10 December 2018
EMA/CHMP/862876/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 10-13 December 2018

Chair: Harald Enzmann Vice-Chair: Bruno Sepodes

10 December 2018, 13:00 – 19:30, room 3A

11 December 2018, 08:30 – 19:30, room 3A

12 December 2018, 08:30 – 19:30, room 3A

13 December 2018, 08:30 – 15:00, room 3A

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).

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

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 10-13 December 2018. See December 2018 CHMP minutes (to be published post January 2019 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 10-13 December 2018

1.3. Adoption of the minutes

CHMP minutes for 12-15 November 2018.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. ropeginterferon alfa-2b - Orphan - EMEA/H/C/004128

AOP Orphan Pharmaceuticals AG; treatment of polycythemia vera

Scope: Oral explanation/Opinion

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

List of Outstanding Issues adopted on 15.11.2018, 26.07.2018. List of Questions adopted on 22.06.2017.

2.1.2. zanamivir - EMEA/H/C/004102

treatment of influenza A or B virus infection

Scope: Oral explanation

Action: Oral explanation to be held on 13 December 2018 at time 09:00

List of Outstanding Issues adopted on 18.10.2018. List of Questions adopted on 26.04.2018.

2.1.3. doxorubicin hydrochloride - EMEA/H/C/004110

treatment of breast and ovarian cancer

Scope: Oral explanation

Action: Oral explanation to be held on 11 December 2018 at time 14:00

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 14.09.2017.

2.1.4. lusutrombopag - EMEA/H/C/004720

treatment of thrombocytopenia

Scope: Oral explanation

Action: Oral explanation to be held on 11 December 2018 at time 09:00

List of Outstanding Issues adopted on 18.10.2018. List of Questions adopted on 31.05.2018.

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

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

Scope: Oral explanation

Action: Oral explanation to be held on 12 December 2018 at time 11:00

List of Outstanding Issues adopted on 22.02.2018, 09.11.2017. List of Questions adopted on 15.12.2016.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

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

Roche Registration GmbH

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

Scope: Oral explanation

Action: Oral explanation to be held on 12 December 2018 at time 14:00

Request for Supplementary Information adopted on 18.10.2018, 26.07.2018.

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

AstraZeneca AB

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

Scope: Oral explanation, Ad Hoc Expert Group Report

Action: Oral explanation to be held on 12 December 2018 at time 09:00

Request for Supplementary Information adopted on 18.10.2018, 31.05.2018.

2.4. Referral procedure oral explanations

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

MAHs: various

Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

Scope: Oral explanation/Opinion

Action: Oral explanation to be held on 10 December 2018 at time 16:00

See 10.6

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. bevacizumab - EMEA/H/C/004697

treatment of adult patients with metastatic carcinoma of the colon or rectum, metastatic breast cancer, unresectable advanced, metastatic or recurrent non-small cell lung cancer, advanced and/or metastatic renal cell cancer, persistent, recurrent, or metastatic carcinoma of the cervix

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 28.06.2018.

3.1.2. miglustat - EMEA/H/C/004904

treatment of adult patients with mild to moderate type 1 Gaucher disease and only in the treatment of patients for whom enzyme replacement therapy is unsuitable

Scope: Opinion

Action: For adoption

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

3.1.3. naldemedine - EMEA/H/C/004256

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.04.2018, 22.02.2018. List of Questions adopted on 20.07.2017.

3.1.4. tobramycin - EMEA/H/C/005086

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

Scope: Opinion

Action: For adoption

List of Questions adopted on 18.10.2018.

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

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 18.10.2018. List of Questions adopted on 31.05.2018.

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

3.2.1. avacopan - Orphan - EMEA/H/C/004487

ChemoCentryx Ltd; induction of response in adult patients with granulomatosis with polyangiitis (Wegener's) (GPA) or microscopic polyangiitis (MPA)

Scope: List of outstanding issues, Letter from applicant dated 05 December 2018 requesting an extension of clock stop to respond to the list of outstanding issues to be adopted in December 2018.

Action: For adoption

List of Questions adopted on 26.04.2018.

3.2.2. pegfilgrastim - EMEA/H/C/004556

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.03.2018.

3.2.3. febuxostat - EMEA/H/C/004773

treatment of hyperuricaemia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.09.2018.

3.2.4. pegvaliase - Orphan - EMEA/H/C/004744

BioMarin International Limited; treatment of adults with phenylketonuria (PKU) who have inadequate blood phenylalanine control

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 26.07.2018.

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

3.3.1. glucagon - EMEA/H/C/003848

treatment of severe hypoglycaemia

Scope: List of questions

Action: For adoption

3.3.2. erlotinib - EMEA/H/C/005071

treatment of lung and pancreatic cancers

Scope: List of questions

Action: For adoption

3.3.3. emapalumab - Orphan - EMEA/H/C/004386

Novimmune B.V.; treatment of paediatric patients with primary haemophagocytic lymphohistiocytosis (HLH)

Scope: List of questions

Action: For adoption

3.3.4. rituximab - EMEA/H/C/004696

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

Scope: List of questions

Action: For adoption

3.3.5. 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

Scope: List of questions

Action: For adoption

3.3.6. ibalizumab - EMEA/H/C/004961

Accelerated assessment

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

Scope: List of questions

Action: For adoption

3.3.7. larotrectinib - Orphan - EMEA/H/C/004919

Accelerated assessment

Bayer AG; treatment of adult and paediatric patients with locally advanced or metastatic solid tumours

Scope: List of questions

Action: For adoption

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

3.4.1. 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: Final list of experts for the SAG Oncology meeting held on 26 November 2018 was adopted via written procedure on 23 November 2018.

Report from SAG.

Action: For adoption

List of questions adopted on 20.09.2018.

3.4.2. levodopa - EMEA/H/C/004786

treatment of symptoms of OFF periods in Parkinson's disease

Scope: Letter from applicant dated 05 December 2018 requesting an extension of clock stop to respond to the list of questions adopted on 20. September 2018.

Action: For adoption

List of Questions adopted on 20.09.2018.

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

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

Scope: Updated list of experts for the SAG HIV Viral Diseases meeting adopted via written procedure on 30.11.2018.

Action: For information

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

3.4.4. sotagliflozin - EMEA/H/C/004889

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

Scope: Ad Hoc Expert Group Report

Action: For adoption

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

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

3.7.1. adalimumab - EMEA/H/C/005253

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

Scope: Withdrawal of initial marketing authorisation application

Action: For information

3.7.2. canakinumab - EMEA/H/C/004754

prevention of major cardiovascular events

Scope: Withdrawal of initial marketing authorisation application

Action: For information

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

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

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

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

Janssen Biologics B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength of 100 mg/ml solution for injection for paediatric use.
C.I.6.a - Extension of indication to include paediatric patients from the age of 2 years and older for the treatment of polyarticular juvenile idiopathic arthritis (pJIA) with Simponi 100 mg/ml solution for injection. As a consequence, sections 4.1, 4.2, 5.1 and section 4.1 of the 50mg strength have been updated accordingly.
C.I.11.z - To update the RMP to version 18.0 to delete the following safety concerns: vasculitis, psoriasis (new onset or worsening of pre-existing), and sarcoidosis/sarcoid like reaction. This change has been agreed by the CHMP in the outcome of variation Type II/068.
C.I.11.z - To update the RMP to version 18.0 to change the due date of the category 3 study MK-8259-050. This change has been agreed by the CHMP in the outcome of MEA033.
In addition, the marketing authorisation holder took the opportunity to:
- update the Product Information in line with the latest QRD template (version 10);
- implement the recommendations stated in the revised Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' with regards to the excipient Sorbitol (E420);
- add a statement in Section 4.4 of the SmPC to record the name and the batch number of the administered product, in line with Good Pharmacovigilance Practice (GVP) Module PII: Biological medicinal products."

Action: For adoption

List of Questions adopted on 20.09.2018.

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

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

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension application to add 2 new strengths of 50 mg and 87.5 mg for solution for injection in a pre-filled syringe with needle guard, for subcutaneous (SC) administration, grouped with a type II variation (C.I.6.a) to include paediatric use of polyarticular Juvenile Idiopathic Arthritis (2 years and above) for solution for injection (50 mg, 87.5 mg and 125 mg).

The above-described changes are grouped

The RMP (version 25.0) is updated in accordance.

In addition, the applicant took the opportunity to implement minor editorial changes in the product information."

Action: For adoption

List of Questions adopted on 26.07.2018.

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. Aimovig - erenumab - EMEA/H/C/004447/X/0001

Novartis Europharm Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Kirsti Villikka

Scope: "Extension application to add a new strength of 140 mg."

