SAWYER, category 1) including reports on long-term safety in relation to body surface area (BSA) (as a measure for exposure variation) and to gender. SAWYER is a Phase Ib adaptive, comparative, randomized, parallel-group, multi-center study of subcutaneous (SC) rituximab versus intravenous (IV) rituximab both in combination with chemotherapy (fludarabine and cyclophosphamide), in patients with previously untreated CLL. Furthermore, the RMP version 19.0 has also been updated accordingly to reflect the removal this commitment. In addition, the Marketing authorisation holder (MAH) took the opportunity to include the changes on the concluded commitment such as the prolonged B-cell depletion and immunogenicity associated with the subcutaneous formulation."	
Mimpara - cinacalcet - EMEA/H/C/000570/II/0062/G Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update to Section 4.4 of the SmPC to provide additional information on switching from etelcalcetide to Mimpara (cinacalcet), upon request by PRAC following the assessment of the etelcalcetide PSUR (dated 14 June 2018). Further, the term 'silica, dental type' has been replaced by 'Amorphous silicon dioxide' in SmPC section 6.1. An updated RMP version 9.0 was provided as part of the application in order to align the RMP with the GVP Module V (template Rev 2) with consequential reclassification of existing safety concerns."	
Parsabiv - etelcalcetide - EMEA/H/C/003995/II/0010 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.8 to add convulsions secondary to hypocalceaemia as uncommon adverse reactions and further information on reports related to hypersensitivity reactions. Editorial correction is made to section 7. The Package Leaflet is update accordingly.Consequentially, RMP (version 2) has been submitted to reclassify some of the existing	

safety concerns."

Tremfya - guselkumab -
EMEA/H/C/004271/II/0005

Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.4 and 4.8 of the SmPC in order to add hypersensitivity and rash as adverse drug reactions with the frequency uncommon, together with a statement describing the characteristics of the serious hypersensitivity events. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted."

XGEVA - denosumab -
EMEA/H/C/002173/II/0065

Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.8 of the SmPC to modify the frequency category of the ADR Atypical Femoral Fracture (AFF) from "rare" to "uncommon" and to add descriptive language regarding latency observed in clinical studies. The Package Leaflet has been updated accordingly. In addition, the MAH is taking the opportunity to remove the black triangle and corresponding text from the Annexes as Xgeva is no longer under additional monitoring, to implement editorial changes in the annexes and to update the contact details of the local representative in Ireland in the Package Leaflet.
An updated RMP (version 33) was provided as part of the application."

Xolair - omalizumab -
EMEA/H/C/000606/II/0093

Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of section 4.6 of the SmPC based on the data from the Xolair Pregnancy Registry (EXPECT) and final study report Q2952g listed as a category 3 study in the RMP; this is an observational study to evaluate pregnancy outcomes and estimate the incidence of spontaneous fetal loss in pregnant women exposed to omalizumab prenatally and to explore the potential risk to newborn infants exposed via breast milk.
The Package Leaflet is proposed to be updated accordingly.

The RMP version 14.0 has also been submitted."

Zejula - niraparib -
EMEA/H/C/004249/II/0006, Orphan

Tesaro UK Limited, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Patrick Batty, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to optimise the starting dose of niraparib and clarify dose modification information, modify the existing warning on haematologic adverse reactions, amend the description of thrombocytopenia and amend existing efficacy and pharmacokinetics information, respectively. The changes are based on the integrated Population clinical report that contains information from the completed Phase 3 NOVA, study submitted s part of the initial MAA, as well as supportive information from the ongoing phase 2 PR-30-5020-C (QUADRA) and phase 1 / 2 300-PN-162-01-001 (TOPACIO) studies. The update of the SmPC posology is based on exposure response study reports to propose alternative dosing strategies that aim to reduce Grade 3/4 thrombocytopenia; the Package Leaflet is updated accordingly. The RMP version 1.1 has also been submitted to reflect the new EU RMP format. Furthermore, the core sections of the RMP have been updated to: align with niraparib PSUR 1, reflect post-authorization experience, inclusion of embolic and thrombotic events as important potential risks and to optimize the starting dose of niraparib to reduce adverse events."

