23 April 2019
EMA/CHMP/232099/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Final agenda for the meeting on 23-26 April 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

23 April 2019, 13:00 – 19:30, room 1C

24 April 2019, 08:30 – 19:30, room 1C

25 April 2019, 08:30 – 19:30, room 1C

26 April 2019, 08:30 – 15:00, room 1C

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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Table of contents

1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 23-26 April 2019. See (current) April 2019 CHMP minutes (to be published post May 2019 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 23-26 April 2019

1.3. Adoption of the minutes

CHMP minutes for 25-28 March 2019

ORGAM minutes for 15 April 2019

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

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

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

Scope: Possible oral explanation/List of outstanding issues

Action: Possible oral explanation to be held on Wednesday, 24 April 2019 at time 11:00

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

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

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

Scope: Possible oral explanation/List of outstanding issues

Action: Possible oral explanation to be held on Wednesday, 24 April 2019 at time 14:00

List of Outstanding Issues adopted on 31.01.2019, 15.11.2018. List of Questions adopted on 31.05.2018.

2.1.3. edaravone - Orphan - EMEA/H/C/004938

Mitsubishi Tanabe Pharma Europe Ltd; treatment of amyotrophic lateral sclerosis (ALS)

Scope: Oral explanation, List of experts for the SAG Neurology meeting scheduled on 15 April 2019 adopted via written procedure on 12 April 2019

Action: Oral explanation to be held on Wednesday, 24 April 2019 at time 09:00

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 20.09.2018.

2.1.4. glutamine - Orphan - EMEA/H/C/004734

Emmaus Medical Europe Ltd; treatment of sickle cell disease

Scope: Oral explanation

Action: Oral explanation to be held on Thursday, 25 April 2019 at time 09:00

List of Outstanding Issues adopted on 31.01.2019. List of Questions adopted on 28.06.2018.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. ambrisentan - EMEA/H/C/004985

treatment of pulmonary arterial hypertension (PAH)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 20.09.2018.

3.1.2. cabazitaxel - EMEA/H/C/004951

treatment of prostate cancer

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 20.09.2018.

3.1.3. avatrombopag - EMEA/H/C/004722

treatment of thrombocytopenia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 20.09.2018.

3.1.4. dolutegravir / lamivudine - EMEA/H/C/004909

treatment of Human Immunodeficiency Virus type 1 (HIV-1)

Scope: Opinion

Action: For adoption

List of Questions adopted on 31.01.2019.

3.1.5. turoctocog alfa pegol - Orphan - EMEA/H/C/004883

Novo Nordisk A/S; Treatment and prophylaxis of bleeding in patients with haemophilia A

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.03.2019, 15.11.2018. List of Questions adopted on 26.07.2018.

3.1.6. pegfilgrastim - EMEA/H/C/004556

reduction in the duration of neutropenia and the incidence of febrile neutropenia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 13.12.2018. List of Questions adopted on 22.03.2018.

3.1.7. cemiplimab - EMEA/H/C/004844

as monotherapy, indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.03.2019, 31.01.2019. List of Questions adopted on 26.07.2018.

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

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

Scope: Opinion

Action: For adoption

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

3.1.9. buprenorphine - EMEA/H/C/004743

Substitution treatment for opioid drug dependence

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.02.2019, 15.11.2018. List of Questions adopted on 22.03.2018.

3.1.10. ioflupane (^{123}I) - EMEA/H/C/004745

indicated for detecting loss of functional dopaminergic neuron terminals in the striatum

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 20.09.2018.

3.1.11. talazoparib - EMEA/H/C/004674

for the treatment of adult patients with germline breast cancer susceptibility gene (BRCA) mutated human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 20.09.2018.

3.1.12. fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/005254

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

Scope: Opinion

Action: For adoption

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

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 15.11.2018.

3.1.14. hydroxycarbamide - EMEA/H/C/004837

prevention of complications of Sickle Cell disease

Scope: Opinion

Action: For adoption

Oral explanation held on 28.03.2019. List of Outstanding Issues adopted on 28.03.2019, 28.02.2019, 15.11.2018. List of Questions adopted on 28.06.2018.

3.1.15. Zynteglo - Autologous CD34^{+} cells encoding $\beta^{A\text{-}T87Q}$-globin gene- Orphan - ATMP - EMEA/H/C/003691

bluebird bio (Netherlands) B.V.; treatment of transfusion-dependent β-thalassaemia (TDT)

Scope: Re-adoption of opinion

Action: For adoption

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

Opinion adopted on 28.03.2019. List of Questions adopted on 25.01.2019.

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

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

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.11.2018.

3.2.2. glucagon - EMEA/H/C/003848

treatment of severe hypoglycaemia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 13.12.2018.

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

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 18.10.2018.

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

3.3.1. arsenic trioxide - EMEA/H/C/005175

treatment of relapsed acute promyelocytic leukaemia (APL)

Scope: List of questions

Action: For adoption

3.3.2. budesonide / glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004983

as a maintenance treatment in adult patients with moderate to very severe chronic obstructive pulmonary disease (COPD)

Scope: List of questions

Action: For adoption

3.3.3. dexmedetomidine - EMEA/H/C/005152

light to moderate sedation

Scope: List of questions

Action: For adoption

3.3.4. tagraxofusp - Orphan - EMEA/H/C/005031

Accelerated assessment

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

Scope: List of questions

Action: For adoption

3.3.5. polatuzumab vedotin - Orphan - EMEA/H/C/004870

Accelerated assessment

Roche Registration GmbH; treatment of mature B cell lymphomas

Scope: List of questions

Action: For adoption

3.3.6. selinexor - Orphan - EMEA/H/C/005127

Accelerated assessment

Karyopharm Europe GmbH; treatment of patients with relapsed refractory multiple myeloma (RRMM)

Scope: List of questions

Action: For adoption

3.3.7. lifitegrast - EMEA/H/C/004653

treatment of moderate to severe dry eye disease in adults for whom prior artificial tears has not been sufficient

Scope: List of questions

Action: For adoption

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

3.4.1. clofarabine - EMEA/H/C/005039

treatment of acute lymphoblastic leukaemia

Scope: Request by the applicant dated 12.04.2019 requesting an extension to the clock stop to respond to the List of Questions adopted on 31.01.2019.

Action: For adoption

List of Questions adopted on 31.01.2019.

3.4.2. rituximab - EMEA/H/C/004696

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

Scope: Amended time table

Action: For adoption

Amended list of questions adopted on 28.03.2019. List of questions adopted on 13.12.2018.

3.4.3. ibalizumab - EMEA/H/C/004961

treatment of adults infected with HIV-1 resistant to at least 1 agent in 3 different classes

Scope: Updated draft list of experts for the SAG HIV/viral meeting scheduled on 11.04.2019 adopted via written procedure on 5 April 2019

Action: For information

Request for supplementary information adopted on 28.02.2019. List of Questions adopted on 11.12.2018.

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

No items

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

No items

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

4.3.1. Humalog - insulin lispro - EMEA/H/C/000088/X/0169

Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: relates to quality

Action: For adoption

4.3.2. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/X/0075/G

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "Extension application to add a new strength of 25 mg granules in sachet in the treatment of cystic fibrosis in children aged 6 to less than 12 months old.
C.I.4 - To update sections 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC, and sections 2 and 3 of the PL for the 150 mg film-coated tablet presentations to bring it in line with the new dosage form (25 mg granules), which supports the extension of indication for children aged 6 to 12 months old. The RMP (version 8.3) is updated in accordance. In addition, the MAH took the opportunity to implement minor updates in the Product Information."

Action: For adoption

4.3.3. Liprolog - insulin lispro - EMEA/H/C/000393/X/0130

Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: relates to quality

Action: For adoption

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

4.4.1. Remsima - infliximab - EMEA/H/C/002576/X/0062

Celltrion Healthcare Hungary Kft.

Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension application to introduce a new pharmaceutical form (solution for injection), a new strength (120 mg) and a new route of administration (subcutaneous use). The RMP (version 9.1) is updated in accordance."

An updated list of questions was adopted via written procedure on 17.04.2019.

Action: For information

List of Questions adopted on 28.03.2019.

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. Empliciti - elotuzumab - EMEA/H/C/003967/II/0012

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of indication to include treatment in combination with pomalidomide and dexamethasone of adult patients with multiple myeloma. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 4.9, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The RMP (version 2.0) is updated to reflect the new indication.", 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 13.12.2018.

5.1.2. Fiasp - insulin aspart - EMEA/H/C/004046/II/0010

Novo Nordisk A/S

Rapporteur: Kristina Dunder, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include treatment of children and adolescents aged 1 year and above based on data from the phase 3b clinical trial NN1218-4101 (assessed as part of PAM P46-002, fulfilled), supported by data from the Clinical Pharmacology trials NN1218-4371 (PAM P46-003, submitted on the 02-Jan-2019) and NN1218-3888 which was included in the initial MAA. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC and the corresponding sections of the Package Leaflet are updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make other non-related minor or editorial changes throughout the EU PI to increase readability/consistency."

Action: For adoption

5.1.3. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0069

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 first line treatment of advanced or metastatic renal cell carcinoma (RCC) as combination therapy of pembrolizumab together with axitinib based on the results of the first Interim Analysis (IA1) from the pivotal study, KN426, an ongoing, Phase 3, randomized, open-label, multicentre, global study, to evaluate the efficacy and safety of pembrolizumab in combination with axitinib versus sunitinib in previously untreated subjects with advanced/metastatic RCC. It also includes supportive data from KEYNOTE-427 Cohort A (pembrolizumab monotherapy) and a Sponsored Study A4061051 (axitinib monotherapy). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated in order to update the safety information. The Package Leaflet is updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The risk management plan (RMP) Version 24.1 is submitted."

Action: For adoption

5.1.4. Lynparza - olaparib - EMEA/H/C/003726/II/0023

AstraZeneca AB

Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include the use of Lynparza as a monotherapy for the maintenance treatment of adult patients with newly diagnosed advanced BRCA-mutated high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete response or partial response) to first-line platinum-based chemotherapy. As a consequence, sections 4.1 (indication and posology) and 4.8 of the SmPC (summary profile and tabulated list of adverse reactions) are updated in order to include information on a single pivotal Phase 3 study (D0818C00001, referred to as SOLO 1). The Package Leaflet is updated in accordance. The updated pooled safety information for this submission has also been incorporated and aligned in the Capsule SmPC and PL.", 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 28.02.2019, 13.12.2018.

5.1.5. Soliris - eculizumab - Orphan - EMEA/H/C/000791/II/0105

Alexion Europe SAS

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication for Soliris to include treatment of adult patients with Neuromyelitis Optica Spectrum Disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody (Ab) positive. As a consequence the SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, Annex II and package leaflet are revised. The updated RMP version 19 has also been submitted."

Action: For adoption

5.1.6. Stelara - ustekinumab - EMEA/H/C/000958/II/0071

Janssen-Cilag International NV

Rapporteur: Jayne Crowe, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension of indication for Stelara to include treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic or have medical contraindications to such therapies. As a consequence, the SmPC, Package Leaflet and RMP have been updated."

Action: For adoption

5.1.7. WS1539
Ebymect - dapagliflozin / metformin - EMEA/H/C/004162/WS1539/0035
Edistride - dapagliflozin - EMEA/H/C/004161/WS1539/0029
Forxiga - dapagliflozin - EMEA/H/C/002322/WS1539/0048
Xigduo - dapagliflozin / metformin - EMEA/H/C/002672/WS1539/0046

AstraZeneca AB

Lead Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: "Update of sections 4.1, 4.2, 4.4, 4.8, and 5.1 of Forxiga, Edistride, Xigduo and Ebymect of the SmPC to modify the current indication for improvement of glycaemic control based on final results from study D1693C00001 (DECLARE), which is listed as a category 3 study in the RMP (Forxiga: MEA 005): - For the prevention of new or worsening HF or CV death - For the prevention of new or worsening nephropathy; The Package Leaflet (PL) are updated accordingly. The updated dapagliflozin Risk Management Plan (RMP) version 17 and dapagliflozin/metformin fixed dose combination (FDC) RMP version 11 have also been submitted. In addition, the Worksharing Applicant took the opportunity to correct a typo error in Edistride marketing authorisation number in section 8 of SmPC and add the latest renewal date for Xigduo in section 9 of SmPC. Besides, the lactose wording in SmPC section 4.4 has been updated in line with the updated excipient guideline. The revised PI also includes proposal for minor administrative changes for consistency throughout the PI."