Action: For adoption

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

No items

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

No items

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

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

5.1.1. Adcetris - brentuximab vedotin - Orphan - EMEA/H/C/002455/II/0055

Takeda Pharma A/S

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of the existing Hodgkin lymphoma (HL) indication to include the frontline treatment of adult patients with CD30+ advanced HL in combination with chemotherapy, based on data from ECHELON-1 (C25003), a phase 3 multi-centre, randomised, open-label study comparing the modified progression-free survival (mPFS) obtained with brentuximab vedotin, doxorubicin, vinblastine and dacarbazine versus the mPFS obtained with doxorubicin, bleomycin, vinblastine and dacarbazine. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 10. The MAH also submitted an updated RMP version 13."

Action: For adoption

Request for Supplementary Information adopted on 20.09.2018, 31.05.2018.

5.1.2. 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

5.1.3. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0060

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, in combination with carboplatin and either paclitaxel or nab-paclitaxel, for the first-line treatment of metastatic squamous NSCLC in adults for Keytruda.
As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Additionally, editorial corrections to section 5.1 of the SmPC are introduced (concerning the procedure EMEA/H/C/003820/II/0052). The RMP version 20.1 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 15.11.2018.

5.1.4. Lynparza - olaparib - EMEA/H/C/003726/II/0020

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 tablets as a montherapy for the treatment of adult patients with BRCA1/2-mutated HER2 negative metastatic breast cancer who have previously been treated with chemotherapy. These patients could have received chemotherapy in the neoadjuvant, adjuvant or metastatic setting.
As a consequence, section 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for Lynparza tablets have been updated. Section 4.8 of Lynparza capsules and relevant sections of the package

leaflet have been updated accordingly. Furthermore, RMP version 16 has also been provided."

Final list of experts for the SAG Oncology meeting held on 26 November 2018 was adopted via written procedure on 23 November 2018.

Report from SAG.

Action: For adoption

Request for Supplementary Information adopted on 20.09.2018, 28.06.2018.

5.1.5. 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 montherapy 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."

Action: For adoption

5.1.6. Mozobil - plerixafor - Orphan - EMEA/H/C/001030/II/0034

Genzyme Europe BV

Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of Indication to include paediatric patients aged 1 to 18 years for Mozobil, as a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018.

5.1.7. Opsumit - macitentan - Orphan - EMEA/H/C/002697/II/0029

Janssen-Cilag International N.V.

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of Indication to include treatment of patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH), based on the pivotal study MERIT-1 (AC-055E201), together with 6 months of efficacy and safety data (cut-off date 17 October 2017) from its ongoing open-label extension study MERIT-2 (AC-055E202), as well as a drug-drug interaction (DDI) study (AC-055-122) of macitentan and rosuvastatine, a DDI

study (AC-055-123) of macitentan and riociguat, and observational data from the OPUS Registry (OPsumit USers Registry; cut-off date of 17 April 2018).
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 are being updated and the Package Leaflet is being updated accordingly. In addition, the MAH took the opportunity to implement editorial changes and to align the annexes with the latest QRD template and to update the contact details of the local representatives in the Package Leaflet.
An updated RMP version 9.2 was provided as part of the application."

Action: For adoption

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

GE Healthcare AS

Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty

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

Action: For adoption

Request for Supplementary Information adopted on 18.10.2018, 28.06.2018.

5.1.9. Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0050

Novartis Europharm Limited

Rapporteur: Concepcion Prieto Yerro

Scope: "Change of the Revolade indication of immune throbocytopaenic purpura to specify the duration of the disease. As a result the SmPC sections 4.1, 4.2, 4.4, 4.8 and 5.1 are being revised. The Package leaflet is being updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 20.09.2018.

5.1.10. Rubraca - rucaparib - Orphan - EMEA/H/C/004272/II/0001

Clovis Oncology UK Limited

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Annika Folin

Scope: "Extension of Indication to include new indication for Rubraca "Rubraca is indicated as monotherapy for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy". As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated with the expanded clinical eficacy and safety data. The Package Leaflet is also updated in accordance.
The updated RMP version 2.0 has also been submitted.

In addition, the applicant took the opportunity to propose the move of one paragraph from section 4.4 to 5.1 in the SmPC for consitency with other SmPC agents in this class with this indication."

Action: For adoption

Request for Supplementary Information adopted on 20.09.2018.

5.1.11. Sprycel - dasatinib - EMEA/H/C/000709/II/0059

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of Indication to include a paediatric indication for Philadelphia chromosome positive acute lymphoblastic leukaemia for Sprycel; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 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 make minor editorial changes to the product information.
The RMP version 16.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 20.09.2018, 31.05.2018.

5.1.12. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0047

PTC Therapeutics International Limited

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension of Indication to include non-ambulatory patients with Duchenne muscular dystrophy; This variation additionally presents, as supportive data, the final results of the long term clinical study PTC-124-GD-019-DMD (an Open-Label Study for Previously Treated Ataluren (PTC124) Patients with Nonsense Mutation Dystrophinopathy), submitted in line with the requirements of the Article 46 of the Paediatric Regulation.
As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.
The RMP version 8.0 has also been submitted."

Action: For adoption

5.1.13. Trimbow - beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004257/II/0002

Chiesi Farmaceutici S.p.A.

Rapporteur: Janet Koenig, PRAC Rapporteur: Jan Neuhauser

Scope: "Extension of Indication for Trimbow to all adult patients with moderate or severe chronic obstructive pulmonary disease (COPD).
As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated in order to add the results of two Phase III studies (Triple 7 and Triple 8);
Triple 7 (CCD-05993AA1-07) is a multinational, multicentre, randomised, open-label, active-controlled, 26-week, 2-arm, parallel group study to evaluate the non-inferiority of fixed

combination of beclomethasone dipropionate plus formoterol fumarate plus glycopyrronium bromide administered via pressurised metered dose inhaler (pMDI) (CHF 5993) versus (vs.) fixed combination of fluticasone furoate plus vilanterol administered via dry powder inhaler (DPI) (Relvar®) plus tiotropium bromide (Spiriva®) for the treatment of patients with Chronic Obstructive Pulmonary Disease (COPD).
Triple 8 (CCD-05993AA1-08) is a 52-week, double blind, double dummy, randomized, multinational, multicentre, 2-arm parallel group, active controlled clinical trial of fixed combination of beclomethasone dipropionate plus formoterol fumarate plus glycopyrronium bromide administered via pMDI (CHF 5993) versus indacaterol/glycopyrronium (Ultibro®) via DPI in patients with Chronic Obstructive Pulmonary Disease (TRIBUTE)
The Package Leaflet and the Risk Management Plan are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 20.09.2018, 28.06.2018.

5.1.14. Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0191

Gilead Sciences Ireland UC

Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli

Scope: "Extension of Indication based on results from interim Week 48 clinical study report (CSR) for Study GS-US-174-0144; a 'Randomized, Double-Blind Evaluation of the Antiviral Efficacy, Safety and Tolerability of Tenofovir Disoproxil Fumarate Versus Placebo in Pediatric Patients with Chronic Hepatitis B Infection'. Following changes have been proposed:

1) Viread film coated tablets (123 mg; 163 mg; 204 mg): new chronic hepatitis B (CHB) indication to include treatment of CHB in paediatric patients aged 6 to < 12 years
2) Viread granules 33 mg/g: extension of the existing CHB indication for Viread granules to include treatment of CHB in paediatric patients aged 2 to < 12 years.

As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC have been updated for Viread 123 mg, 163 mg and 204 mg. Sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated for Viread 245 mg, whereas Sections 4.1, 4.2, 4.4, 5.1 and 5.2. have been updated for Viread granules 33 mg/g.

The Package Leaflet has been updated accordingly for all the products concerned."

Action: For adoption

5.1.15. WS1372
OPDIVO - nivolumab - EMEA/H/C/003985/WS1372/0053
Yervoy - ipilimumab - EMEA/H/C/002213/WS1372/0057

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of Indication to include first-line treatment of adult patients with metastatic Non-Small Cell Lung Carcinoma (NSCLC) for OPDIVO and Yervoy; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add information from the

pivotal study CA209227 (an open-label, randomised phase 3 trial of nivolumab, or nivolumab plus ipilimumab, or nivolumab plus platinum doublet chemotherapy versus platinum doublet chemotherapy in subjects with chemotherapy-naïve stage IV or recurrent NSCLC). The Package Leaflet and RMP (version 14.0 for Opdivo and version 21.0 for Yervoy) are updated in accordance. In addition, the MAH has taken the opportunity to introduce minor editorial and formatting revisions in the PI."

Action: For adoption

Request for Supplementary Information adopted on 26.07.2018.