Zykadia - ceritinib -
EMEA/H/C/003819/II/0026

Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin, "Update of section 4.5 of the SmPC in order to update the safety information based on final results from study CLDK378A2103, a Post Authorisation Measure Study (MEA 002) which evaluated the effects of ceritinib daily dosing on the pharmacokinetics of the probe drugs midazolam and warfarin, which are metabolised by CYP3A4 and CYP2C9 respectively, in patients with ALK-positive advanced tumors including NSCLC. The Package Leaflet is updated accordingly. The RMP version 14 has also been submitted."

WS1461

Glyxambi-EMEA/H/C/003833/WS1461/0017
Jentadueto-EMEA/H/C/002279/WS1461/0047
Trajenta-EMEA/H/C/002110/WS1461/0035
Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 , 4.8 and 5.1 of the SmPC to update the warnings related to acute pancreatitis and bullous pemphigoid and the efficacy and safety information based on final results from study listed as a category 3 in the RMP "A multicenter, international, randomized, parallel group, double blind, placebo-controlled CArdiovascular Safety & Renal Microvascular outcomE study with LINAgliptin, 5 mg once daily in patients with type 2 diabetes mellitus at high vascular risk (CARMELINA)". The RMP have also been updated accordingly for all products (Trajenta and Jentadueto version 12, Glyxambi version 4.0) and to be in accordance with the revision 2 of the RMP template."

WS1476
Epclusa-EMEA/H/C/004210/WS1476/0028
Harvoni-EMEA/H/C/003850/WS1476/0070
Sovaldi-EMEA/H/C/002798/WS1476/0052
Vosevi-EMEA/H/C/004350/WS1476/0016
Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "Submission of the final report from study GS-US-334-0154, listed as a category 3 study in the RMP. This is a phase 2b randomized, open-label study of 200mg or 400mg sofosbuvir + ribavirin for 24 Weeks in genotype 1 or 3 HCV-infected subjects with renal insufficiency. The RMPs have also been submitted for each of the products in this work-sharing procedure."

B.6.11. PRAC assessed procedures

PRAC Led
alli - orlistat - EMEA/H/C/000854/II/0058
Glaxo Group Ltd, Informed Consent of Xenical, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey,

"Submission of the final report for non-interventional PASS study 204675 "Evaluating the effectiveness of the revised alli pack information in helping pharmacy staff within the EU supply alli appropriately" listed as a category 3 study in the RMP.
In addition, the MAH took the opportunity to update the RMP template in accordance to GVP module V Rev 2 (RMP version 17)."

PRAC Led

Emtriva - emtricitabine -
EMEA/H/C/000533/II/0127

Gilead Sciences Ireland UC, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "C.I.11: Submission of an updated RMP version 9.1 in order to implement Revision 2 of the EU-RMP template and update the safety concerns accordingly. In addition, updates have been made to the Antiretroviral Pregnancy Registry and the Mitochondrial Collaborative Committee (MITOC) study (A Cross-Sectional Study of HIV Negative Children Aged 18-24 Months Born to HIV-1 Infected Mothers in Europe: A European Study Sponsored by the Collaborative Committee for Mitochondrial Toxicity in Children (MITOC)). Finally, the RMP is also updated to reflect the approved transfer of the Marketing Authorisation from Gilead Sciences International Ltd, Cambridge (GSIL) to Gilead Sciences Ireland UC, Cork (GSIUC)."

PRAC Led

Invokana - canagliflozin -
EMEA/H/C/002649/II/0039

Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Provision of final Study Report for non-interventional PASS Study RRA-21430; Acute Pancreatitis Retrospective Observational Epidemiology Cohort Study: Acute pancreatitis in patients with T2DM who are new users of canagliflozin as compared with new users of other AHAs: a retrospective cohort study using large claims databases in the US."