Action: For adoption

5.1.8. WS1542
Bretaris Genuair - aclidinium - EMEA/H/C/002706/WS1542/0040
Eklira Genuair - aclidinium - EMEA/H/C/002211/WS1542/0040

AstraZeneca AB

Lead Rapporteur: Ewa Balkowiec Iskra, Lead Co-Rapporteur: Peter Kiely

Scope: "Extension of indication to include reduction of COPD exarcerbations for Eklira Genuair and Bretaris Genuair; as a consequence, sections 4.1, 4.4, 4.8 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Worksharing Applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet for Bretaris Genuair and to implement minor editorial changes in section 4.4, 4.6, 5.3 of the SmPC and section 2 of the PL for both Eklira Genuair and Bretaris Genuair."

Action: For adoption

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

No items

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. lisocabtagene maraleucel - PRIME – Orphan – ATMP - H0004731/0004

Celgene Europe Ltd; intended for the treatment of adult patients with relapsed or refractory large B-cell lymphoma including diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL), and follicular lymphoma grade 3B (FL3B) after at least 2 lines of therapy

Scope: Request for combination pack

Action: For adoption

8.1.2. isatuximab - Orphan - H0004977

sanofi-aventis groupe; Isatuximab in combination with pomalidomide and dexamethasone is indicated for the treatment of patients with refractory or relapsed multiple myeloma who have received at least 2 lines of prior therapy including lenalidomide and a proteasome inhibitor

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

Action: For adoption

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

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Tyverb - lapatinib - EMEA/H/C/000795/II/0059

Novartis Europharm Limited

Rapporteur: Filip Josephson

Scope: "Update of section 5.1 of the SmPC in order to update Table 8 based on updated/corrected results from study EGF114299/LAP016A2307, an interventional study with progression free survival rate as primary objective, original report submitted during procedure EMEA/H/C/00795/II/0051."

Action: For discussion

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

Celgene Europe BV

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: Letter from third party regarding the opinion adopted on 28.03.2019

Action: For information

10. Referral procedures

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

10.1.1. Lartruvo – olaratumab – EMEA/H/A-20/1479/C/4216/015

Eli Lilly Nederland B.V.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Daniela Melchiorri

Scope: Opinion

Action: For adoption

Review of benefit-risk balance following preliminary results of the ANNOUNCE study (I5B-MC-JGDJ) which did not meet the primary endpoint of prolongation of overall survival in the study population.

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

10.2.1. Norethisterone Ethinylestradiol-meta-analysis - EMEA/H/A-5(3)/1477

MAH various

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

Scope: Opinion

Action: For adoption

Request of the UK for a CHMP opinion on a recently published meta-analysis study on the developmental effect of norethisterone acetate and ethinylestradiol and any potential clinical implications on the human foetus.

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

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

MAHs: Galderma Nordic AB

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

Scope: Re-examination, Appointment of Re-examination Rapporteurs

Action: For adoption

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

11. Pharmacovigilance issue

11.1. Early Notification System

April 2019 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

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. CHMP co-opted member

Call for nomination of a CHMP co-opted member with the area of expertise:

Expertise in biostatistics, principally on clinical trial methodology, and at least basic knowledge of the EU regulatory framework

Action: For information

14.1.2. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 8-11 April 2019

Action: For information

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for April 2019

Action: For adoption

14.1.3. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 15-17 April 2019

Action: For information

14.1.4. Paediatric Committee (PDCO)

PIPs reaching D30 at April 2019 PDCO

Action: For information

Report from the PDCO meeting held on 23-26 April 2019

Action: For information

14.1.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 15-17 April 2019

Action: For information

14.1.6. 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 23-25 April 2019

Action: For information

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

14.2.1. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 5 April 2019. Table of conclusions

Action: For information

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

14.2.2. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP April 2019 meeting to CHMP for adoption:

- 6 reports on products in scientific advice and protocol assistance
- 5 reports on products in pre-authorisation procedures

Action: For adoption

14.3. Cooperation within the EU regulatory network

14.3.1. Antimicrobial Advice ad hoc Expert Group (AMEG)

Scope: Overview of comments received by stakeholders during the public consultation on the AMEG scientific advice on the impact on public health and animal health of the use of antibiotics in animals - preliminary risk profiling for new antimicrobials

Action: For information

14.3.2. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Henrike Potthast

CMDh question to PKWP - Biowaiver for oral solutions with the "same concentration"

Action: For adoption

14.4. Cooperation with International Regulators

No items

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

No items

14.6. CHMP work plan

No items

14.7. Planning and reporting

No items

14.8. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Preparedness of the system and capacity increase

Action: For discussion

16. 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)*

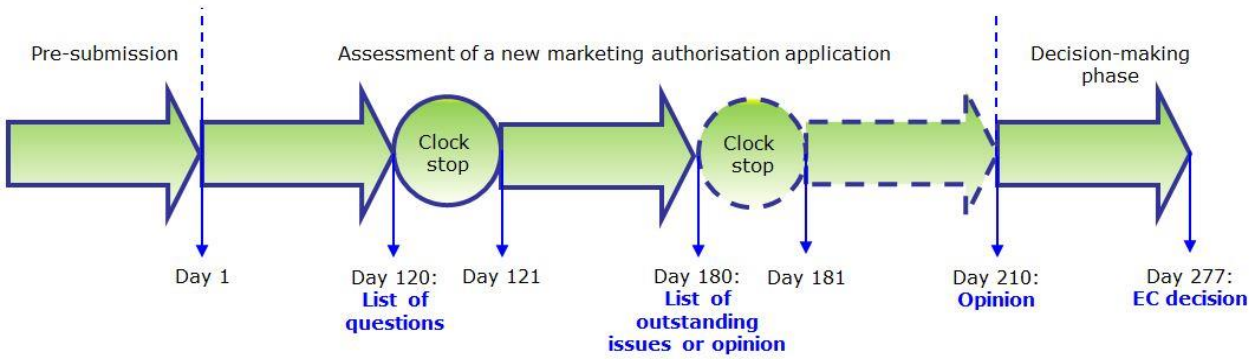
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

23 April 2019
EMA/CHMP/232100/2019

Final Annex to 23-26 April 2019 CHMP Agenda

Pre submission and post authorisations issues

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Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for
April 2019: **For adoption**

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

Final Outcome of Rapporteurship allocation for
April 2019: **For adoption**

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

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

Increlex - mecasermin -
EMEA/H/C/000704/S/0055
Ipsen Pharma, Rapporteur: Outi Mäki-Ikola,
PRAC Rapporteur: Kirsti Villikka
Request for Supplementary Information adopted
on 28.02.2019.

Kolbam - cholic acid -
EMEA/H/C/002081/S/0029, Orphan
Retrophin Europe Ltd, Rapporteur: Constantinos
Markopoulos, PRAC Rapporteur: Agni Kapou

Obizur - susoctocog alfa -
EMEA/H/C/002792/S/0023
Baxalta Innovations GmbH, Rapporteur: Andrea
Laslop, PRAC Rapporteur: Brigitte
Keller-Stanislawski
Request for Supplementary Information adopted
on 28.02.2019.

Orphacol - cholic acid -
EMEA/H/C/001250/S/0026, Orphan
Laboratoires CTRS, Rapporteur: Constantinos
Markopoulos, PRAC Rapporteur: Sofia Trantza
Request for Supplementary Information adopted
on 28.02.2019.

SCENESSE - afamelanotide -
EMEA/H/C/002548/S/0023, Orphan
Clinuvel Europe Limited, Rapporteur: Janet

Koenig, PRAC Rapporteur: Martin Huber

Vyndaqel - tafamidis - EMEA/H/C/002294/S/0047, Orphan
Pfizer Europe MA EEIG, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Ghania Chamouni
Request for Supplementary Information adopted on 28.03.2019.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Adjupanrix - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - EMEA/H/C/001206/R/0062
GlaxoSmithkline Biologicals SA, Informed Consent of Pandemrix (EXP), Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Imbruvica - ibrutinib - EMEA/H/C/003791/R/0049, Orphan
Janssen-Cilag International NV, Rapporteur: Filip Josephson, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Nikica Mirošević Skvrce

Instanyl - fentanyl - EMEA/H/C/000959/R/0049
Takeda Pharma A/S, Rapporteur: Alexandre Moreau, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Ghania Chamouni
Request for Supplementary Information adopted on 31.01.2019.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Accofil - filgrastim - EMEA/H/C/003956/R/0026
Accord Healthcare S.L.U., Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Sol Ruiz, PRAC Rapporteur: Kirsti Villikka

Busulfan Fresenius Kabi - busulfan - EMEA/H/C/002806/R/0010
Fresenius Kabi Deutschland GmbH, Generic, Generic of Busilvex, Rapporteur: John Joseph Borg, PRAC Rapporteur: Eva A. Segovia

Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/R/0063
ViiV Healthcare B.V., Rapporteur: Filip

Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber
Request for Supplementary Information adopted on 28.02.2019.

Trulicity - dulaglutide - EMEA/H/C/002825/R/0036
Eli Lilly Nederland B.V., Rapporteur: Martina Weise, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Amelia Cupelli

Vargatef - nintedanib - EMEA/H/C/002569/R/0025
Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Agni Kapou

Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/R/0028
Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 28.03.2019.

B.2.3. Renewals of Conditional Marketing Authorisations

Bavencio - avelumab - EMEA/H/C/004338/R/0008, Orphan
Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark

Translarna - ataluren - EMEA/H/C/002720/R/0051, Orphan
PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Liana Gross-Martirosyan

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 8-11 April 2019 PRAC:

Signal of recurrent thrombosis in patients with antiphospholipid syndrome

DOACs (Rivaroxaban; apixaban; dabigatran; edoxaban) – Xarelto, Pradaxa, Eliquis, Lixiana, Roteas – PRAC recommendation on a variation

Action: For adoption

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its April 2019 meeting:

EMEA/H/C/PSUSA/00000954/201809
(denosumab (indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer))
CAPS:
Prolia (EMEA/H/C/001120) (denosumab), Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "From: 26/09/2017 To: 26/09/2018"

EMEA/H/C/PSUSA/00001749/201809
(insulin aspart)
CAPS:
Fiasp (EMEA/H/C/004046) (insulin aspart), Novo Nordisk A/S, Rapporteur: Kristina Dunder
NovoMix (EMEA/H/C/000308) (insulin aspart), Novo Nordisk A/S, Rapporteur: Kristina Dunder
NovoRapid (EMEA/H/C/000258) (insulin aspart), Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "From: 01/10/2017 To: 30/09/2018"

EMEA/H/C/PSUSA/00002653/201809
(rivaroxaban)
CAPS:
Xarelto (EMEA/H/C/000944) (rivaroxaban), Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "From: 15/09/2017 To: 15/09/2018"

EMEA/H/C/PSUSA/00010052/201809
(vortioxetine)
CAPS:
Brintellix (EMEA/H/C/002717) (vortioxetine), H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Laurence de Fays, "From: 29/09/2017 To: 29/09/2018"

EMEA/H/C/PSUSA/00010055/201809
(alemtuzumab)
CAPS:

Lemtrada (EMEA/H/C/003718) (alemtuzumab), Sanofi Belgium, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "13-Sep-2017 – 12-Sep-2018"

EMEA/H/C/PSUSA/00010317/201809
(naloxegol)
CAPS:
Moventig (EMEA/H/C/002810) (naloxegol), Kyowa Kirin Holdings B.V., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ronan Grimes, "16-Mar-2018 – 15-Sept-2018"

EMEA/H/C/PSUSA/00010366/201809
(naltrexone / bupropion)
CAPS:
Mysimba (EMEA/H/C/003687) (naltrexone hydrochloride / bupropion hydrochloride), Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber, "From: 10/09/2017 To: 09/09/2018"

EMEA/H/C/PSUSA/00010480/201809
(dexamethasone (centrally authorised product indicated in symptomatic multiple myeloma))
CAPS:
Neofordex (EMEA/H/C/004071) (dexamethasone), Laboratoires CTRS, Rapporteur: Greg Markey, PRAC Rapporteur: Ghania Chamouni, "17-Sep-2017 – 16-Sep-2018"

EMEA/H/C/PSUSA/00010635/201809
(avelumab)
CAPS:
Bavencio (EMEA/H/C/004338) (avelumab), Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark, "From: 22/03/2018 To: 22/09/2018"

EMEA/H/C/PSUSA/00010637/201809
(trientine)
CAPS:
Cuprior (EMEA/H/C/004005) (trientine), GMP-Orphan SA, Rapporteur: Jayne Crowe, PRAC Rapporteur: Ana Sofia Diniz Martins, "06-Mar-2018 – 05-Sep-2018"

EMEA/H/C/PSUSA/00010655/201809
(niraparib)
CAPS:
Zejula (EMEA/H/C/004249) (niraparib), Tesaro Bio Netherlands B.V., Rapporteur: Bjorg Bolstad,

PRAC Rapporteur: Jan Neuhauser, "From: 25/03/2018 To: 25/09/2018"

EMEA/H/C/PSUSA/00010662/201809
(ocrelizumab)
CAPS:
Ocrevus (EMEA/H/C/004043) (ocrelizumab), Roche Registration GmbH, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Brigitte Keller-Stanislawski, "From: 27/03/2018 To: 27/09/2018"

B.4. EPARs / WPARs

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

Apealea - paclitaxel -
EMEA/H/C/004154/II/0003/G
Oasmia Pharmaceutical AB, Rapporteur: Bart Van der Schueren

Benlysta - belimumab -
EMEA/H/C/002015/II/0064/G
GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder

Benlysta - belimumab -
EMEA/H/C/002015/II/0068
GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder

Benlysta - belimumab -
EMEA/H/C/002015/II/0069/G
GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder

Docetaxel Kabi - docetaxel -
EMEA/H/C/002325/II/0022
Fresenius Kabi Deutschland GmbH, Generic, Generic of Taxotere, Rapporteur: Alexandre Moreau
Request for Supplementary Information adopted on 11.04.2019.