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

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

Celgene Europe BV

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

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

Letter from applicant dated 04 December 2018 requesting an extension of clock stop to respond to the request for supplementary information.

Action: For adoption

Request for supplementary information adopted on 18.10.2018.

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

No items

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. entrectinib - H0004936

Treatment of adult and paediatric patients with neurotrophic tyrosine receptor kinase (NTRK) fusion-positive locally advanced or metastatic solid tumours, who have progressed following prior therapies, or as initial therapy when there are no acceptable standard therapies. Treatment of patients with ROS1-positive metastatic NSCLC.

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

Action: For adoption

8.1.2. cefiderocol - H0004829

Treatment of infections caused by carbapenem-resistant Gram-negative bacteria in adults with limited treatment options

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

Action: For adoption

8.1.3. cefiderocol - H0005242

Treatment of infections caused by aerobic Gram-negative bacteria in adult patients with limited treatment options

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

Action: For adoption

8.1.4. polatuzumab vedotin - Orphan - H0004870

Roche Registration GmbH; Treatment of relapsed and refractory patients with diffuse large B cell lymphoma.

Polatuzumab vedotin in combination with bendamustine and rituximab is indicated for the treatment of previously treated patients with diffuse large B-cell lymphoma who are not candidates for hematopoietic stem cell transplant

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

Action: For adoption

8.1.5. selinexor - Orphan - H0005127

Karyopharm Europe GmbH; is indicated in combination with dexamethasone, for the treatment of patients with relapsed refractory multiple myeloma (RRMM) who have received at least three prior lines of therapy and whose disease is refractory to at least one proteasome inhibitor (PI), one immunomodulatory agent (IMiD), and one anti-CD38 monoclonal antibody (mAb), and to their most recent treatment regimen (penta-refractory MM)

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

Action: For adoption

8.1.6. arsenic trioxide - H0005175

is indicated for induction of remission, and consolidation in adult patients with:
- Newly diagnosed low-to-intermediate risk acute promyelocytic leukaemia (APL) (white blood cell count, ⩽ 10 x 103/µl) in combination with all-trans-retinoic acid (ATRA)
- Relapsed/refractory acute promyelocytic leukaemia (APL)(Previous treatment should have included a retinoid and chemotherapy)
characterised by the presence of the t(15;17) translocation and/or the presence of the Pro-Myelocytic Leukaemia/Retinoic-Acid-Receptor-alpha (PML/RAR-alpha) gene.
The response rate of other acute myelogenous leukaemia subtypes to arsenic trioxide has not been examined.

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

Tesaro UK Limited

Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Patrick Batty,

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

Request for supplementary information

Action: For adoption

9.1.2. Deltyba - delamanid - Orphan - EMEA/H/C/002552/R/0033

Otsuka Novel Products GmbH,

Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams

Scope: Request for Supplementary Information

Action: For adoption

9.1.3. Ocrevus - ocrelizumab - EMEA/H/C/004043

Roche Registration GmbH,

Rapporteur: Mark Ainsworth, Co-Rapporteur: Daniela Melchiorri

Scope: PASS 3 study

Action: For discussion

9.1.4. Adenuric - febuxostat - EMEA/H/C/000777/II/0051

Menarini International Operations Luxembourg S.A.,

Rapporteur: Andrea Laslop

Scope: "Update of section 5.1 of the SmPC in order to include the results of the clinical safety study CARES (TMX-67_301), to compare the cardiovascular outcomes of febuxostat and allopurinol in subjects with gout and cardiovascular comorbidities; this is a Multicenter, Randomized, Active-Control, Phase 3B Study.
In addition, the Marketing authorisation holder (MAH) took the opportunity to provide a consolidated Module 2.7.6 in order to list all the synopsis of individual studies in a unique tabular format."

PRAC Advice

Action: For adoption

Request for Supplementary Information adopted on 04.10.2018.

10. Referral procedures

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

No items

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

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

MAH various

Rapporteur: TBC, Co- Rapporteur: TBC

Scope: Start of procedure, Appointment of rapporteurs, Time table

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

10.4.1. Syner-KINASE 10 000 IU - EMEA/H/A-29(4)/1472

Syner-Medica Ltd

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Sol Ruiz

Scope: List of outstanding issues

Action: For adoption

RMS: UK; CMS: DE, ES, FR, NL; Mutual Recognition Procedure number: UK/H/6520/01-05/MR, Disagreements regarding benefit/risk balance, safety and manufacturing.

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

No items

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

10.6.1. Fosfomycin containing medicinal products – EMEA/H/A-31/1476

MAH various

Rapporteur: TBC, Co-rapporteur: TBC

Scope: Start of procedure, Appointment of rapporteurs, Time table

Action: For adoption

Need to re-evaluate the benefit-risk ratio of the approved indications considering the current scientific knowledge. Furthermore, the appropriate dose and duration of administration for both oral and intravenous formulations need to be discussed as well as the adequacy of safety relevant information and information about pharmacological properties.

The German National Competent Authority triggered a referral under Article 31 of Directive 2001/83 based on interest of the Union, requesting an opinion to CHMP on the benefit-risk of fosfomycin-containing products and on the need for regulatory measures to be taken.

10.6.2. Metamizole containing medicinal products – metamizole sodium - EMEA/H/A-31/1469

MAH various

Rapporteur: Ewa Balkowiec, Co-rapporteur: Janet Koenig

Scope: List of outstanding issues/Opinion

Action: For adoption

The Polish National Competent Authority triggered a referral under Article 31 of Directive

2001/83 based on interest of the Union, requesting an opinion to CHMP on whether the scientific data regarding the maximum daily dose and contraindications concerning pregnancy and breastfeeding are adequately presented in the product information of metamizole containing medicinal products.

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

MAHs: various

Overall Rapporteur: Martina Weise, Co-Rapporteurs: Candesartan: Kristina Dunder, Irbesartan: Concepcion Prieto Yerro, Losartan: Johann Lodewijk Hillege, Olmesartan: Milena Stain, Valsartan: Daniela Melchiorri

Scope: List of outstanding issues/Opinion

Action: For adoption

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

MAHs: various

Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

Scope: Oral explanation/Opinion

Action: For adoption

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

See 2.4

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

MAH various

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

Scope: Letter from MAH

Action: For information

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

10.6.6. Gadolinium-containing contrast agents (GdCA): Gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP) - EMEA/H/A-31/1097

Applicant: various

Lead Rapporteur: Patrick Batty

Scope: Interim Analysis Report Study ALS-Gd64/001 ("Bone study") submission as a post-authorisation measure resulting from the 2010 Article 20 and Article 31 referral procedures for gadolinium-containing contrast agents.

Time table

Action: For adoption

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: List of outstanding issues/Opinion

Action: For adoption

This procedure concerns a Type II Quality WS variation (SE/H/xxxx/WS/190). The notification received by the reference member state (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

December 2018 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

Seating plan under Romanian EU presidency from January 2019 until June 2019

Action: For information

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 26-29 November 2018

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 05-07 December 2018
Action: For information

14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at December 2018 PDCO

Action: For information

Report from the PDCO meeting held on 11-14 December 2018

Action: For information

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 04-06 December 2018
Action: For information

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 10-12 December 2018

Action: For information

Request to Pharmacokinetics Working Party to draft a product-specific guideline for demonstration of bioequivalence for etonogestrel/ethinylestradiol containing contraceptive

rings

Action: For adoption

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

14.3.1. Scientific Advice Working Party (SAWP)

Chair: Robert Hemmings

Report from the SAWP meeting held on 26-29 November 2018. 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.