PRAC Led

JETREA - ocriplasmin -
EMEA/H/C/002381/II/0042/G

Oxurion NV, Rapporteur: Greg Markey, PRAC

Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, “C.I.13z: Submission of the final report from ‘ORBIT study (TG-MV-018): Ocriplasmin Research to Better Inform Treatment (ORBIT)’. This is a multicenter, prospective, observational study which assesses clinical outcomes and safety of JETREA® administered in a real-world setting for the treatment of symptomatic VMA.
C.I.13z: Submission of the final report from ‘Use of Intravitreal JETREA® in Clinical Practice: A European Prospective Drug Utilisation Study (TG-MV-017)’ listed as a category 3 study in the RMP. This study is a European, multicentre, observational study. The study includes two parts, a drug utilisation study (DUS) and the Patient Educational Material Evaluation Survey (PEMES). The main objective of the DUS is to document JETREA utilisation patterns in real-life clinical practice. The objective of the PEMES is to assess the effectiveness of the risk minimisation measures (i.e. the patient educational material [PEM] provided to patients prior to the injection of JETREA).
C.I.13z: Submission of the final report from ‘INJECT: INvestigation of JETREA® in Patients with Confirmed Vitreomacular Traction’. This is a non-interventional, multi-centre, worldwide study in patients treated with JETREA® (ocriplasmin) for the approved indication in their country. The aim of the study is to evaluate safety, clinical effectiveness, and HRQoL outcomes in a real world setting among a large population of patients exposed to ocriplasmin across different countries according to country’s approved indications.
In addition, RMP V7.2 has been updated accordingly and the second revision of the RMP template has been implemented as well.”

PRAC Led

Onglyza - saxagliptin -
EMEA/H/C/001039/II/0048

AstraZeneca AB, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP version 14 in order to introduce the new template (EMA/PRAC/613102/2015, GVP Module V, revision 2) and to reclassify or remove some of the safety concerns.”

PRAC Led

Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0040

Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Provision of final Study Report for non-interventional PASS Study RRA-21430; Acute Pancreatitis Retrospective Observational Epidemiology Cohort Study: Acute pancreatitis in patients with T2DM who are new users of canagliflozin as compared with new users of other AHAs: a retrospective cohort study using large claims databases in the US."

B.6.12. CHMP-CAT assessed procedures

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0027, ATMP

"Update of section 4.8 of the SmPC in order to add granulomatous dermatitis as new adverse drug reaction with an uncommon frequency and to update the adverse reaction dyspnoea from dyspnoea exertional to dyspnoea under common frequency."

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

PRAC Led

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0028, ATMP

"Submission of an updated RMP version 4.0 in order to align the important identified and potential risks and missing information with the revised guideline Good Pharmacovigilance Practices Module V (Revision 2), resulting in the reclassification and removal of a number of identified and potential risks and missing information."

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

WS1460

Viagra-EMEA/H/C/000202/WS1460/0099

Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, "To update Section 4.7 "Effects on the ability to drive and use machines " of the current Viagra, Ververti and sildenafil Pfizer (sildenafil citrate) Summaries of Product

Characteristics (SmPCs), to align the content of the SmPC with the requirement of the current European Union (EU) Quality Review of Documents (QRD) template. The package leaflet (PL) has already been updated accordingly."	
WS1466/G **Atripla-EMEA/H/C/000797/WS1466/0133/G** **Biktarvy-EMEA/H/C/004449/WS1466/0002/G** **Descovy-EMEA/H/C/004094/WS1466/0035/G** **Emtriva-EMEA/H/C/000533/WS1466/0126/G** **Eviplera-EMEA/H/C/002312/WS1466/0094/G** **Genvoya-EMEA/H/C/004042/WS1466/0052/G** **Odefsey-EMEA/H/C/004156/WS1466/0036/G** **Stribild-EMEA/H/C/002574/WS1466/0098/G** **Truvada-EMEA/H/C/000594/WS1466/0152/G** Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings	
WS1471/G **Infanrix hexa-EMEA/H/C/000296/WS1471/0248/G** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren,	
WS1481 **Mircera-EMEA/H/C/000739/WS1481/0071** **NeoRecormon-EMEA/H/C/000116/WS1481/0100** Roche Registration GmbH, Lead Rapporteur: Martina Weise	
WS1485/G **Competact-EMEA/H/C/000655/WS1485/0072/G** **Glubrava-EMEA/H/C/000893/WS1485/0058/G** Takeda Pharma A/S, Lead Rapporteur: Peter Kiely,	
WS1486 **Aluvia-EMEA/H/W/000764/WS1486/0106** **Kaletra-EMEA/H/C/000368/WS1486/0173**	

Norvir-EMEA/H/C/000127/WS1486/0151
AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Joseph Emmerich, “To update sections 4.4 Special warnings and precautions for use and 4.8 Undesirable effects of the SmPC with the risk of autoimmune hepatitis as recommended by PRAC (EPITT no: 18956).”