Request for supplementary information adopted with a specific timetable.

Entyvio - vedolizumab -
EMEA/H/C/002782/II/0039
Takeda Pharma A/S, Rapporteur: Daniela

Melchiorri	
Flixabi - infliximab - EMEA/H/C/004020/II/0031 Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 27.09.2018.	
Ilumetri - tildrakizumab - EMEA/H/C/004514/II/0005/G Almirall S.A, Rapporteur: Jan Mueller-Berghaus	
Lymphoseek - tilmanocept - EMEA/H/C/002085/II/0017 Norgine B.V., Rapporteur: Jayne Crowe	
Nucala - mepolizumab - EMEA/H/C/003860/II/0023 GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely	
Orencia - abatacept - EMEA/H/C/000701/II/0125 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola	
Praxbind - idarucizumab - EMEA/H/C/003986/II/0014/G Boehringer Ingelheim International GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 04.04.2019. Request for Supplementary Information adopted on 14.02.2019.	Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0145 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus	
ProQuad - measles, mumps, rubella and varicella vaccine (live) - EMEA/H/C/000622/II/0132 MSD Vaccins, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 04.04.2019.	Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Repaglinide Accord - repaglinide - EMEA/H/C/002318/II/0009/G Accord Healthcare S.L.U., Generic, Generic of NovoNorm, Rapporteur: Agnes Gyurasics	
Repatha - evolocumab - EMEA/H/C/003766/II/0026/G Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 17.01.2019, 19.07.2018.	
Simponi - golimumab - EMEA/H/C/000992/II/0087/G Janssen Biologics B.V., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 21.03.2019.	
Synagis - palivizumab - EMEA/H/C/000257/II/0118 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Mark Ainsworth Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 14.02.2019.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TachoSil - human thrombin / human fibrinogen - EMEA/H/C/000505/II/0092 Takeda Austria GmbH, Rapporteur: Jan Mueller-Berghaus	
Trulicity - dulaglutide - EMEA/H/C/002825/II/0033 Eli Lilly Nederland B.V., Rapporteur: Martina Weise Opinion adopted on 04.04.2019. Request for Supplementary Information adopted on 07.02.2019.	Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tysabri - natalizumab - EMEA/H/C/000603/II/0113/G Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 04.04.2019.	Request for supplementary information adopted with a specific timetable.
Visudyne - verteporfin - EMEA/H/C/000305/II/0098/G Novartis Europharm Limited, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 04.04.2019.	Request for supplementary information adopted with a specific timetable.
Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0054/G Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez Request for Supplementary Information adopted on 14.02.2019.	

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

Aclasta - zoledronic acid - EMEA/H/C/000595/II/0072 Novartis Europharm Limited, Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.1 upon request of the CHMP following assessment of P46/036 based on final results from study ZOL446H2337; this is a randomised, double-blind, placebo-controlled efficacy and safety study of intravenous zoledronic acid administered twice yearly compared to placebo in children with glucocorticoid-induced osteoporosis (GIO) which was part of the main clinical measure of the Aclasta Paediatric Investigational Plan (PIP). In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet."	
Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0151 Amgen Europe B.V., Rapporteur: Martina Weise, "Submission of the final analysis of clinical study report (CSR, 10 May 2018) for Study 20110226 to fulfil the post-marketing authorization measure (category 3 pharmacovigilance activity in the Aranesp EU Risk Management Plan (RMP). Study 20110226 is a phase 3, multicenter, randomized, double-blind, parallel group study - START-CKD: Strategies Using Darbepoetin alfa to Avoid Transfusions in Chronic Kidney." Request for Supplementary Information adopted on 04.04.2019.	Request for supplementary information adopted with a specific timetable.
AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0022 sanofi-aventis groupe, Rapporteur: Martina Weise, "Submission of the final report of the nonclinical 7-Week oral administration juvenile toxicity study in the rat (JUV0024 Aubagio), which is part of the agreed PIP for Aubagio (EMEA-001094-PIP01-10)."	
Biktarvy - bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449/II/0011 Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the pooling of 96-week data from two randomized, double-blind, active	

controlled studies GS-US-380-1489 and GS-US-380-1490 in HIV-1 infected, antiretroviral treatment-naïve adults receiving Biktarvy compared with each of the comparator treatment groups (i.e. pooled Biktarvy (BVY) vs abacavir /dolutegravir /lamivudine and pooled BVY vs dolutegravir + emtricitabine/tenofovir alafenamide). In addition the Marketing Authorisation Holder (MAH) took the opportunity to introduce some minor linguistic amendments in the SmPC and the Package Leaflet" Request for Supplementary Information adopted on 28.03.2019.	
CellCept - mycophenolate mofetil - EMEA/H/C/000082/II/0146 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of sections 4.7 and 4.8 of the SmPC to update the safety information based on the reassessment of all available evidence from clinical trials and post-marketing experience, in order to present adverse drug reactions (ADRs) rather than adverse events (AEs). Additionally, section 5.2 of the SmPC is updated based on current literature on the pharmacokinetics in geriatric patients. The Package Leaflet and Labelling are updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to introduce minor editorial changes throughout the PI and to bring the PI in line with the latest QRD template version 10."	
Cerdelga - eliglustat - EMEA/H/C/003724/II/0021, Orphan Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study PKM14281, A Randomized, Three-Period Crossover Study of Single and Repeated Doses for Three Different Strengths of Eliglustat in Healthy Adult, CYP2D6 Extensive and Poor Metabolizers, to characterize dose proportionality of 21, 42 and 84 mg eliglustat dosage strengths, in line with CHMP recommendation." Request for Supplementary Information adopted on 21.03.2019.	
Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0099	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 4.5 of the SmPC in order to update the safety information for the concomitant administration of Cervarix with meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine (Nimenrix), based on results from study MENACWY-TT-054. This is a phase III, open, randomised, controlled, multicentre study aimed to assess the immunogenicity and reactogenicity of Nimenrix administered alone as compared to Nimenrix co-administered with HPV vaccine Cervarix or co-administered with Cervarix and tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed (Boostrix) in female adolescents and adults at 9 to 25 years of age; as requested in the CHMP conclusion of procedure P46/093. The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the package leaflet to correct inconsistencies related to the indication in males." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 14.02.2019.	recommendation.
Cyramza - ramucirumab - EMEA/H/C/002829/II/0030 Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, "Update of section 4.8 of the SmPC in order to add haemangioma and thrombotic microangiopathy (TMA) as new adverse drug reactions as common and rare, respectively based on review of clinical trials, post-marketing cases and the published scientific literature. 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, Latvia and Lithuania in the Package Leaflet." Opinion adopted on 04.04.2019.	Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746/II/0003 Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Submission of the final week 96 report from study P021, a phase 3 multicenter, double-blind, randomized active comparator-controlled clinical trial to evaluate	

the safety and efficacy of MK-1439A once-daily versus ATRIPLA once-daily in treatment-naïve HIV-1 infected patients."	
Dynastat - parecoxib - EMEA/H/C/000381/II/0075 Pfizer Europe MA EEIG, Duplicate, Duplicate of Xapit (SRD), Rapporteur: Jayne Crowe, "Update section 4.4 of the SmPC in regard of the co-administration of NSAIDs and antiplatelet drugs as a class, and the association with an increased risk of gastrointestinal bleeding. The opportunity has been taken for minor editorial amendments to be made in the SmPC, Labelling and Package Leaflet." Opinion adopted on 04.04.2019. Request for Supplementary Information adopted on 17.01.2019.	Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
ELOCTA - efmoroctocog alfa - EMEA/H/C/003964/II/0030 Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2 and 4.8 of the SmPC in order to remove the class wording that no data are available in previously untreated patients and update the frequency category for blood and lymphatic system disorders in previously untreated patients following interim results from study 997HA306, this is an ongoing open-label, single-arm, multicentre study evaluating the safety and efficacy of rFVIIIFc in paediatric previously untreated patients with severe haemophilia A when used according to local standard of care; the Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to delete the non-mandatory list of local representatives." Request for Supplementary Information adopted on 04.04.2019, 31.01.2019.	Request for supplementary information adopted with a specific timetable.
Fasenra - benralizumab - EMEA/H/C/004433/II/0013 AstraZeneca AB, Rapporteur: Fátima Ventura, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the final results from study D3250C00021 (BORA) listed as a category 3 in the RMP; this is a randomised phase 3 study to evaluate the safety and tolerability of benralizumab in asthmatic adults and adolescents on inhaled corticosteroid plus	Request for supplementary information adopted with a specific timetable.

long-acting β2 agnostic. In addition, section 4.2 of the SmPC is updated to reflect the extended PIP waiver age group" Request for Supplementary Information adopted on 11.04.2019, 14.02.2019.	
Kalydeco - ivacaftor - EMEA/H/C/002494/II/0076, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro, "Update of sections 4.4 and 5.1 of the SmPC to clarify the classification of the G970R CFTR mutation as a splicing mutation, based on data from the Study 770-112 G970R substudy (previously submitted in procedure II/54) and an additional mRNA analysis (report N052)." Request for Supplementary Information adopted on 28.02.2019.	
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." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 13.12.2018.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Luminity - perflutren - EMEA/H/C/000654/II/0026 Lantheus EU Limited, Rapporteur: Peter Kiely, "Submission of the final report from study Luminity 422, a category 3 study in the RMP, in order to fulfil MEA 004.4. This is a phase IV, multi-centre, parallel-group, randomised, cross-over trial to compare the efficacy of Luminity and SonoVue in the evaluation of left ventricular border definition." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 14.02.2019.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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	Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

method. This variation fulfils the commitment made in REC 002." Opinion adopted on 04.04.2019. Request for Supplementary Information adopted on 13.12.2018.	
Orgalutran - ganirelix - EMEA/H/C/000274/II/0043 Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, "Update of sections 4.4 and 4.8 of the SmPC to include anaphylaxis (including anaphylactic shock), angioedema, and urticaria under hypersensitivity reactions. In addition, the MAH took the opportunity to include minor editorial corrections in the SmPC and to update the list of local representatives (PT and NL) in the Package Leaflet."	
Pifeltro - doravirine - EMEA/H/C/004747/II/0003 Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Submission of the final week 96 report from study P021, a phase 3 multicenter, double-blind, randomized active comparator-controlled clinical trial to evaluate the safety and efficacy of MK-1439A once-daily versus ATRIPLA once-daily in treatment-naïve HIV-1 infected patients."	
Rubraca - rucaparib - EMEA/H/C/004272/II/0009, Orphan Clovis Oncology Ireland Limited, Rapporteur: Jorge Camarero Jiménez, "Submission of a final report CHVI-283298 describing development and qualification of a test method capable of confirming the absence of monomethyl sulfate (MMS) in fulfilment of a regulatory recommendation." Opinion adopted on 11.04.2019.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0012 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 4.8 of the SmPC in order to add "hypersensitivity reactions including rash, urticaria and angioedema" as an adverse drug reaction with frequency "rare". This update is based on data from clinical trials, literature and post-marketing surveillance reports. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted	

on 14.03.2019.