14.3.2. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP December 2018 meeting to CHMP for adoption:

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

Action: For adoption

14.3.3. Antimicrobial Advice ad hoc Expert Group (AMEG)

Scope: Draft scientific advice by the Antimicrobial Advice Ad Hoc Expert Group (AMEG) on the preliminary risk profiling for new antimicrobials (EMA/682199/2017)

Action: For adoption for 3 months public consultation

Scope: Draft scientific advice by the Antimicrobial Advice Ad Hoc Expert Group (AMEG) on the categorisation of antimicrobials (EMA/682198/2017)

Action: For discussion

Background information: request from the European Commission for the update of the AMEG advice on the impact on public health and animal health of the use of antibiotics in animals (link)

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

14.7.1. CHMP 2019 Work Plan

CHMP: Harald Enzmann

Action: For adoption

14.8. Planning and reporting

14.8.1. New marketing authorisation applications for 2018 with and without appointed rapporteurs

Action: For information

14.9. Others

14.9.1. EMA relocation to Amsterdam, the Netherlands

Action: For discussion

15. Any other business

15.1. AOB topic

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)*

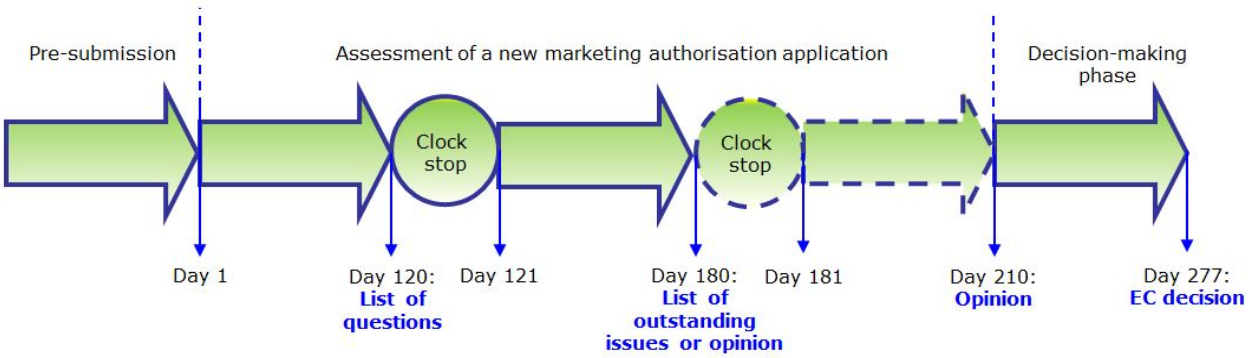
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

10 December 2018
EMA/CHMP/862846/2018 Corr[1]

Annex to 10-13 December 2018 CHMP Agenda

Pre submission and post authorisation issues

[1] Correction in section B.4.

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

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for December 2018: **For adoption**

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

Final Outcome of Rapporteurship allocation for December 2018: **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

ATryn - antithrombin alfa -
EMEA/H/C/000587/S/0035
Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli

Strensiq - asfotase alfa -
EMEA/H/C/003794/S/0032, Orphan
Alexion Europe SAS, Rapporteur: Greg Markey, PRAC Rapporteur: Rhea Fitzgerald

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Renvela - sevelamer carbonate -
EMEA/H/C/000993/R/0046
Genzyme Europe BV, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Laurence de Fays
Request for Supplementary Information adopted on 15.11.2018.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Ebilfumin - oseltamivir -

EMEA/H/C/003717/R/0012
Actavis Group PTC ehf, Generic, Generic of Tamiflu, Rapporteur: Milena Stain, PRAC Rapporteur: Kirsti Villikka

Jardiance - empagliflozin -
EMEA/H/C/002677/R/0040
Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Eva A. Segovia
Request for Supplementary Information adopted on 18.10.2018.

Mekinist - trametinib -
EMEA/H/C/002643/R/0029
Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty

Mepact - mifamurtide -
EMEA/H/C/000802/R/0047, Orphan
Takeda France SAS, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 18.10.2018.

SIMBRINZA - brinzolamide / brimonidine -
EMEA/H/C/003698/R/0014
Novartis Europharm Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Rhea Fitzgerald

SYLVANT - siltuximab -
EMEA/H/C/003708/R/0029, Orphan
Janssen-Cilag International NV, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Brigitte Keller-Stanislawski

B.2.3. Renewals of Conditional Marketing Authorisations

Bosulif - bosutinib -
EMEA/H/C/002373/R/0035
Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Martin Huber

Deltyba - delamanid - See 9.1
EMEA/H/C/002552/R/0033, Orphan
Otsuka Novel Products GmbH, Rapporteur: Greg

Markey, PRAC Rapporteur: Julie Williams

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 26-29 November 2018 PRAC:

Canagliflozin; dapagliflozin; empagliflozin; ertugliflozin – Signal of Fournier's gangrene– PRAC recommendation on a variation / DHPC

Action: For adoption

Certolizumab pegol; etanercept; golimumab; infliximab – Signal of lichenoid skin reactions for tumour necrosis factor alfa (TNFα) inhibitors - PRAC recommendation on a variation

Action: For adoption

Dulaglutide; exenatide; liraglutide – Signal of diabetic ketoacidosis- 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 December 2018 meeting:

EMEA/H/C/PSUSA/00000015/201804
(abiraterone)
CAPS:
Zytiga (EMEA/H/C/002321) (abiraterone acetate), Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia, "28 April 2017 to 27 April 2018"

EMEA/H/C/PSUSA/00000424/201804
(bortezomib)
CAPS:
Bortezomib Accord (EMEA/H/C/003984) (bortezomib), Accord Healthcare Limited, Rapporteur: Milena Stain
Bortezomib Hospira (EMEA/H/C/004207) (bortezomib), Pfizer Europe MA EEIG, Rapporteur: Milena Stain
Bortezomib SUN (EMEA/H/C/004076) (bortezomib), Sun Pharmaceutical Industries Europe B.V., Rapporteur: Katarina Vučić
VELCADE (EMEA/H/C/000539) (bortezomib),

Janssen-Cilag International NV, Rapporteur: Daniela Melchiorri
NAPS:
BORTEZOMIB GLENMARK - GLENMARK PHARMACEUTICALS S.R.O.
, PRAC Rapporteur: Amelia Cupelli, “26/04/2017 - 25/04/2018”

EMEA/H/C/PSUSA/00001069/201804
(artenimol / piperaquine tetraphosphate)
CAPS:
Eurartesim (EMEA/H/C/001199) (piperaquine tetraphosphate / artenimol), Alfasigma S.p.A., Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, “28/04/2017 - 27/04/2018”

EMEA/H/C/PSUSA/00001200/201804
(efavirenz)
CAPS:
Stocrin (EMEA/H/C/000250) (efavirenz), Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes
Sustiva (EMEA/H/C/000249) (efavirenz), Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes
NAPS:
EFAVIRENZ CREO PHARMA LIMITED - CREO PHARMA LTD
, PRAC Rapporteur: Ana Sofia Diniz Martins, “17 April 2017 to 16 April 2018”

EMEA/H/C/PSUSA/00002833/201804
(sunitinib)
CAPS:
Sutent (EMEA/H/C/000687) (sunitinib), Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, “01 May 2017 through 30 April 2018”

EMEA/H/C/PSUSA/00002839/201803
(tacrolimus (systemic formulations))
CAPS:
Advagraf (EMEA/H/C/000712) (tacrolimus), Astellas Pharma Europe B.V., Rapporteur: Jayne Crowe
Envarsus (EMEA/H/C/002655) (tacrolimus), Chiesi Farmaceutici S.p.A., Rapporteur: John Joseph Borg
Modigraf (EMEA/H/C/000954) (tacrolimus), Astellas Pharma Europe B.V., Rapporteur: Kristina Dunder
NAPS:
ADOPORT - LEK PHARMACEUTICALS D.D. LJUBLJANA

ADOPORT - SANDOZ FARMACÊUTICA LDA., SANDOZ S.P.A., SANDOZ FARMACÉUTICA, S.A., SANDOZ, SANDOZ N.V., LEK PHARMACEUTICALS D.D. LJUBLJANA, SANDOZ LTD
ADPORT - SANDOZ A/S, SANDOZ B.V., SANDOZ GMBH
CRILOMUS - HEXAL AG
ENVARSUS - CHIESI FARMACEUTICI S.P.A.
PROGRAF - ASTELLAS D.O.O.
PROGRAF - ASTELLAS PHARMA EUROPE B.V.
TACROLIMUS SANDOZ - SANDOZ B.V.
ПРОГРАФ - ASTELLAS PHARMA D.O.O.
, PRAC Rapporteur: Ronan Grimes, “01st April 2015 to 31st March 2018”

EMEA/H/C/PSUSA/00009118/201805
(decitabine)
CAPS:
Dacogen (EMEA/H/C/002221) (decitabine), Janssen-Cilag International N.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, “02/05/2017 - 01/05/2018”

EMEA/H/C/PSUSA/00010395/201805
('tolvaptan (indicated for adults with autosomal dominant polycystic kidney disease (ADPKD)))
CAPS:
Jinarc (EMEA/H/C/002788) (tolvaptan), Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, “2017-11-19 to 2018-05-18”

EMEA/H/C/PSUSA/00010644/201805
(atezolizumab)
CAPS:
Tecentriq (EMEA/H/C/004143) (atezolizumab), Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “18 November 2017 to 17 May 2018”

EMEA/H/C/PSUSA/00010668/201805
(emicizumab)
CAPS:
Hemlibra (EMEA/H/C/004406) (emicizumab), Roche Registration GmbH, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Amelia Cupelli, “16 November 2017 to 15 May 2018”