WS1487
Blitzima-EMEA/H/C/004723/WS1487/0017
Ritemvia-EMEA/H/C/004725/WS1487/0017
Rituzena-EMEA/H/C/004724/WS1487/0018
Truxima-EMEA/H/C/004112/WS1487/0019
Celltrion Healthcare Hungary Kft., Duplicate, Duplicate of Truxima, Lead Rapporteur: Sol Ruiz, “B.II.f.1.b) 5 - To extend the shelf-life of the finished product from 30 months to 36 months. The change only applies to the 100 mg presentations.

WS1492
Stribild-EMEA/H/C/002574/WS1492/0104
Truvada-EMEA/H/C/000594/WS1492/0155
Viread-EMEA/H/C/000419/WS1492/0195
Gilead Sciences Ireland UC, Lead Rapporteur: Joseph Emmerich, “To updated the SmPC section 4.8 with final safety data from Study GS-US-104-0352 following the outcome of P46 FUM 277 for Viread. Even though the request was made for Viread, data from this study are also included in the Truvada and Stribild PI therefore these have been updated accordingly.
Furthermore, as safety data from Study GS-US-104-0352 are also present in Section 5.1 of the SmPC, this section was accordingly updated.
For Truvada and Stribild, the MAH has taken this opportunity to update the lactose information text in Section 4.4 of the SmPC and Section 2 of the PIL in line with the latest EC excipient guideline. The chance was already submitted for Viread within procedure EMEA/H/C/000419/II/0191.
Additionally, for Viread a minor administrative edit was made in Section 4.5 of the SmPC, and for all products minor administrative edits were made to Annex III.A.

The requested worksharing procedure proposed amendments to the Summary of Product Characteristics, Labelling and Package Leaflet.”	
WS1507 **Abseamed-EMEA/H/C/000727/WS1507/0078** **Binocrit-EMEA/H/C/000725/WS1507/0078** **Epoetin alfa** **Hexal-EMEA/H/C/000726/WS1507/0077** Sandoz GmbH, Lead Rapporteur: Alexandre Moreau, “To align the Instruction For Use (IFU) to include additional information concerning myelodysplastic syndromes (MDS). The annexes are also brought in line with the QRD general principles regarding the SmPC information for a generic/hybrid/biosimilar product”	
WS1514 **HyQvia-EMEA/H/C/002491/WS1514/0044** **Kiovig-EMEA/H/C/000628/WS1514/0084** Baxalta Innovations GmbH, Lead Rapporteur: Jan Mueller-Berghaus	

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

Time Tables – starting & ongoing procedures: For information

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

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

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

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

G. ANNEX G

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

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

Qualification of Biomarkers:

HTA:

G.2. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 15-18 October 2018 CHMP plenary:

Pneumology-Allergology		
1.	(SME);Treatment of peanut allergy	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Infectious diseases		
2.	Treatment of cytomegalovirus (CMV) infection	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Oncology		
3.	(SME); Treatment of patients with unresectable or metastatic melanoma who have previously been treated with at least two systemic therapies, including a PD-1 blocking antibody and if BRAF V600 mutation positive, a BRAF inhibitor	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Endocrinology-Gynaecology-Fertility-Metabolism		
4.	(SME);Treatment of Hutchinson-Gilford Progeria Syndrome and Progeroid Laminopathies	The CHMP denied eligibility to PRIME and adopted the critical summary report.

Cardiovascular diseases		
5.	(SME); Treatment of acute ischemic stroke	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Dermatology		
6.	(SME); Treatment of Epidermolysis Bullosa	The CHMP denied eligibility to PRIME and adopted the critical summary report.

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

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