Strensiq - asfotase alfa - EMEA/H/C/003794/II/0035/G, Orphan

Alexion Europe SAS, Rapporteur: Daniela Melchiorri, "Update of sections 4.4, 4.6, 4.8 and 5.2 of the SmPC with the results of the integrated safety analysis of pooled asfotase alfa clinical studies, and section 5.1 of the SmPC with the final results of study ENB-002-08/ENB-003-08 (an open-label, non-randomised, non-controlled study) and study ENB-010-10 (a controlled, open label study to evaluate the efficacy, safety, and PK of asfotase alfa in infants and children ≤ 5 years of age with hypophosphatasia (HPP)). The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and Package Leaflet."
Request for Supplementary Information adopted on 28.02.2019.

Telzir - fosamprenavir - EMEA/H/C/000534/II/0094/G

ViiV Healthcare B.V., Rapporteur: Joseph Emmerich, "Update of sections 4.3 and 4.5 of the SmPC in order to implement information on a drug-drug interaction between fosamprenavir (with or without ritonavir) and the antipsychotic lurasidone and update of sections 4.4 and 4.5 of the SmPC in order to implement information on a drug-drug interaction between fosamprenavir (with or without ritonavir) and various antineoplastic agents (including dasatinib, nilotinib, ibrutinib, vinblastine, everolimus), based on an assessment of recent safety data. The Package Leaflets are updated accordingly."
Request for Supplementary Information adopted on 31.01.2019.

Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0102

Genzyme Europe BV, Rapporteur: Peter Kiely, "Update of sections 4.4 and 5.1 of the SmPC in order to update the safety information with HiLo and ESTIMABL1 long term follow-up data study results as well as fulfil FUM35. Additionally, the sodium content provision wording in the Package Leaflet is aligned to the Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use" (SANTE-2017-11668).

Few editorial changes are also made and the name of an excipient in the German translation is also corrected."	
Translarna - ataluren - EMEA/H/C/002720/II/0046, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update information on patients with moderate to severe renal impairment based on results from study PTC124-GD-032-HV (MEA010). In addition the MAH took the opportunity to amend section 5.2 to propose correction of the biotransformation statement. The Package leaflet is updated accordingly." Request for Supplementary Information adopted on 28.02.2019, 20.09.2018.	
Tyverb - lapatinib - EMEA/H/C/000795/II/0059 Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update Table 8 based on updated/corrected results from study EGF114299/LAP016A2307, an interventional study with progression free survival rate as primary objective, original report submitted during procedure EMEA/H/C/00795/II/0051."	See agenda 9.1
Victoza - liraglutide - EMEA/H/C/001026/II/0050 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.1 of the SmPC, based on the phase 3b study NN2211-4315 (LIRA-ADD2SGLT2i), to include data on liraglutide vs placebo as add-on to SGLT2 inhibitors (+/- metformin) in subjects with type 2 diabetes mellitus. The Package Leaflet has been updated accordingly."	
Xeloda - capecitabine - EMEA/H/C/000316/II/0081 Roche Registration GmbH, Rapporteur: Janet Koenig, "Update of sections 4.2 and 4.8 of the SmPC in order to update the safety information with an adverse drug reaction that may occur upon accidental exposure to Xeloda crushed or cut tablets. The Package Leaflet is updated accordingly. In addition, the MAH is taking the opportunity to make some editorial changes to the Product Information."	

Request for Supplementary Information adopted on 28.03.2019.	
Xeloda - capecitabine - EMEA/H/C/000316/II/0083 Roche Registration GmbH, Rapporteur: Janet Koenig, "Update of section 4.6 of the SmPC in order to add advice on post treatment contraception period and wash out period before initiation of breastfeeding. The Package leaflet is updated accordingly."	
Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0009, Orphan Ipsen Pharma, Rapporteur: Martina Weise, "Update of sections 4.2 and 5.2 of the SmPC in order to add PK information in subjects with mild, moderate and severe renal impairment based on study D-FR-01017-002 (A Phase I, open-label study to compare the pharmacokinetics of telotristat ethyl and its metabolite in subjects with impaired renal function to healthy subjects with normal renal function after a single dose of telotristat etiprate) (MEA005). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 28.02.2019.	
XGEVA - denosumab - EMEA/H/C/002173/II/0068 Amgen Europe B.V., Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC based on post-marketing experience to include the new ADR 'lichenoid drug eruptions' with a frequency category of 'uncommon'. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in Ireland and Portugal in the Package Leaflet." Opinion adopted on 11.04.2019.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0042 Pfizer Ireland Pharmaceuticals, Rapporteur: Alar Irs, "Update of section 4.8 of the SmPC to include revised frequency of the adverse drug reaction (ADR) eosinophilia from not known to rare. The Package leaflet is updated accordingly." Request for Supplementary Information adopted on 31.01.2019.	
WS1429 **Descovy-EMEA/H/C/004094/WS1429/**	

0032
Genvoya-EMEA/H/C/004042/WS1429/0048
Odefsey-EMEA/H/C/004156/WS1429/0033

Gilead Sciences Ireland UC, Lead Rapporteur: Greg Markey, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with data in patients on chronic haemodialysis from the Study GS-US-292-1825; this is a Phase 3b Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of E/C/F/TAF Fixed Dose Combination (FDC) in HIV-1 Infected Subjects on Chronic Hemodialysis.
The Package Leaflet is updated accordingly.
In addition, the Worksharing Applicant (WSA) took the opportunity to introduce changes to the lactose wording for Genvoya and Odefsey and an administrative correction to the Genvoya Patient information leaflet (PIL) in order to add "lurasidone" to the second list of contra-indicated drugs appearing in the PIL.
The WSA has also taken the opportunity to introduce some minor administrative amendments throughout the product information for all three products as well as to implement some minor linguistic amendments (MLAs) to the translations of the respective product information annexes:
- Genvoya: DE, ES, FI, HR, HU, IS, IT, NO, SL and SV languages
- Descovy: DA, DE, ES, FR, HR, NL, NO, PT and SL languages
- Odefsey: CS, DE, LV, MT, NL, PL, SL and SV languages."
Request for Supplementary Information adopted on 28.02.2019, 20.09.2018.

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."
Request for Supplementary Information adopted on 13.12.2018.

WS1523 **Epclusa-EMEA/H/C/004210/WS1523/0031** **Harvoni-EMEA/H/C/003850/WS1523/0072** **Sovaldi-EMEA/H/C/002798/WS1523/0054** **Vosevi-EMEA/H/C/004350/WS1523/0022** Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, "Update of sections 4.3, 4.4 and 4.5 of the SmPC in order to implement additional guidance on the use of sofosbuvir-based therapy with concomitant drugs, based on final results from study GS-US-334-2130. This was a phase I study to evaluate the effects of cytochrome P450 and drug transporter inducers on sofosbuvir and probe drug pharmacokinetics in healthy subjects. The Package Leaflet is updated accordingly. In addition, the Worksharing Applicant (WSA) took the opportunity to introduce minor editorial changes throughout the Product Information." Request for Supplementary Information adopted on 14.02.2019.	
WS1527/G **Cymbalta-EMEA/H/C/000572/WS1527/0078/G** **Duloxetine Lilly-EMEA/H/C/004000/WS1527/0014/G** **Xeristar-EMEA/H/C/000573/WS1527/0081/G** **Yentreve-EMEA/H/C/000545/WS1527/0063/G** Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim, Yentreve, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, "C.I.4 (Type II) - Update of sections 4.4 and 4.6 of the SmPC in order to add a warning on the risk of postpartum haemorrhage based on final results from study F1J-MC-B057 listed as a category 3 in the RMP; this is an observational study to assess maternal and foetal outcomes following exposure to duloxetine. The Package Leaflet is updated accordingly. C.I.11.z (Type IB) - to stop enrolment of Study F1J-MC-B034 (study B034), another study included in the current EU-RMP Version 12.4 as an additional pharmacovigilance activities to address missing information regarding duloxetine exposure due to pregnancy. The RMP version 13 has also been submitted. In addition, the Worksharing Applicant (WSA)	Request for supplementary information adopted with a specific timetable.

took the opportunity to correct the term "sucrase-isomaltase" in section 4.4 of the SmPC in line with the Annex to the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017 corr. 1*) and to bring the PI in line with the latest QRD template version 10. The Xeristar 30 mg SmPC & Xeristar 60 mg SmPC and the Yentreve 20 mg SmPC & Yentreve 40 mg SmPC have been combined in a single SmPC, respectively, following the Policy on combined SmPCs (EMA/333423/2015)." Request for Supplementary Information adopted on 11.04.2019.	

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: Anette Kirstine Stark, "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 31.01.2019, 18.10.2018.	
Flebogamma DIF - human normal immunoglobulin - EMEA/H/C/000781/II/0059/G Instituto Grifols, S.A., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 4.8 of the SmPC for Flebogamma DIF 100 mg/ml in order to update the safety information based on the final results from study IG0601: A multi-center, prospective, open-label, clinical trial to assess the safety and the efficacy of a new intravenous immune globulin (IGIV3I Grifols 10%) in patients with idiopathic (immune) thrombocytopenic purpura. The Package Leaflet is updated	

accordingly. Update of section 4.8 of the SmPC to revise the adverse drug reactions for both strengths based on all completed studies previously submitted. The Package Leaflet is updated accordingly. Update of SmPC according to the Guideline on core SmPC for human normal immunoglobulin for intravenous administration (IVIg) which came into effect on 01 January 2019. With this submission, the MAH proposes the following changes in alignment with the guideline: - Inclusion of Chronic inflammatory demyelinating polyneuropathy (CIDP) and Multifocal motor neuropathy (MMN) as new therapeutic indications - Modification of Secondary immunodeficiencies (SID) therapeutic indication definition. The Package Leaflet is updated accordingly. The RMP version 7.0 has also been submitted."	
Hulio - adalimumab - EMEA/H/C/004429/II/0004 Mylan S.A.S, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study (FKB327-003) listed as a category 3 study in the RMP. This is an open-label extension study to compare the long term efficacy, safety, immunogenicity and pharmacokinetics of Hulio and Humira in patients with rheumatoid arthritis on concomitant methotrexate (ARABESC-OLE). The RMP version 2.0 is updated accordingly." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 17.01.2019.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
IMVANEX - smallpox vaccine (live modified vaccinia virus ankara) - EMEA/H/C/002596/II/0036 Bavarian Nordic A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "Update of sections 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 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 Annex II is updated accordingly. Minor consequential changes to	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

section 4.4 of the SmPC are introduced and the Package Leaflet is updated accordingly. The RMP version 7.2 has also been submitted." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 14.02.2019, 04.10.2018.	
Intuniv - guanfacine - EMEA/H/C/003759/II/0015 Shire Pharmaceuticals Ireland Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Maria del Pilar Rayon, "Update of section 4.5 of the SmPC in order to remove the statement on potential drug interactions with drugs that inhibit OCT1 based on final results from study V8953M-SPD503; this is a non-clinical study (Transporter Interaction - OCT1 inhibition); The RMP version 3.0 has also been submitted." Request for Supplementary Information adopted on 11.04.2019, 14.02.2019.	Request for supplementary information adopted with a specific timetable.
Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0036 GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné, "Update of section 4.4 of the SmPC in order to indicate that protection against Plasmodium falciparum malaria wanes over time and vaccination may delay the acquisition of natural immunity. In addition, section 5.1 of the SmPC has been updated with long-term efficacy data. This update is based on final results from study MALARIA-076 listed as a category 3 study in the RMP. This was an open extension to the phase III, multi-centre study MALARIA-055 PRI (110021) to evaluate long-term efficacy, safety and immunogenicity of the GSK Biologicals' candidate malaria vaccine in infants and children. The RMP version 4.3 has also been submitted." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 14.02.2019, 31.10.2018.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Movymia - teriparatide - EMEA/H/C/004368/II/0010 STADA Arzneimittel AG, Duplicate, Duplicate of Terrosa, Rapporteur: Milena Stain, PRAC Rapporteur: Ronan Grimes, "Submission of the final clinical study report from Study	Request for supplementary information adopted with a specific timetable.