B.4. EPARs / WPARs

Erleada - apalutamide - EMEA/H/C/004452 Janssen-Cilag International N.V., treatment of non metastatic castration resistant prostate cancer (NM CRPC), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Fexinidazole Winthrop - fexinidazole - EMEA/H/W/002320, Article 58 sanofi-aventis groupe, treatment of human African trypanosomiasis (HAT), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Macimorelin Aeterna Zentaris - macimorelin - EMEA/H/C/004660 Aeterna Zentaris GmbH, Diagnosis of Adult growth hormone deficiency (AGHD), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Silodosin Recordati - silodosin - EMEA/H/C/004964 Recordati Ireland Ltd, treatment of prostatic hyperplasia (BPH), Generic, Generic of Urorec, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Canakinumab - EMEA/H/C/004754 prevention of major cardiovascular events, **WPAR**	For information only. Comments can be sent to the EPL in case necessary.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0020, Orphan Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop Opinion adopted on 22.11.2018. Request for Supplementary Information adopted on 20.09.2018.	Positive Opinion adopted by consensus on 22.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
ATryn - antithrombin alfa - EMEA/H/C/000587/II/0036 Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 29.11.2018.	
Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/002333/II/0069 GSK Vaccines S.r.l, Rapporteur: Kristina Dunder Opinion adopted on 06.12.2018.	Positive Opinion adopted by consensus on 06.12.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cinryze - C1 esterase inhibitor (human) - EMEA/H/C/001207/II/0064 Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 25.10.2018.	
Darzalex - daratumumab - EMEA/H/C/004077/II/0023, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac	
Dupixent - dupilumab - EMEA/H/C/004390/II/0006/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 29.11.2018. Request for Supplementary Information adopted on 25.10.2018, 19.07.2018.	Positive Opinion adopted by consensus on 29.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Entyvio - vedolizumab - EMEA/H/C/002782/II/0036/G Takeda Pharma A/S, Rapporteur: Greg Markey	
Entyvio - vedolizumab - EMEA/H/C/002782/II/0037 Takeda Pharma A/S, Rapporteur: Greg Markey Opinion adopted on 29.11.2018.	Positive Opinion adopted by consensus on 29.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Fasenra - benralizumab - EMEA/H/C/004433/II/0008 AstraZeneca AB, Rapporteur: Nithyanandan Nagercoil Request for Supplementary Information adopted on 08.11.2018.	
Foclivia - influenza virus surface antigens (inactivated) of strain a/vietnam/1194/2004 (h5n1) - EMEA/H/C/001208/II/0038/G Seqirus S.r.l, Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 08.11.2018.	
Fulvestrant Mylan - fulvestrant - EMEA/H/C/004649/II/0005 Mylan S.A.S, Generic, Generic of Faslodex,	Request for supplementary information adopted with a specific timetable.

Rapporteur: Natalja Karpova Request for Supplementary Information adopted on 06.12.2018.	
Humira - adalimumab - EMEA/H/C/000481/II/0184/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 06.12.2018.	Request for supplementary information adopted with a specific timetable.
Imfinzi - durvalumab - EMEA/H/C/004771/II/0001 AstraZeneca AB, Rapporteur: Sinan B. Sarac	
InductOs - dibotermin alfa - EMEA/H/C/000408/II/0093 Medtronic BioPharma B.V., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 29.11.2018.	Request for supplementary information adopted with a specific timetable.
Inflectra - infliximab - EMEA/H/C/002778/II/0070/G Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey	
KANJINTI - trastuzumab - EMEA/H/C/004361/II/0006/G Amgen Europe B.V., BREDA, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 06.12.2018.	Request for supplementary information adopted with a specific timetable.
Kevzara - sarilumab - EMEA/H/C/004254/II/0010/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus	
MULTAQ - dronedarone - EMEA/H/C/001043/II/0041 sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 13.09.2018.	
MVASI - bevacizumab - EMEA/H/C/004728/II/0005/G Amgen Europe B.V., Duplicate, Duplicate of KYOMARC, Rapporteur: Svein Rune Andersen Opinion adopted on 29.11.2018.	Positive Opinion adopted by consensus on 29.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Myalepta - metreleptin - EMEA/H/C/004218/II/0003, Orphan Aegerion Pharmaceuticals B.V., Rapporteur: Bart	

Van der Schueren	
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0015, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren	
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0086/G Pfizer Europe MA EEIG, Rapporteur: Greg Markey Request for Supplementary Information adopted on 06.12.2018.	Request for supplementary information adopted with a specific timetable.
NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0026/G Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 22.11.2018. Request for Supplementary Information adopted on 27.09.2018, 19.07.2018.	Positive Opinion adopted by consensus on 22.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Obizur - susoctocog alfa - EMEA/H/C/002792/II/0022/G Baxalta Innovations GmbH, Rapporteur: Nithyanandan Nagercoil	
Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0007 Roche Registration GmbH, Rapporteur: Mark Ainsworth Opinion adopted on 22.11.2018.	Positive Opinion adopted by consensus on 22.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Omidria - phenylephrine / ketorolac - EMEA/H/C/003702/II/0008/G Omeros London Limited, Rapporteur: Jayne Crowe Request for Supplementary Information adopted on 29.11.2018.	Request for supplementary information adopted with a specific timetable.
Pheburane - sodium phenylbutyrate - EMEA/H/C/002500/II/0019 Eurocept International B.V., Rapporteur: Jayne Crowe	
Remsima - infliximab - EMEA/H/C/002576/II/0060/G Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey	
SIRTURO - bedaquiline - EMEA/H/C/002614/II/0030, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson Request for Supplementary Information adopted	

on 08.11.2018.	
Stelara - ustekinumab - EMEA/H/C/000958/II/0070/G Janssen-Cilag International NV, Rapporteur: Greg Markey	
Vizarsin - sildenafil - EMEA/H/C/001076/II/0029 KRKA, d.d., Novo mesto, Generic, Generic of Viagra, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 22.11.2018.	Request for supplementary information adopted with a specific timetable.
Zinplava - bezlotoxumab - EMEA/H/C/004136/II/0013 Merck Sharp & Dohme B.V., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 29.11.2018.	Positive Opinion adopted by consensus on 29.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zinplava - bezlotoxumab - EMEA/H/C/004136/II/0014 Merck Sharp & Dohme B.V., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 06.12.2018.	Positive Opinion adopted by consensus on 06.12.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1393/G **Hexacima-EMEA/H/C/002702/WS1393/0080/G** **Hexaxim-EMEA/H/W/002495/WS1393/0085/G** **Hexyon-EMEA/H/C/002796/WS1393/0084/G** Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 22.11.2018. Request for Supplementary Information adopted on 11.10.2018, 19.07.2018.	Positive Opinion adopted by consensus on 22.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1438/G **Hexacima-EMEA/H/C/002702/WS1438/0083/G** **Hexaxim-EMEA/H/W/002495/WS1438/0088/G** **Hexyon-EMEA/H/C/002796/WS1438/0087/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 06.12.2018. Request for Supplementary Information adopted on 04.10.2018.	Positive Opinion adopted by consensus on 06.12.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1462	Positive Opinion adopted by consensus on

Rixathon-EMEA/H/C/003903/WS1462/0014 **Riximyo-EMEA/H/C/004729/WS1462/0014** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 06.12.2018. Request for Supplementary Information adopted on 11.10.2018.	06.12.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1478 **Saxenda-EMEA/H/C/003780/WS1478/0019** **Victoza-EMEA/H/C/001026/WS1478/0048** **Xultophy-EMEA/H/C/002647/WS1478/0027** Novo Nordisk A/S, Lead Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 06.12.2018.	Request for supplementary information adopted with a specific timetable.
WS1479/G **Halimatoz-EMEA/H/C/004866/WS1479/0001/G** **Hefiya-EMEA/H/C/004865/WS1479/0001/G** **Hyrimoz-EMEA/H/C/004320/WS1479/0001/G** Sandoz GmbH, Lead Rapporteur: Milena Stain, Lead PRAC Rapporteur: Ulla Wändel Liminga Request for Supplementary Information adopted on 22.11.2018.	Request for supplementary information adopted with a specific timetable.
WS1480 **Rixathon-EMEA/H/C/003903/WS1480/0015** **Riximyo-EMEA/H/C/004729/WS1480/0015** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 29.11.2018.	Request for supplementary information adopted with a specific timetable.
WS1499 **Fluenz Tetra-EMEA/H/C/002617/WS1499/0085** **Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/WS1499/0018** AstraZeneca AB, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 22.11.2018.	Positive Opinion adopted by consensus on 22.11.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1502 **Fertavid-EMEA/H/C/001042/WS1502/0042** **Puregon-EMEA/H/C/000086/WS1502/0100** Merck Sharp & Dohme B.V., Lead Rapporteur: Nithyanandan Nagercoil Request for Supplementary Information adopted on 06.12.2018.	Request for supplementary information adopted with a specific timetable.
WS1503/G **Prezista-EMEA/H/C/000707/WS1503/0100/G** **Rezolsta-EMEA/H/C/002819/WS1503/0029/G** **Symtuza-EMEA/H/C/004391/WS1503/0013/G** Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege	
WS1538 **Aflunov-EMEA/H/C/002094/WS1538/0046** **Foclivia-EMEA/H/C/001208/WS1538/0041** Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri	