RGB1023O31; a Phase III, multi-centre, randomised, active-controlled, parallel-group, comparative efficacy/safety study. An updated RMP version 1.3 was provided as part of the application."
Request for Supplementary Information adopted on 11.04.2019.

OPDIVO - nivolumab - EMEA/H/C/003985/II/0060/G

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to include information from studies CA209171 (A Phase 2, single-arm, open-label, multicentre clinical trial with nivolumab monotherapy in subjects with advanced or metastatic squamous (Sq) cell non-small cell lung cancer (NSCLC) who have received at least one prior systemic regimen for the treatment of Stage IIIb/IV Sq NSCLC) and CA209172 (A Phase 2, single-arm, open-label, multicentre clinical trial with nivolumab monotherapy in subjects with histologically confirmed Stage III (unresectable) or Stage IV melanoma progressing after prior treatment containing an anti-CTLA-4 monoclonal antibody). In addition the MAH take the occasion to update annex II to reflect already fulfilled requirement regarding biomarkers data (ANX 005.3, ANX 006, ANX 023, ANX 024, ANX 026 and ANX 027). The RMP has been updated accordingly (submitted version 13.4)."
Request for Supplementary Information adopted on 28.03.2019.

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0022

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.2 and 5.2 of the SmPC in order to add 2 dosing regimens, 840 mg every 2 weeks and 1680 mg every 4 weeks administered as an IV infusion for the approved indications, based on results of population pharmacokinetics modelling and simulation analyses (report No. 1085557) and supported by exposure-response analyses (report No. 1087176). The package leaflet is updated accordingly.
An updated RMP is also provided in order to reflect the proposed new dosing regimens, and to

align the indication statement for metastatic urothelial carcinoma with the SmPC. Moreover, the due date for submission of RMP commitments and an Annex II condition are proposed to be updated."	
Terrosa - teriparatide - EMEA/H/C/003916/II/0009 Gedeon Richter Plc., Rapporteur: Milena Stain, PRAC Rapporteur: Ronan Grimes, "Submission of the final clinical study report from Study RGB1023O31; a Phase III, multi-centre, randomised, active-controlled, parallel-group, comparative efficacy/safety study. An updated RMP version 1.3 was provided as part of the application." Request for Supplementary Information adopted on 11.04.2019.	Request for supplementary information adopted with a specific timetable.
Uptravi - selexipag - EMEA/H/C/003774/II/0022 Janssen-Cilag International N.V., Rapporteur: Martina Weise, PRAC Rapporteur: Adrien Inoubli, "Update of Sections 4.2, 4.4 and 4.5 of the SmPC in order to update the safety information based on the final results from study AC-065-117 a listed category 3 study in the RMP which is a clinical pharmacology drug-drug interaction (DDI) study, evaluating the effect of clopidogrel a moderate inhibitor of CYP2C8, on the pharmacokinetics of selexipag and its active metabolite ACT-333679. The package leaflet is updated accordingly. The RMP version 6.1 has also been submitted. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to correct minor discrepancies in the SmPC." Request for Supplementary Information adopted on 11.04.2019, 14.02.2019.	Request for supplementary information adopted with a specific timetable.
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	Request for supplementary information adopted with a specific timetable.

13 has also been submitted." Request for Supplementary Information adopted on 11.04.2019, 14.02.2019, 04.10.2018.	
WS1490 **IKERVIS-EMEA/H/C/002066/WS1490/0014** **Verkazia-EMEA/H/C/004411/WS1490/0001** Santen Oy, Lead Rapporteur: Peter Kiely, Lead PRAC Rapporteur: Jan Neuhauser, "Submission of an updated RMP version 7.0 in order to implement RMP revision 2 template, as a consequence safety concerns have been updated: all safety concerns were moved from important safety concerns to the new section of Risks not considered important for inclusion in the list of safety concerns in the RMP. The milestones for VERKAZIA PASS have also been updated. In addition, the MAH is proposing to align IKERVIS SmPC section 4.4 on concomitant therapy and effects on immune system with VERKAZIA SmPC in order to harmonize the routine risk minimization measures for both products. The MAH took this opportunity to implement the latest QRD template and the safety features for IKERVIS." Request for Supplementary Information adopted on 11.04.2019, 14.02.2019.	Request for supplementary information adopted with a specific timetable.
WS1518 **Epclusa-EMEA/H/C/004210/WS1518/0034** **Harvoni-EMEA/H/C/003850/WS1518/0077** **Sovaldi-EMEA/H/C/002798/WS1518/0055** **Vosevi-EMEA/H/C/004350/WS1518/0025** Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC (Epclusa, Harvoni), sections 4.2, 4.4, 5.1 and 5.2 (Sovaldi) and 4.2, 4.8 and 5.2 (Vosevi) in order to add new information regarding the use of the sofosbuvir-containing products in patients with renal impairment, based on final results from studies GS-US-342-4062, GS-US-337-4063 and GS-US-334-0154, listed as a category 3 study in the RMP and study GS-US-338-1125. Study GS-US-342-4062 was a phase 2, multi-centre, open-label study to evaluate the	Request for supplementary information adopted with a specific timetable.

efficacy and safety of sofosbuvir/velpatasvir for 12 weeks in subjects with chronic HCV infection who are on dialysis for end stage renal disease. Study GS-US-337-4063 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of ledipasvir/sofosbuvir in subjects with genotype 1, 4, 5 and 6 chronic HCV infection who are on dialysis for end stage renal disease. Study GS-US-334-0154 was a phase 2b, open label study of 200 mg or 400 mg Sofosbuvir+ribavirin for 24 weeks in Genotype 1 or 3 HCV infected subjects with renal insufficiency. Study GS-US-338-1125 was a phase 1, open-label, parallel-group, single-dose study to evaluate the pharmacokinetics of voxilaprevir in subjects with normal renal function and severe renal impairment. The Package Leaflet is updated accordingly. The RMPs have also been submitted for each of the products in this work-sharing procedure." Request for Supplementary Information adopted on 11.04.2019.	

B.5.4. PRAC assessed procedures

PRAC Led **Adasuve - loxapine - EMEA/H/C/002400/II/0030** Ferrer Internacional s.a., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the category 3 final report from Drug Utilization study AMDC-204-403 EU (A Multinational Retrospective Medical Record Review to Evaluate Utilization Patterns of Adasuve-Staccato loxapine for inhalation in agitated persons in routine clinical care). An updated RMP version 9.1 is proposed accordingly." Request for Supplementary Information adopted on 11.04.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Bydureon - exenatide - EMEA/H/C/002020/II/0054** AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

study report, upon request by PRAC following the assessment of MEA 11.5, from study H8O-MC-B015 extension/ D5550R00003; 'Incidence of Pancreatic Malignancy and Thyroid Neoplasm in Type 2 Diabetes Mellitus Patients who Initiate Exenatide Compared to Other Antihyperglycemic Drugs', as well as the feasibility study 'Incidence of pancreatic cancer and thyroid neoplasm among type 2 diabetes patients who initiated Bydureon (exenatide) as compared with those who initiated other glucose lowering drugs'. An updated RMP (version 32) was agreed during the procedure." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 17.01.2019.	
PRAC Led **Flixabi - infliximab - EMEA/H/C/004020/II/0039** Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Update of the RMP to replace the current registries with one company-sponsored initiated registry (PERFUSE) and three IBD registries (CEDUR, CREDIT, and DREAM)" Request for Supplementary Information adopted on 11.04.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Humira - adalimumab - EMEA/H/C/000481/II/0185** AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from The Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT) registry, an ongoing long-term observational cohort study initiated in Germany in 2001 by The German Society of Rheumatology to investigate the long-term safety, effectiveness, and costs of biologic therapies for rheumatoid arthritis, listed as a category 3 study in the RMP." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 17.01.2019.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Kengrexal - cangrelor - EMEA/H/C/003773/II/0015**	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP (version 3.1) in order to revise the objectives, the safety concerns to address and the milestones for a study listed as category 3 in the RMP: a multicentre retrospective observational study of patients undergoing percutaneous coronary intervention (PCI) who receive cangrelor and transition to either clopidogrel, prasugrel or ticagrelo (ARCANGELO – Italian prospective study on cangrelor). The protocol synopsis of the PASS is included in the Annex to the RMP. In addition, the RMP and the list of safety concerns are revised in accordance with the GVP Module V guideline (rev. 2)." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 14.03.2019, 14.02.2019, 06.09.2018.	recommendation.
PRAC Led **Kyprolis - carfilzomib - EMEA/H/C/003790/II/0034, Orphan** Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Nikica Mirošević Skvrce, PRAC-CHMP liaison: Selma Arapovic Dzakula, "Update of the RMP (v.10.1) for Kyprolis to align with the revised guideline GVP Module V (Revision 2), resulting in the reclassification and removal of a number of identified and potential risks and missing information." Opinion adopted on 11.04.2019.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Ozempic - semaglutide - EMEA/H/C/004174/II/0006** Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 3.1 in order to reflect that final protocols for Studies NN9535-4447 and NN9535-4352 have been provided (included as milestones under 'additional pharmacovigilance activities' in the RMP). Further the RMP is updated in line with the new template in accordance with Guideline on GVP Module V – Risk management systems (Rev 2)." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 14.02.2019.	
PRAC Led **Prolia - denosumab - EMEA/H/C/001120/II/0078/G** Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 27 in order to add a retrospective cohort database study as a new category 3 study, upon request by PRAC following the assessment of EMEA/H/C/PSUSA/000954/201709, in order to further characterize the potential increased risk of cerebrovascular events (e.g. stroke) and other serious cardiovascular events in subjects with osteoporosis. Further, the important identified and potential risks and missing information in the RMP have been updated in accordance with the Guideline on GVP Module V – Risk management systems (Rev 2)." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 17.01.2019.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Prolia - denosumab - EMEA/H/C/001120/II/0081** Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 26 in order to amend the study objectives for the category 3 study 20090522 to include the study population 'men and women who receive denosumab with glucocorticoid exposure'. The amended protocol for study 20090522 has also been added to the appropriate annex of the RMP." Opinion adopted on 11.04.2019.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Remicade - infliximab - EMEA/H/C/000240/II/0218** Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final study report on Remicade for the RABBIT Cohort 2 portion of the registry. Rheumatoide Arthritis - Beobachtung der Biologika-Therapie (RABBIT) is a German RA registry established as a prospective	Request for supplementary information adopted with a specific timetable.

observational cohort study on the long-term safety and effectiveness of biologic disease-modifying anti-rheumatic drugs in patients with RA. RMP (v19) was updated with the conclusion of the study. The MAH also revised the list of safety concerns in the RMP as requested in the assessment of LEG 156." Request for Supplementary Information adopted on 11.04.2019, 17.01.2019.	
PRAC Led **Simponi - golimumab - EMEA/H/C/000992/II/0085** Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study (CNTO148ART4002) listed as a category 3 study in the RMP. This is an observational phase 4 study using the Optum Research Database (ORD) to estimate the long-term safety profile in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) who are initiating Simponi treatment and/or other types of biologic and non-biologic treatments. In addition, the RMP (version 19.0) is updated to reflect the final study report from study CNTO148ART4002 and to revise the list of safety concerns in accordance with the GVP Module V guideline (rev. 2)." Request for Supplementary Information adopted on 11.04.2019, 17.01.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS1510 Mirapexin-EMEA/H/C/000134/WS1510/0089 Sifrol-EMEA/H/C/000133/WS1510/0080** Boehringer Ingelheim International GmbH, Lead Rapporteur: Mark Ainsworth, Lead PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "To introduce RMP version 10.0, the RMP has been converted into the new RMP template as per GVP Module V Revision 2 (EMA/838713/2011 Rev 2). In addition, the applicant takes the opportunity to adapt the medical search strategies and data retrieval approach without any impact on the overall safety conclusion." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 14.02.2019.	
PRAC Led **WS1521** **Kivexa-EMEA/H/C/000581/WS1521/0079** **Trizivir-EMEA/H/C/000338/WS1521/0112** **Ziagen-EMEA/H/C/000252/WS1521/0105** ViiV Healthcare B.V., Lead PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, "Submission of an RMP version 1.0 combining the RMPs for Ziagen, Kivexa and Trizivir into one abacavir active-substance RMP and revision of the important identified /potential risk for abacavir containing products in accordance with the revised GVP on RMP version 2, based on the post-marketing data." Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 14.02.2019.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1568** **Relvar Ellipta-EMEA/H/C/002673/ WS1568/0043** **Revinty Ellipta-EMEA/H/C/002745/ WS1568/0041** GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of the final report from study HZC102972 listed as a category 3 study in the RMP. This is a post-authorisation safety study to further characterise the important potential risk of decreased bone mineral density (BMD) and associated fractures with FF/VI in the treatment of chronic obstructive pulmonary disease (COPD) by evaluating the effect of the inhaled corticosteroid fluticasone furoate (FF) on bone mineral density by comparing fluticasone furoate (FF)/vilanterol (VI) treatment with VI treatment in subjects with moderate COPD." Request for Supplementary Information adopted on 11.04.2019.	Request for supplementary information adopted with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0003, Orphan, ATMP

Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, "Update of the sections 4.8, 5.1 of the SmPC to add information based on Phase 1/2 Multicenter Study Evaluating the Safety and Efficacy of KTE-C19 in Subjects with Refractory Aggressive Non-Hodgkin Lymphoma (ZUMA-1), an addendum presenting 24-month analysis. The Package Leaflet has been updated accordingly. Furthermore, editorial changes have been introduced throughout the PI." Request for Supplementary Information adopted on 22.03.2019, 25.01.2019.	
YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0006, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus	

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

WS1493/G **Rivastigmine 1A Pharma-EMEA/H/C/001181/WS1493/0025/G** **Rivastigmine Hexal-EMEA/H/C/001182/WS1493/0026/G** **Rivastigmine Sandoz-EMEA/H/C/001183/WS1493/0027/G** Hexal AG, Informed Consent of Exelon, Lead Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 24.01.2019.	
WS1498/G **Infanrix hexa-EMEA/H/C/000296/WS1498/0252/G** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 04.04.2019.	Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1525 **Hexacima-EMEA/H/C/002702/WS1525/0086** **Hexaxim-EMEA/H/W/002495/WS1525/**	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

0091 **Hexyon-EMEA/H/C/002796/WS1525/0090** Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 11.04.2019. Request for Supplementary Information adopted on 14.02.2019.	
WS1564 **Fiasp-EMEA/H/C/004046/WS1564/0011** **NovoMix-EMEA/H/C/000308/WS1564/0097** **NovoRapid-EMEA/H/C/000258/WS1564/0125** **Ryzodeg-EMEA/H/C/002499/WS1564/0031** Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder Opinion adopted on 04.04.2019.	Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1571 **Keppra-EMEA/H/C/000277/WS1571/0174** UCB Pharma S.A., Lead Rapporteur: Koenraad Norga	
WS1578 **M-M-RVAXPRO-EMEA/H/C/000604/WS1578/0093** **ProQuad-EMEA/H/C/000622/WS1578/0131** MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 04.04.2019.	Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1579 **Axura-EMEA/H/C/000378/WS1579/0081** **Memantine Merz-EMEA/H/C/002711/WS1579/0017** Merz Pharmaceuticals GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro	
WS1580 **Juluca-EMEA/H/C/004427/WS1580/0012** **Tivicay-EMEA/H/C/002753/WS1580/0046** ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson Opinion adopted on 11.04.2019.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1584 **Nuwiq-EMEA/H/C/002813/WS1584/0029** **Vihuma-EMEA/H/C/004459/WS1584/**	

0011 Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus	
WS1604 **Filgrastim** **Hexal-EMEA/H/C/000918/WS1604/0048** **Zarzio-EMEA/H/C/000917/WS1604/0049** Hexal AG, Duplicate, Duplicate of Zarzio, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 04.04.2019.	Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Mosquirix-EMEA/H/W/002300/WS1556/0040/G **Shingrix-EMEA/H/C/004336/WS1556/0014/G** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 11.04.2019.	Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hexacima-EMEA/H/C/002702/WS1574/0087 **Hexaxim-EMEA/H/W/002495/WS1574/0092** **Hexyon-EMEA/H/C/002796/WS1574/0091** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus	

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

PRAC Led **OPDIVO - nivolumab -** **EMEA/H/C/003985/II/0062** Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus Withdrawal request submitted on 03.04.2019.	The MAH withdrew the procedure on 03.04.2019.

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

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

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

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dapagliflozin / saxagliptin / metformin hydrochloride - EMEA/H/C/004910
to improve glycaemic control when metformin with or without sulphonylurea (SU) does not provide adequate glycaemic control and where simultaneous addition of dapagliflozin and saxagliptin is considered necessary - to improve glycaemic control when metformin with or without sulphonylurea (SU) and either dapagliflozin or saxagliptin does not provide adequate glycaemic control - when already being treated with dapagliflozin and saxagliptin and metformin.
List of Questions adopted on 15.11.2018.

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deferasirox - EMEA/H/C/005014
treatment of chronic iron overload,
List of Questions adopted on 15.11.2018.

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erlotinib - EMEA/H/C/005071
treatment of lung and pancreatic cancers
List of Questions adopted on 13.12.2018.

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etanercept - EMEA/H/C/004711
Rheumatoid arthritis, Juvenile idiopathic arthritis, Psoriatic arthritis, Axial spondyloarthritis, Ankylosing spondylitis, Non-radiographic axial spondyloarthritis, Plaque psoriasis, Paediatric plaque psoriasis
List of Questions adopted on 20.09.2018.

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levodopa - EMEA/H/C/004786
treatment of symptoms of OFF periods in Parkinson’s disease
List of Questions adopted on 20.09.2018.

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siponimod - EMEA/H/C/004712
treatment of secondary progressive multiple sclerosis (SPMS)
List of Questions adopted on 31.01.2019.

Nucala - mepolizumab - EMEA/H/C/003860/X/0018

GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski
List of Questions adopted on 31.01.2019.

delafloxacin - EMEA/H/C/004860
treatment of Acute Bacterial Skin and Skin Structure Infection (ABSSSI) in adults
List of Questions adopted on 20.09.2018.

tigecycline - EMEA/H/C/005114
Treatment of soft tissue and intra-abdominal infections
- complicated skin and soft tissue infections, excluding diabetic foot infections
- complicated intra-abdominal infections
should be used only in situations where it is known or suspected that other alternatives are not suitable
List of Questions adopted on 13.12.2018.

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

Evoltra - clofarabine - EMEA/H/C/000613/S/0063
Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Firdapse - amifampridine - EMEA/H/C/001032/S/0064, Orphan
BioMarin International Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Lamzede - velmanase alfa - EMEA/H/C/003922/S/0004, Orphan
Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jan Neuhauser

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

Cosentyx - secukinumab - EMEA/H/C/003729/R/0050
Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Eva A. Segovia

Duavive - estrogens conjugated / bazedoxifene - EMEA/H/C/002314/R/0021

Pfizer Europe MA EEIG, Rapporteur: Martina Weise, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber

Firdapse - amifampridine - EMEA/H/C/001032/R/0062, Orphan
BioMarin International Limited, Rapporteur: Kristina Dunder, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Ulla Wändel Liminga

Lynparza - olaparib - EMEA/H/C/003726/R/0029
AstraZeneca AB, Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli

Otezla - apremilast - EMEA/H/C/003746/R/0027
Celgene Europe BV, Rapporteur: Peter Kiely, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Eva A. Segovia

Rasagiline ratiopharm - rasagiline - EMEA/H/C/003957/R/0014
Teva B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Ana Sofia Diniz Martins

Rixubis - nonacog gamma - EMEA/H/C/003771/R/0029
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski

Trevicta - paliperidone - EMEA/H/C/004066/R/0022
Janssen-Cilag International NV, Informed Consent of Xeplion, Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga

Zalmoxis - nalotimagene carmaleucel - EMEA/H/C/002801/R/0015, Orphan, ATMP
MolMed S.p.A, Rapporteur: Johannes Hendrikus Ovelgonne, Co-Rapporteur: Sol Ruiz, CHMP Coordinators: Paula Boudewina van Hennik and Maria Concepcion Prieto Yerro, PRAC Rapporteur: Brigitte Keller-Stanislawski

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

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

Dupixent - dupilumab - EMEA/H/C/004390/II/0017 sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Kimmo Jaakkola, "Extension of Indication to include a new indication in adults patients with Chronic rhinosinusitis with nasal polyposis. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated RMP is submitted (V 4.0)"	
OFEV - nintedanib - EMEA/H/C/003821/II/0026, Orphan Boehringer Ingelheim International GmbH, Rapporteur: Jayne Crowe, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce, "Extension of indication to include new indication for OFEV for the treatment of Systemic Sclerosis associated Interstitial Lung Disease (SSc-ILD). As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The MAH takes this opportunity to also introduce minor linguistic corrections to the Annexes for France and Sweden. The RMP version 7.0 has also been submitted." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	
Suliqua - insulin glargine / lixisenatide - EMEA/H/C/004243/II/0011 sanofi-aventis groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "Extension of indication to include treatment in combination with metformin of adults with type 2 diabetes mellitus to improve glycaemic control when this has not been provided by metformin alone or metformin combined with another oral glucose lowering medicinal product or basal insulin, based on the phase 3 Study EFC13794; a 26-week randomized, open-label, active controlled, parallel-group, study assessing the efficacy and safety of the insulin glargine/lixisenatide fixed ratio combination in	

adults with Type 2 Diabetes inadequately controlled on GLP-1 receptor agonist and metformin (alone or with pioglitazone and/or SGLT2 inhibitors), followed by a fixed ratio combination single-arm 26-week extension period. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated and the Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to update the contact details of the local representatives in Denmark, the Netherlands and the UK in the Package Leaflet and to implement minor editorial changes in the annexes. An updated RMP version 4.0 was provided as part of the application."	
Toujeo - insulin glargine - EMEA/H/C/000309/II/0108 Sanofi-Aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Extension of indication to include new population for Toujeo. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance."	
WS1550 **Docetaxel Zentiva-EMEA/H/C/000808/ WS1550/0058** **Taxotere-EMEA/H/C/000073/WS1550/ 0131** Aventis Pharma S.A., Lead Rapporteur: Alexandre Moreau, Lead Co-Rapporteur: Janet Koenig, Lead PRAC Rapporteur: Ghania Chamouni, "Extension of indication to include in combination with androgen-deprivation therapy (ADT), with or without prednisone or prednisolone, for the treatment of patients with metastatic hormone-sensitive prostate cancer for Taxotere and Docetaxel Zentiva; as a consequence, sections 4.1, 4.2, 4.4 and 4.8 of the SmPC are updated. The Package Leaflet is updated accordingly. The RMP version has also been submitted. In addition, the Worksharing Applicant took the opportunity to update information impacting the local representatives in the packages leaflets."	

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Adcetris - brentuximab vedotin -
EMEA/H/C/002455/II/0066, Orphan
Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik

BeneFIX - nonacog alfa -
EMEA/H/C/000139/II/0160
Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus

Hemoblast - thrombin -
EMEA/H/D/002769/II/0006/G
BSI Group, Rapporteur: Daniela Melchiorri

Hulio - adalimumab -
EMEA/H/C/004429/II/0010/G
Mylan S.A.S, Rapporteur: Bart Van der Schueren

Keppra - levetiracetam -
EMEA/H/C/000277/II/0178/G
UCB Pharma S.A., Rapporteur: Koenraad Norga

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0073
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri

Ogivri - trastuzumab -
EMEA/H/C/004916/II/0006/G
MYLAN S.A.S, Rapporteur: Koenraad Norga

Onpattro - patisiran -
EMEA/H/C/004699/II/0004/G, Orphan
Alnylam Netherlands B.V., Rapporteur: Kristina Dunder

Ovitrelle - choriogonadotropin alfa -
EMEA/H/C/000320/II/0078
Merck Europe B.V., Rapporteur: Paula Boudewina van Hennik

Thyrogen - thyrotropin alfa -
EMEA/H/C/000220/II/0104/G
Genzyme Europe BV, Rapporteur: Peter Kiely

Zessly - infliximab -
EMEA/H/C/004647/II/0007
Sandoz GmbH, Rapporteur: Bjorg Bolstad

Zytiga - abiraterone acetate -
EMEA/H/C/002321/II/0056/G
Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez

WS1620

Humalog-EMEA/H/C/000088/WS1620/0175
Liprolog-EMEA/H/C/000393/WS1620/0136
Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder

WS1625/G
Blitzima-EMEA/H/C/004723/WS1625/0025/G
Ritemvia-EMEA/H/C/004725/WS1625/0025/G
Truxima-EMEA/H/C/004112/WS1625/0028/G
Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz

Hexacima-EMEA/H/C/002702/WS1575/0088/G
Hexaxim-EMEA/H/W/002495/WS1575/0093/G
Hexyon-EMEA/H/C/002796/WS1575/0092/G
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

Hexacima-EMEA/H/C/002702/WS1592/0089/G
Hexaxim-EMEA/H/W/002495/WS1592/0094/G
Hexyon-EMEA/H/C/002796/WS1592/0093/G
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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

Advagraf - tacrolimus - EMEA/H/C/000712/II/0054
Astellas Pharma Europe B.V., Rapporteur: Jayne Crowe, "Update of section 4.2 of the SmPC to include a more clear statement for physicians regarding the potential risk of uncontrolled substitution between different tacrolimus formulations, even with those where BE has been proven, in order to minimise the risk of under or over exposure to tacrolimus."