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

Adenuric - febuxostat - EMEA/H/C/000777/II/0051 Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, “Update of section 5.1 of the SmPC in order to include the results of the clinical safety study CARES (TMX-67_301), to compare the cardiovascular outcomes of febuxostat and allopurinol in subjects with gout and cardiovascular comorbidities; this is a Multicenter, Randomized, Active-Control, Phase 3B Study. In addition, the Marketing authorisation holder (MAH) took the opportunity to provide a consolidated Module 2.7.6 in order to list all the synopsis of individual studies in a unique tabular format.” Request for Supplementary Information adopted on 04.10.2018.	
Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0021, Orphan	

Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Update of sections 4.8 and 5.1 of the SmPC to include new clinical efficacy and safety data on long-term treatment with Alprolix. The submission includes integrated evaluation of data from the extension study (9HB01EXT (BYOND) which was submitted in a previous P46 procedure) and the pivotal parent studies. The PIL is updated accordingly. In addition, the MAH took the opportunity to update the product information to comply with the latest version of the “Excipients in the labelling and package leaflet of medicinal products for human use"guideline. The list of local representatives has been updated and other minor editorial changes have been included in the PIL.”

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

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

Brineura - cerliponase alfa - EMEA/H/C/004065/II/0007, Orphan

BioMarin International Limited, Rapporteur: Martina Weise, “Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update the safety information of Brineura in relation to device-related complications and meningitis, and to include meningitis as a possible adverse reaction, based on data collected from clinical trials and post-marketing experience. The package leaflet is updated accordingly.” Request for Supplementary Information adopted on 04.10.2018.

Brineura - cerliponase alfa - EMEA/H/C/004065/II/0011, Orphan

BioMarin International Limited, Rapporteur: Martina Weise, “Update of section 4.4 of the SmPC to include a warning in relation to the access device use life following a review of the global safety database for all device-related events. The PL is updated accordingly.” Request for Supplementary Information adopted on 18.10.2018.

Cyramza - ramucirumab -
EMEA/H/C/002829/II/0023/G
Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, “Submission of the final report from study Study I4T-MC-JVCZ Randomized Phase 2 Trial Evaluating Alternative Ramucirumab Doses in Combination with Paclitaxel in Second-Line Metastatic or Locally Advanced, Unresectable Gastric or Gastroesophageal Junction Adenocarcinoma and Study I4T-MC-JVDB Randomized Phase 2 Trial Evaluating Pharmacokinetics and Safety of Four Ramucirumab Dosing Regimens in Second Line Gastric or Gastroesophageal Junction Adenocarcinoma in fulfilment with Annex II condition linked to Cyramza Marketing Authorisation. Annex II of the product information has been updated accordingly.” Request for Supplementary Information adopted on 13.09.2018, 14.06.2018.

Epivir - lamivudine -
EMEA/H/C/000107/II/0108
ViiV Healthcare UK Limited, Rapporteur: Joseph Emmerich, “Update of section 4.2 of the SmPC in order to correct the posology of paediatric patients at least 3 months of age and weighting less than 25 kg with renal impairment.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the PI in relation to sodium and propylene glycol content in line with QRD. The package leaflet is updated in accordance.”

Ferriprox - deferiprone -
EMEA/H/C/000236/II/0128
Apotex Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, “Update section 4.4 of the SmPC and the patient/carer reminder card in order to update and change the recommended frequency of ANC monitoring throughout Ferriprox treatment from a weekly basis to every week for the first six months of Ferriprox therapy, once every two weeks after six months of Ferriprox therapy, and to monthly after one year of therapy. The package leaflet has been updated accordingly. The RMP version 13.2 has also been submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update minor linguistic amendments in the HU and MT product

information."

Halaven - eribulin -
EMEA/H/C/002084/II/0047
Eisai GmbH, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add Hypocalcaemia as new adverse reaction with frequency 'common' as a result of a cumulative review on the matter requested during EMEA/H/C/PSUSA/00001254/201711 procedure (LEG 021). The Package Leaflet is updated accordingly."

IBRANCE - palbociclib -
EMEA/H/C/003853/II/0011
Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC to update the clinical efficacy data from pivotal Phase 3 Study A5481008 (PALOMA-2), a study of IBRANCE in combination with letrozoleto, to include the results from recent analyses of the study with a data cutoff date of 31 May 2017. In addition, the MAH took the oportunity to update section 4.2 to include that when coadministered with an aromatase inhibitor, the later should be administered according to the dose schedule reported in the Summary of Product Characteristics."
Request for Supplementary Information adopted on 27.09.2018, 26.07.2018, 17.05.2018.

Isentress - raltegravir -
EMEA/H/C/000860/II/0078/G
Merck Sharp & Dohme B.V., Rapporteur: Greg Markey, "Submission of the final reports from 3 in vitro studies evaluating the inhibitory effect of raltegravir at higher concentrations on OATP1B3, OCT1, OCT2, MATE1 and MATE2-K transporters and CYP2B6, CYP2D6, UGT2B7 enzyme activities, and a final CSR to assess the drug-drug interaction (DDI) potential of raltegravir at a 1,200 mg once daily clinical dose, according to the request from the CHMP following the assessment of X/59."
Request for Supplementary Information adopted on 13.09.2018.

Ivemend - fosaprepitant -
EMEA/H/C/000743/II/0040
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of sections 4.4 of the SmPC in order to update the safety information related

to Infusion Site Reactions (ISR) based on reports of post-marketing experience resulting the cumulative search of the company global safety data base for serious adverse events (interventional, spontaneous, literature and non-interventional study reports) which led to a safety labelling change notification issued by the FDA on the 23rd January2018; the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include edits in the SmPC previously and in the Package Leaflet." Request for Supplementary Information adopted on 11.10.2018.	
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0042/G Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Submission of an updated RMP version 8 in order to remove MotHER pharmacovigilance activities [MEA 011] from the European Union Risk Management Plan (EU RMP) and use the Global Enhanced Pharmacovigilance (PV) Pregnancy Program to fulfil the commitment (c.1.11.b) and to change the due date of final results for the provision of the final study report for BO27938 (KATHERINE), a category 3 study in the RMP (c.1.11.z). A randomized, multicenter, open label Phase III study to evaluate the efficacy and safety of Trastuzumab emtansine versus trastuzumab as adjuvant therapy for patients with Her2-positive primary breast cancer who have residual tumor present pathologically in the breast or axillary lymph nodes following preoperative therapy to address the following safety concerns: Left ventricular dysfunction, safety in elderly patients, immunogenicity (Anti-therapeutic Antibodies [ATAs] In addition, the MAH takes the opportunity to update the RMP in line with the version 2.0 or new GVP Module V. and include an update of Kadcyla Educational Material to reflect changes in the Prescribing information following the renewal of the marketing authorisation."	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0062 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Update of sections 4.2 and 5.1 of the SmPC to add an alternative dosing regimen of	

400 mg every 6 weeks (Q6W) for all approved indications and indications currently under review in addition to the currently approved 200 mg every Q3W, based on modeling and simulation analysis. No new clinical or pre-clinical studies are being submitted as part of the current application. The Package Leaflet (section 3) is updated accordingly."

Lartruvo - olaratumab - EMEA/H/C/004216/II/0012, Orphan

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

Latuda - lurasidone - EMEA/H/C/002713/II/0022

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

Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029/II/0003/G

AstraZeneca AB, Rapporteur: Romaldas Mačiulaitis, "1) type II (C.I.4): Update of sections 4.8 and 5.1 of the SmPC in order to update the information based on final results from study ZS-005 (category 3 PASS study in the RMP). This is an open-label, multicentre, multi-dose, prospective maintenance study to investigate the long-term safety and efficacy of Lokelma (sodium zirconium cyclosilicate) in subjects with hyperkalaemia.
2) type II (C.I.4): Update of section 4.5 of the SmPC in order to add information regarding the use with drugs that have the potential for drug-drug interaction based on an increase in gastric PH.
The Package Leaflet has been updated accordingly."
Request for Supplementary Information adopted on 04.10.2018, 28.06.2018.

LUTATHERA - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123/II/0005, Orphan

Advanced Accelerator Applications, Rapporteur: Robert James Hemmings, “Update of the SmPC section 5.1 to include information on the quality of life based on analysis of Netter-I Quality of Life data.”

Request for Supplementary Information adopted on 20.09.2018.

Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0038

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

Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0083

Pfizer Europe MA EEIG, Rapporteur: Greg Markey, “Update of section 4.4 of the SmPC in order to include a safety warning of the risk for invasive disease caused by Meningococcal polysaccharide serogroups A, C, W-135 and Y because of the use of Nimenrix with concomitant treatment of eculizumab.”

Request for Supplementary Information adopted on 18.10.2018.

Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0084

Pfizer Europe MA EEIG, Rapporteur: Greg Markey, “Update of section 4.2 of the SmPC in order to update the posology information in infants, following the final results from study MenACWY-TT-087 (Study 087); this is a phase IIIb, controlled, randomised, open study aimed to demonstrate the immunogenicity and safety of Nimenrix in healthy infants, given on a 3+1 primary and booster (2, 4, 6 and 15-18 months of age), a 1+1 primary and booster (6 and 15-18

months of age) or as a single dose at 15-18 months of age. The Package Leaflet is updated accordingly. The MAH took the opportunity to include editorial changes in sections 4.4 and 4.8 of the SmPC." Request for Supplementary Information adopted on 18.10.2018.	
Ongentys - opicapone - EMEA/H/C/002790/II/0015 Bial - Portela & Cª, S.A., Rapporteur: Greg Markey, "Submission of the analytical data results on M10 in patients treated once daily for more than 6 months using a validated analytical method. This variation fulfills the commitment made in REC 002."	
OPDIVO - nivolumab - EMEA/H/C/003985/II/0057 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, "Update of section 5.1 of the SmPC in order to include descriptive efficacy data available from study CA209374 (A Phase 3b/4 Safety Trial of Nivolumab (BMS-936558) in Subjects With Advanced or Metastatic Renal Cell Carcinoma)."	
Resolor - prucalopride - EMEA/H/C/001012/II/0046 Shire Pharmaceuticals Ireland Limited, Rapporteur: Greg Markey, "Update of section 4.8 of the SmPC in order to add migraine and vertigo as uncommon adverse events, based on a reanalysis of the integrated safety information of 16 double-blind, placebo-controlled studies. In addition, the Marketing authorisation holder (MAH) made editorial revision proposals for sections 4.4, 4.6 and 5.2 for alignment with Company Core Data Sheet version 12 and QRD templated wording. The MAH also took the opportunity to propose minor editorial changes to Package Leaflet and sections 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC."	
Revestive - teduglutide - EMEA/H/C/002345/II/0043, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Mark Ainsworth, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC based on the final CSR of study TED-C14-006 ("a 24-Week Double-blind, Safety, Efficacy, and Pharmacodynamic Study Investigating Two	

Doses of Teduglutide in Pediatric Subjects Aged 1 Year Through 17 Years With Short Bowel Syndrome who are Dependent on Parenteral Support"; a category 3 study in the RMP). The Package Leaflet is updated accordingly."
Request for Supplementary Information adopted on 15.11.2018, 20.09.2018, 26.07.2018, 31.05.2018.

Rubraca - rucaparib - EMEA/H/C/004272/II/0002, Orphan
Clovis Oncology UK Limited, Rapporteur: Jorge Camarero Jiménez, "Submission of the final study report (QS-CLV-010) on the exploratory population pharmacokinetic analysis of rucaparib undertaken to test additional semi-mechanistic absorption and distribution models."
Request for Supplementary Information adopted on 18.10.2018.

Stelara - ustekinumab - EMEA/H/C/000958/II/0066
Janssen-Cilag International NV, Rapporteur: Greg Markey, "Update of section 4.8 of the SmPC to add allergic alveolitis and eosinophilic pneumonia as rare adverse reaction. The PL is updated accordingly."
Request for Supplementary Information adopted on 27.09.2018.

Stribild - elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil - EMEA/H/C/002574/II/0097
Gilead Sciences Ireland UC, Rapporteur: Robert James Hemmings, "Submission of the final report from study GS-US-236-0112, a phase 2/3, open-label study of the pharmacokinetics, safety and antiviral activity of the elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate single tablet regimen (STR) in HIV-1 infected antiretroviral treatment-naive adolescents. This submission fulfils the post-authorisation measures MEA 019 and P46 020."
Request for Supplementary Information adopted on 11.10.2018.

Sutent - sunitinib - EMEA/H/C/000687/II/0070
Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include paediatric study results (from studies A6181196 and

ACNS1021) performed in compliance with a paediatric investigation plan (PIP).”
Request for Supplementary Information adopted on 08.11.2018, 27.09.2018.

Tyverb - lapatinib - EMEA/H/C/000795/II/0057
Novartis Europharm Limited, Rapporteur: Filip Josephson, “Update of section 4.6 of the SmPC in order to update the safety information on pregnancy and breast-feeding following review of the company Core Data Sheet (CDS).The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Estonia and Lithuania in the Package Leaflet. Moreover, the MAH took the opportunity to make minor editorial changes/clarification in labelling for bottle presentations.”

Venclyxto - venetoclax - EMEA/H/C/004106/II/0016, Orphan
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, “Submission of the report from study M13-982 listed as a category 3 study in the RMP. This is a Phase 2 Open-Label Study of the Efficacy of ABT199 (GDC-0199) in Subjects with Relapsed/Refractory or Previously Untreated Chronic Lymphocytic Leukemia Harboring the 17p Deletion.”
Request for Supplementary Information adopted on 13.09.2018.

Vosevi - sofosbuvir / velpatasvir / voxilaprevir - EMEA/H/C/004350/II/0018
Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, “Update of section 5.1 of the SmPC based on final results from study GS-US-367-4181. This is an open-label study to evaluate the safety and efficacy of sofosbuvir/velpatasvir/voxilaprevir fixed-dose combination for 12 weeks in subjects who participated in a prior Gilead-sponsored HCV treatment study.”

Zostavax - shingles (herpes zoster) vaccine (live) - EMEA/H/C/000674/II/0117
MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.5 and 5.1 of the SmPC to include that Zostavax can be given concomitantly with pneumococcal vaccine and to reflect the results of an observational post-marketing study

comparing the effectiveness of Zostavax when co-administrated with a 23-valent pneumococcal polysaccharide vaccine (Bruxvoort K et al. 2018). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet."
Request for Supplementary Information adopted on 20.09.2018.

Zykadia - ceritinib -
EMEA/H/C/003819/II/0027
Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, "C.I.13: Submission of the final Biomarker annual update report from phase II studies (A2201 and Study A2203) in order to fulfil the following Post-Marketing Measure identified by the CHMP: To submit a yearly update of the biomarker program for ceritinib."

WS1401
Genvoya-EMEA/H/C/004042/WS1401/0047
Stribild-EMEA/H/C/002574/WS1401/0094
Tybost-EMEA/H/C/002572/WS1401/0044
Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings, "Update of section 4.6 the SmPC for Tybost, Stribild and Genvoya based on pharmacokinetics data in pregnancy from IMPAACT study P1026s (ClinicalTrials.gov ID NCT00042289); this is an ongoing, nonrandomized, open-label, parallel-group, multi-centre phase 4 prospective study of antiretroviral (ARV) pharmacokinetics (PK) and safety in HIV-1 infected pregnant women that includes an arm for EVG/COBI. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10."
Request for Supplementary Information adopted on 11.10.2018, 12.07.2018.

WS1454
Zypadhera-EMEA/H/C/000890/WS1454/0035
Zyprexa-EMEA/H/C/000115/WS1454/0127
Zyprexa
Velotab-EMEA/H/C/000287/WS1454/0095
Eli Lilly Nederland B.V., Duplicate, Duplicate of

Olansek (SRD), Lead Rapporteur: Outi Mäki-Ikola, “Update section 4.8 of the SmPC to add stuttering as adverse drug reaction based on data from clinical trials and spontaneous reporting. PL is updated accordingly. In addition, the MAH took this opportunity to revised wording of section 5.2 on pharmacokinetics of olanzapine in hepatically impaired patients to improve clarity.
In addition, the list of local representatives in the PL is being revised.”
Request for Supplementary Information adopted on 18.10.2018.

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

WS1472
Exviera-EMEA/H/C/003837/WS1472/0040
Viekirax-EMEA/H/C/003839/WS1472/0049
AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, “Submission of the final report from study M12-999 listed as a category 3 study in the RMP. This is an open-label, phase 2 study to evaluate the safety and efficacy of the combination of of ombitasvir/paritaprevir/ritonavir with or without dasabuvir and with or without ribavirin (RBV) in adult liver or renal transplant recipients with Hepatitis C Virus (HCV) GT1 or GT4 infection (CORAL I).”
Request for Supplementary Information adopted on 18.10.2018.