Brilique - ticagrelor - EMEA/H/C/001241/II/0044
AstraZeneca AB, Rapporteur: Johann Lodewijk

Hillege, "Update of section 4.4 of the SmPC in order to add a warning on Thrombotic Thrombocytopenic Purpura (TTP) and update of section 4.8 of the SmPC to include TTP as new adverse drug reaction with a frequency 'unknown', based on a safety review. The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make some formatting corrections throughout the product information."	
Brilique - ticagrelor - EMEA/H/C/001241/II/0045 AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to add a new warning on interference with laboratories tests regarding platelet function tests to diagnose heparin induced thrombocytopenia (HIT) based on as safety review."	
Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0046 Merck Sharp & Dohme B.V., Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.3, 4.4 and 4.9 of the SmPC in order to revise the current text regarding Ovarian Hyperstimulation Syndrome (OHSS) to add clarity and remove clinical advice describing specific clinical interventions for reducing OHSS that have become outdated, based on post-marketing data and literature review. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder to include some editorial changes to the Package Leaflet."	
EXJADE - deferasirox - EMEA/H/C/000670/II/0066 Novartis Europharm Limited, Rapporteur: Alexandre Moreau, "To update the Exjade SmPC (Section 5.1) to reflect the results of clinical study CICL670A2302 (TELESTO) with Exjade in patients with myelodysplatic syndrome (MDS)."	
Exviera - dasabuvir - EMEA/H/C/003837/II/0044 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Update of section 4.3 of the SmPC to contraindicate the concomitant use with apalutamide, a strong CYP3A inducer, as well as to update section 4.5 of	

the SmPC on the interaction with apalutamide based on approved product information. The Package Leaflet is updated accordingly."	
Eylea - aflibercept - EMEA/H/C/002392/II/0052 Bayer AG, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the SmPC in order to reflect the final results from ALTAIR (SN17668) study; this is a randomized, open-label phase 4 study evaluating the efficacy and safety of repeated doses of intravitreal aflibercept with variable treatment intervals in Japanese subjects with neovascular age-related macular degeneration. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to include minor editorial changes in section 5.1 of the SmPC."	
IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0027, Orphan CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.4 of the SmPC to update the warning with regards to inhibitor development. Section 4.8 of the SmPC and the PL has been updated accordingly."	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0074 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Submission of the final CSR version 03 for KEYNOTE-013 summarising final data from the rrcHL cohort."	
Repatha - evolocumab - EMEA/H/C/003766/II/0033 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to update the safety information with regards to the adverse reaction "Influenza-like illness" with a frequency of Uncommon following the assessment of influenza-like illness with evolocumab in both the clinical database and postmarketing database. The Package Leaflet Section 4 was updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to implement changes to the package leaflet Section 2 subsequent to the revised Annex to the EC guideline on excipients in the labelling (EMA/CHMP/302620/2017) to update the wording for sodium."	

Saxenda - liraglutide - EMEA/H/C/003780/II/0023

Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information regarding hypoglycaemia in patients with type 2 diabetes mellitus treated with insulin based on the final results from the Phase 3b clinical trial NN8022-4272 (SCALE Insulin), undertaken to investigate the effect and safety of liraglutide 3.0 mg in subjects with overweight or obesity and type 2 diabetes mellitus treated with basal insulin. The Package Leaflet is updated accordingly."

Sutent - sunitinib - EMEA/H/C/000687/II/0074

Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, "Submission of the final analyses of the overall survival data, and the additional biomarker analyses collected from Study A6181202 (multi-centre, single-arm, open-label, Phase 4 clinical trial of sunitinib in patients with progressive, advanced/metastatic, well-differentiated, unresectable pancreatic neuroendocrine tumours (pNET))."

Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391/II/0017/G

Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update the safety information based on week-96 results from studies TMC114FD2HTX3001 (AMBER) "A Phase 3, randomized, active-controlled, double-blind study to evaluate efficacy and safety of D/C/F/TAF once daily fixed-dose combination regimen versus a regimen consisting of DRV/COBI FDC co-administered with FTC/TDF FDC in ARV treatment-naïve HIV-1 infected subjects", and study TMC114IFD3013 (EMERALD)) "A Phase 3, randomized, active-controlled, open-label study to evaluate switching to a D/C/F/TAF once-daily single-tablet regimen versus continuing the current regimen consisting of a boosted protease inhibitor combined with FTC/TDF in virologically-suppressed, HIV-1 infected subjects.", both listed as category 3 studies in the RMP. The Package Leaflet is updated

accordingly. The RMP version 5.0 (in version 2 of the RMP template) has also been submitted to reflect the study results and revise due dates for category 3 studies GS-US-311-1717 and GS-US-292-0109. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update section 4.2 of the SmPC and Package Leaflet to include advice in the event of vomiting in line with the approved Genvoya SmPC, make minor editorial changes in the SmPC; as well as to update the list of local representatives in the Package Leaflet in line with the latest QRD template version 10.0."	
Taltz - ixekizumab - EMEA/H/C/003943/II/0026/G Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, "Type II- C.I.4 -Update of section 5.1 of the SmPC based on results of study RHCF - a 52-Week Multicenter, Randomized, Open-Label, Parallel-Group Study Evaluating the Efficacy and Safety of Ixekizumab versus Adalimumab in Patients with Psoriatic Arthritis Who Are Biologic Disease-Modifying Anti-Rheumatic Drug Naïve. Type II- C.I.4 -Update of section 4.5 of the SmPC based on results of study RHBU – a study evaluating of the effect of ixekizumab on the pharmacokinetics of cytochrome P450 substrates in patients with moderate-to-severe plaque psoriasis."	
Verzenios - abemaciclib - EMEA/H/C/004302/II/0003 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC in order to add a criterion for discontinuing abemaciclib in the event of specific hepatic changes based on available safety data. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make editorial changes to section 5.1 of the SmPC."	
Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0053 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Update of section 4.3 of the SmPC to contraindicate the concomitant use with lomitapide, a CYP3A4 substrate, and apalutamide, a strong CYP3A inducer, as well as to update section 4.5 of the SmPC on the potential interactions with apalutamide, encorafenib, ibrutinib and	

lomitapide based on approved product informations. The Package Leaflet is updated accordingly."

XALKORI - crizotinib - EMEA/H/C/002489/II/0062

Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Submission of the review of the PK profile of the crizotinib lactam metabolite, PF-06260182 in subjects or patients treated with single agent crizotinib, and discussion of the clinical relevance of these findings derived from the following reports: A8081001, A8081002, A8081005, A8081006, A8081007, A8081012, A8081014 and A8081020, in order to fulfil a CHMP recommendation. Based on the data discussed as part of this variation, no update of the SmPC is warranted."

XGEVA - denosumab - EMEA/H/C/002173/II/0069

Amgen Europe B.V., Rapporteur: Kristina Dunder, "Update of SmPC sections 4.2, 4.8, 5.1 and 5.2 based on the final analysis from study 20062004; a phase 2, open-label, single-group study to evaluate the safety and pharmacokinetics of denosumab in adult and adolescent subjects with giant cell tumour of bone (GCTB). The final CSR for study 20062004 was previously assessed by CHMP as part of procedure P46 027 and the finalisation of the study addresses the final PIP measure. Further, section 4.8 of the SmPC is being updated to include the new ADR 'alopecia' with a frequency of 'common', upon request by PRAC following the assessment of PSUSA/00009119/201809. In addition, the MAH took the opportunity to update the description of ONJ incidence in section 4.8 of the SmPC in order to express events per 100 patient years without a percentage sign. The Package Leaflet has been updated accordingly."

WS1588
Aluvia-EMEA/H/W/000764/WS1588/0109
Kaletra-EMEA/H/C/000368/WS1588/0177
Norvir-EMEA/H/C/000127/WS1588/0154

AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.3 and 4.5 of the SmPC in order to include information on the contraindication with neratinib and interactions with abemaciclib, neratinib, glecaprevir/pibrentasvir. In addition,

the Worksharing Applicant (WSA) took the opportunity to update section 4.5 of the Kaletra and Aluvia SmPCs to add information on the interaction of lopinavir/ritonavir with sofosbuvir/velpatasvir/voxilaprevir. The Package Leaflets are updated accordingly."	
WS1598 **Cymbalta-EMEA/H/C/000572/WS1598/0079** **Duloxetine Lilly-EMEA/H/C/004000/WS1598/0016** **Xeristar-EMEA/H/C/000573/WS1598/0082** **Yentreve-EMEA/H/C/000545/WS1598/0064** Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim, Yentreve, Lead Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 5.1 to reflect on the data obtained from the paediatric study HMGW, submitted the final report for the paediatric Study HMGW, a Phase 3b, Randomised, Double-Blind, Placebo-Controlled, Clinical Trial of Duloxetine in adolescent Juvenile Primary Fibromyalgia Syndrome (JPFS) population."	
WS1613 **Epclusa-EMEA/H/C/004210/WS1613/0039** **Vosevi-EMEA/H/C/004350/WS1613/0029** Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to add new information regarding co-administration with atorvastatin, based on final results from study GS-US-342-4034. Study GS-US-342-4034 was a phase 1 study to evaluate the effect of sofosbuvir/velpatasvir fixed dose combination on the pharmacokinetics of atorvastatin. The Package Leaflet is updated accordingly. In addition, the Worksharing Applicant took the opportunity to amend Annex II of the Product Information with regards to the due date for submission of study DAA-PASS. This study is designed to evaluate the recurrence of hepatocellular carcinoma and the date has been postponed from Q2 2021 to Q2 2023, as approved in the framework of WS1476. Furthermore, the MAH implemented minor editorial updates throughout the Product	

Information.”	
WS1617 **Filgrastim Hexal-EMEA/H/C/000918/ WS1617/0050** **Zarzio-EMEA/H/C/000917/WS1617/0051** Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.4 and 6.6 of the SmPC in order to remove the latex warning based on company and post marketing data. The Package Leaflet is updated accordingly.”	

B.6.10. CHMP-PRAC assessed procedures

Brinavess - vernakalant - EMEA/H/C/001215/II/0035 Correvio, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information following updates to the Company Core Safety Datasheet (CCDS) based on the results of an integrated safety analysis performed on data of existing clinical studies with a stronger emphasis on treatment-related ADRs and an incidence rate above one percent. The Package Leaflet was updated accordingly. The RMP version 7.0 has also been submitted and incorporates the results from the new safety analysis. In addition the results from completed observational Cohort SPECTRUM study (A Prospective Observational Registry Study to Characterise Normal Conditions of Use, Dosing and Safety Following Administration of Vernakalant IV Sterile Concentrate: PASS Protocol 6621-049) currently under assessment within Brinavess II/34 were included in the updated RMP. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update sections 4.2, 4.4, 4.6, 4.7, 4.8, 5.1, 5.2, 5.3, 6.4 of the SmPC, Annex II, Labelling sections 3 and 5, Package Leaflet sections 2, 4, 5 and 6 to include editorial changes, to correct typographical errors and to bring the PI in line with the latest QRD template version 10 and well as to update statements related to the excipients in the SmPC and Package Leaflet in line with the EC Guideline on "Excipients in the Labelling and Package Leaflet of medicinal products for human use” of	

March 2018 and the EMA Annex to the EC Guideline of October 2017 (SANTE-2017-11668)."

Darzalex - daratumumab - EMEA/H/C/004077/II/0027, Orphan

Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.4. and 4.8 of the SmPC to add new safety information on the recently identified risk of Hepatitis B reactivation (HBV). Consequently the PIL is proposed to be updated. A revision of the RMP (v. 5) is included in the submission. The MAH also proposes a DHPC to inform prescribers on the newly identified risk."

IBRANCE - palbociclib - EMEA/H/C/003853/II/0019/G

Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark,"Update of section 4.8 of the SmPC in order to include ILD/pneumonitis as ADRs based on a safety cumulative review together with reclassification of the risk from potential to identified in the RMP (version 1.6). The Package Leaflet is updated accordingly. The MAH has also submitted the updated RMP version 1.6 in order to remove long term use from missing information in the list of safety concerns. In addition, the MAH is proposing to change the due date for submission of the final CSR of study A5481027 listed as a Category 3 study in the RMP."

Iclusig - ponatinib - EMEA/H/C/002695/II/0051, Orphan

Incyte Biosciences Distribution B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of the RMP to version 19, including deletion of previously agreed safety concerns. These deletions are proposed in line with the guideline on Good Pharmacovigilance Practices (GVP) Module V on RMP (revision 2 - dated on 31 March 2017). Other updates include: review of the categorisation of the posterior reversible encephalopathy syndrome (PRES) risk in the RMP in line with the request from PSUSA/00010128/201712; correction of the category (from Category 3 to 1) of the study AP24534-14-203, an imposed Annex II condition; revision of the due date for the

submission of this study report to August 2021, as described in the Iclusig PI, and as agreed as part of procedure EMEA/H/C/002695/ANX/016."

Inovelon - rufinamide - EMEA/H/C/000660/II/0052, Orphan
Eisai GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of section 4.2 of the SmPC in order to include an additional method of administration via feeding tube for Inovelon oral suspension. This fulfills the CHMP recommendation to evaluate the feasibility of administrating the rufinamide oral suspension via an enteral feeding tube adopted with variation II/45.
The RMP version 11 has been submitted."

Pelgraz - pegfilgrastim - EMEA/H/C/003961/II/0005
Accord Healthcare S.L.U., Rapporteur: Sol Ruiz, PRAC Rapporteur: Menno van der Elst

PREVYMIS - letermovir - EMEA/H/C/004536/II/0011, Orphan
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.4 and 4.5 of the SmPC in order to update the safety information following the final results of a clinical pharmacology trial entitled "A Study to Assess the Effect of Rifampin on the Single-Dose and Steady-State Pharmacokinetics of MK-8228 in Healthy Adult Subjects" (MK-8228-038) listed as a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 2.1 has also been submitted."

ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0151
Pfizer Europe MA EEIG, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "To update sections 4.8 Undesirable effects and 5.1 Pharmacodynamic effects of the SmPC based on the final results from study 3082B2-313 (B1831001 - "An Open-Label Study to Evaluate Prophylaxis Treatment, and to Characterize the Efficacy, Safety, and Pharmacokinetics of B-Domain Deleted Recombinant Factor VIII Albumin Free (Moroctocog Alfa [AF_CC]) in Children with Hemophilia A") listed as an additional pharmacovigilance activity in the Risk Management Plan (RMP; MEA 116). The RMP

version 13.0 has also been submitted.
In addition, the SmPC is being brought in line with the revised guidelines on core SmPC for human plasma derived and recombinant coagulation factor VIII products (Revision 3) in sections 4.2 Posology and Method of Administration, 4.4 Special warnings and special precautions for use, 4.8 Undesirable effects and 5.1 Pharmacodynamic effects."

Signifor - pasireotide - EMEA/H/C/002052/II/0041/G, Orphan
Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of section 4.8 of the SmPC based on the final CSR from Study CSOM230B2219; a multi-center, randomized, open-label, Phase IV study to investigate the management of pasireotide-induced hyperglycemia with incretin based therapy or insulin in adult patients with Cushing's disease or acromegaly (listed as a category 3 study in the RMP).
A revised RMP version 7.0, updated in line with the revised GVP Module V, including changes to the safety concerns, was provided as part of the application."

Spinraza - nusinersen - EMEA/H/C/004312/II/0014, Orphan
Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga, "C.I.13: Submission of the final report from Phase 2 Study SM202 (EMBRACE or CS7) listed as a category 3 study in the RMP. This is a Phase 2, randomized, double-blind, sham-procedure-controlled study to assess the safety and tolerability and explore the efficacy of ISIS 396443 (BIIB058) administered intrathecally in subjects with spinal muscular atrophy who are not eligible to participate in the clinical studies ISIS 396443-CS3B or ISIS 396443-CS4 due to age at screening and/or SMN2 copy number.
An updated RMP version 10.1 has also been submitted."

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0024
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.2, 4.4, and 4.8 of the SmPC in order to add a

warning regarding the risk of immune-related myositis identified during a comprehensive analysis of patients treated with Tecentriq. The additional risk minimisations in Annex 2D are also updated. Furthermore a DHPC is being proposed to inform about the risk of immune-related myositis. The Package Leaflet is updated accordingly. The RMP version 11.0 has also been submitted."

B.6.11. PRAC assessed procedures

PRAC Led
Edurant - rilpivirine - EMEA/H/C/002264/II/0034
Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 8.0 in order to remove 'bleeding disorders' as an important potential risk as agreed by PRAC during procedure PSUSA/00009282/201805. In addition, the MAH took the opportunity to remove some of the safety concerns and remove/reclassify additional pharmacovigilance activities (category 4) in line with the revision 2 of the RMP template."

PRAC Led
Hulio - adalimumab - EMEA/H/C/004429/II/0009
Mylan S.A.S, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 2.2 in order to do the following change:
As part of Post-Authorization Measures (category 3 according to the RMP), the applicant has to submit the study protocol on a longitudinal observational study of patients with rheumatoid arthritis treated with biologic and other new advanced targeted therapies by 31 March 2019 (Ref No.MEA/PRO 002). The applicant now proposes to use a different registry (RABBIT) than previously the previously agreed BSRBR-RA."

PRAC Led
Kiovig - human normal immunoglobulin - EMEA/H/C/000628/II/0091
Baxter AG, Rapporteur: Jan Mueller-Berghaus,

PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 9.0 in order to include the new indication chronic inflammatory demyelinating polyradiculoneuropathy [CIDP] and update the list of safety concerns (implementation of new specifications from GCP Module V (Rev 2)."

PRAC Led

Kisplyx - lenvatinib - EMEA/H/C/004224/II/0024

Eisai GmbH, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Bjorg Bolstad, "Submission of an updated RMP version 11.1 in order to update the study design for Study E7080-G000-218 (MEA 007) from double-blind to open label as requested by the CHMP from post authorisation measure MEA 06.1. In addition the MAH is taking the opportunity to introduce minor administrative changes to the RMP."

PRAC Led

Ozurdex - dexamethasone - EMEA/H/C/001140/II/0035

Allergan Pharmaceuticals Ireland, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "C.I.13: Submission of the final report from study CMO-EPI-EYE-0522 listed as a category 3 study in the RMP. This is an observational, cross-sectional study conducted in France, Germany, Spain, and the UK having as primary objective the assessment of the effectiveness of the educational material provided to the treating physicians."

PRAC Led

Revlimid - lenalidomide - EMEA/H/C/000717/II/0110, Orphan

Celgene Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final results of the CC-5013-PASS-001 study report dated 2 Nov 2018, for the non-interventional post-authorisation safety study (PASS) of patients treated with lenalidomide."

PRAC Led

Xadago - safinamide - EMEA/H/C/002396/II/0031

Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of an updated RMP version 6.0 in order to implement RMP rev 2 template and introduce changes to pre-clinical, clinical and post-marketing exposure information and update the due date of DUS Z7219N02 from July 2019 to 28 February 2020 ."

PRAC Led
WS1608
Filgrastim Hexal-EMEA/H/C/000918/ WS1608/0049
Zarzio-EMEA/H/C/000917/WS1608/0050
Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "The scope of the above mentioned variation application is to align on the due dates and deliverables for the post-authorization measure, MEA007. The due date is extended from Dec 2019 to March 2020, to combines the annual safety report (ASR) with the 5-year interim clinical study report (CSR) in 2020 and the final CSR in 2024 and for the MEA to cover the entire duration of study EP06-501."

B.6.12. CHMP-CAT assessed procedures

Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0005/G, ATMP
CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, , "Update of the product information to reflect the study results of the 36-month follow up data for trial cod 16 HS 13 and the final study report with 60-month follow-up data for trial cod 16 HS 14.
Study cod 16 HS 13, is a Prospective, randomised, open label, multicentre Phase-III clinical trial to compare the efficacy and safety of the treatment with the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) with microfracture in subjects with cartilage defects of the knee with a defect size between 1 and 4 cm2.
Study cod 16 HS 14, is a Prospective, randomised, open label, multicentre Phase-II clinical trial to investigate the efficacy and safety of the treatment of large defects (4-10 cm2) with

three different doses of the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) in subjects with cartilage defects of the knee."

YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0007, Orphan, ATMP
Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

B.6.13. CHMP-PRAC-CAT assessed procedures

Zalmoxis - nalotimagene carmaleucel - EMEA/H/C/002801/II/0016, Orphan, ATMP
MolMed S.p.A, Rapporteur: Johannes Hendrikus Ovelgonne, Co-Rapporteur: Sol Ruiz, CHMP Coordinators: Paula Boudewina van Hennik and Maria Concepcion Prieto Yerro, PRAC Rapporteur: Brigitte Keller-Stanislawski, "The MAH is proposing to terminate the study TK008 (specific obligation for the CMA) and replace it with study TK013"

B.6.14. PRAC assessed ATMP procedures

PRAC Led
Alofisel - darvadstrocel - EMEA/H/C/004258/II/0006, Orphan, ATMP
Takeda Pharma A/S, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 7 in order to propose replacement of the observational PASS study (Category 3) with two separate studies: a long-term safety extension of the ADMIRE-CD II study and a retreatment PASS. The European multi-database linkage study is added for the assessment of the potential risk of tumorigenicity."

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

WS1595
Kalydeco-EMEA/H/C/002494/WS1595/

0078
Symkevi-EMEA/H/C/004682/WS1595/
0009
Vertex Pharmaceuticals (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, "To provide a final Environmental Risk Assessment report."

WS1610/G
Silodyx-EMEA/H/C/001209/WS1610/
0034/G
Urorec-EMEA/H/C/001092/WS1610/
0037/G
Recordati Ireland Ltd, Lead Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur: Amelia Cupelli, "To align the annexes and RMP of Urorec and Silodyx with the changes approved for the new, recently authorised product Silodosin Recordati, as listed below:

- combined SmPC for both strengths 4mg and 8mg hard capsules
- updates to QRD template version 10
- Deletion of the additional risk minimisation activities about IFIS from Annex II of the Product Information, in accordance with the outcome of the PSUSA procedure and RMP version 11.5

In addition, in order to have the same approved RMP for the mentioned medicinal products; it is submitted for Urorec and Silodyx the RMP version 11.5 that has been approved for Silodosin Recordati (EMEA/H/C/004964)."

WS1619
Cymbalta-EMEA/H/C/000572/WS1619/
0080
Duloxetine Lilly-EMEA/H/C/004000/
WS1619/0017
Xeristar-EMEA/H/C/000573/WS1619/
0083
Yentreve-EMEA/H/C/000545/WS1619/
0065
Eli Lilly Nederland B.V., Lead Rapporteur: Maria Concepcion Prieto Yerro

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WS1622/G
Thymanax-EMEA/H/C/000916/WS1622/
0042/G
Valdoxan-EMEA/H/C/000915/WS1622/
0044/G
Les Laboratoires Servier, Lead Rapporteur: Bjorg Bolstad

WS1628
Aflunov-EMEA/H/C/002094/WS1628/0051
Foclivia-EMEA/H/C/001208/WS1628/0046
Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

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

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

G. ANNEX G

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

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

Final Scientific Advice (Reports and Scientific Advice letters):

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 23-26 April 2019 CHMP plenary:

G.3.2. List of procedures starting in April 2019 for May 2019 CHMP adoption of outcomes

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