WS1473
Exviera-EMEA/H/C/003837/WS1473/0041
Viekirax-EMEA/H/C/003839/WS1473/0050
AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, “Submission of the

final report from study M14-004 listed as a category 3 study in the RMP. This is a multipart, open-label study to evaluate the safety and efficacy of ombitasvir/paritaprevir/ritonavir with or without dasabuvir coadministered with and without ribavirin in adults with Genotype 1 or 4 Chronic Hepatitis C Virus infection and Human Immunodeficiency Virus, Type 1 co-infection (TURQUOISE-I)."
Request for Supplementary Information adopted on 18.10.2018.

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

WS1495
Lyrica-EMEA/H/C/000546/WS1495/0096
Pregabalin
Pfizer-EMEA/H/C/003880/WS1495/0026
Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect information from study A0081042 A Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study of the Efficacy and Safety of Pregabalin as Adjunctive Therapy in Children 1 Month through less than 4 Years of Age with Partial Onset Seizures. This submission relates to paediatric studies submitted according to Article 46 of the paediatric regulation (EC) No 1901/2006."

WS1506/G
Nuwiq-EMEA/H/C/002813/WS1506/0026

/G

Vihuma-EMEA/H/C/004459/WS1506/0009/G

Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.2, 4.8 and 5.1 of the SmPC based on clinical data from studies GENA-21 and GENA-13. The Package Leaflet is updated accordingly.”

B.5.3. CHMP-PRAC assessed procedures

CYLTEZO - adalimumab - EMEA/H/C/004319/II/0004

Boehringer Ingelheim International GmbH, Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga, “Submission of the final report from study 1297.3 listed as a category 3 study in the RMP. This is an interventional trial to generate long-term safety, efficacy, and immunogenicity data for the administration of the proposed biosimilar Cyltezo in patients with moderate to severe rheumatoid arthritis.” Request for Supplementary Information adopted on 06.09.2018.

Dacogen - decitabine - EMEA/H/C/002221/II/0033, Orphan

Janssen-Cilag International N.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, “Update of section sections 4.2, 4.8, 5.1 and 5.2 of the SmPC to reflect the results from paediatric study DACOGENAML2004 titled ‘Phase 1-2 Safety and Efficacy Study of DACOGEN in sequential administration with Cytarabine in children with relapsed or refractory acute myeloid leukemia’, provided as per the requirement of article 46. The RMP version 3.1 (in line with the revision 2 of the RMP template) has also been submitted.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.4 of the SmPC to align the safety warning related to sodium excipient with the Annex to the revised European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use'. The Package Leaflet is updated in accordance. Moreover, the contact details of the local representative in Slovenia have been updated in the Package Leaflet.” Request for Supplementary Information adopted

on 18.10.2018, 26.07.2018, 31.05.2018.

Darzalex - daratumumab - EMEA/H/C/004077/II/0020, Orphan

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

Darzalex - daratumumab - EMEA/H/C/004077/II/0021, Orphan

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

ELOCTA - efmoroctocog alfa - EMEA/H/C/003964/II/0026

Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Julie Williams, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to add a statement for a once-weekly prophylaxis dose and to update the safety information based on the final results from study 8HA01EXT listed as a category 3 study in the RMP; this is a interventional study that evaluated the long-term safety (particularly immunogenicity) and efficacy of ELOCTA in the prevention and treatment of bleeding episodes and for perioperative management. This variation is a follow-up of P46/005 submitted on 16.04.18
RMP version 2.1 was submitted and followed revision 2 of the template."
Request for Supplementary Information adopted on 18.10.2018.

Entyvio - vedolizumab - EMEA/H/C/002782/II/0034

Takeda Pharma A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Adam Przybylkowski, "Update of section 5.1 of the SmPC in order to provide the final efficacy results up to week 348 regarding

clinical study c13008, listed as a category 3 study in the RMP. This is a Phase 3, Open-label Study to Determine the Long-term Safety and Efficacy of Vedolizumab in subjects with Ulcerative Colitis and Crohn's Disease.
The RMP version 4 has also been submitted."
Request for Supplementary Information adopted on 04.10.2018.

Entyvio - vedolizumab - EMEA/H/C/002782/II/0035

Takeda Pharma A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Adam Przybylkowski, "Update of sections 4.2, 4.4, 4.6, 5.1 and 5.3 of the SmPC in order to update the safety information following review of Company Core Data Sheet and literature review. Update of sections 4.6 and 5.3. is proposed with regards to the information on lactation, based on findings from non-Takeda, recently published data. In addition, the MAH proposed clarifications to other sections of the SmPC.
The Package Leaflet is updated accordingly.
The MAH also took the opportunity to correct typographical errors, spelling mistakes and other minor updates to the local languages Product Information."

MabThera - rituximab - EMEA/H/C/000165/II/0157

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Update of Annex II section D of the product information, resulting from the obligation fulfilment for the rituximab subcutaneous formulation at a dose of 1400 mg by the submission of the final clinical study report for study BO22334 (SABRINA, category 1) including reports on long-term safety in relation to body surface area (BSA) (as a measure for exposure variation) and to gender. SABRINA is a two-stage Phase III, international, multi-centre, randomized, controlled, open-label study investigating the pharmacokinetics (PK), efficacy and safety of rituximab SC in combination with cyclophosphamide, doxorubicin, vincristine, prednisolone (CHOP) chemotherapy or cyclophosphamide, vincristine, prednisolone (CVP) chemotherapy versus rituximab IV in combination with CHOP or CVP chemotherapy followed by maintenance treatment with either rituximab SC or rituximab IV.)

Furthermore, the RMP version 19.0 has also been updated accordingly to reflect the removal this commitment. In addition, the Marketing authorisation holder (MAH) took the opportunity to include other changes to the RMP including the fulfilment of the previous information on concluded commitments such as the prolonged B-cell depletion and immunogenicity associated with the subcutaneous formulation."	
MabThera - rituximab - EMEA/H/C/000165/II/0158 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Update of Annex II section D of the product information, resulting from the obligation fulfilment for the rituximab subcutaneous formulation at a dose of 1400 mg by the submission of the final clinical study report for study BO25341 (SAWYER, category 1) including reports on long-term safety in relation to body surface area (BSA) (as a measure for exposure variation) and to gender. SAWYER is a Phase Ib adaptive, comparative, randomized, parallel-group, multi-center study of subcutaneous (SC) rituximab versus intravenous (IV) rituximab both in combination with chemotherapy (fludarabine and cyclophosphamide), in patients with previously untreated CLL. Furthermore, the RMP version 19.0 has also been updated accordingly to reflect the removal this commitment. In addition, the Marketing authorisation holder (MAH) took the opportunity to include the changes on the concluded commitment such as the prolonged B-cell depletion and immunogenicity associated with the subcutaneous formulation."	
Mimpara - cinacalcet - EMEA/H/C/000570/II/0062/G Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update to Section 4.4 of the SmPC to provide additional information on switching from etelcalcetide to Mimpara (cinacalcet), upon request by PRAC following the assessment of the etelcalcetide PSUR (dated 14 June 2018). Further, the term 'silica, dental type' has been replaced by 'Amorphous silicon dioxide' in SmPC section 6.1. An updated RMP version 9.0 was provided as part of the application in order to align the RMP with	

the GVP Module V (template Rev 2) with consequential reclassification of existing safety concerns."

Onivyde - irinotecan hydrochloride trihydrate - EMEA/H/C/004125/II/0008, Orphan

Baxalta Innovations GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: David Olsen, "Update of sections 1, 2, 4.2, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC in order to reflect the expression of strength based on irinotecan anhydrous free-base. The Labelling and Package Leaflet are updated accordingly. In addition the MAH took the opportunity to introduce minor editorial changes. The updated RMP version 2.1 has also been submitted."

Request for Supplementary Information adopted on 15.11.2018, 18.10.2018, 20.09.2018.

Parsabiv - etelcalcetide - EMEA/H/C/003995/II/0010

Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.8 to add convulsions secondary to hypocalceaemia as uncommon adverse reactions and further information on reports related to hypersensitivity reactions. Editorial correction is made to section 7. The Package Leaflet is update accordingly. Consequentially, RMP (version 2) has been submitted to reclassify some of the existing safety concerns."

Reyataz - atazanavir / atazanavir sulfate - EMEA/H/C/000494/II/0117

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, "Submission of the final reports from studies AI424397 (PRINCE I) and AI424451 (PRINCE II) listed as a category 3 studies in the RMP. These studies were phase IIIb, prospective, single arm, open-label, international, multicentre studies to evaluate the safety, efficacy and pharmacokinetics of atazanavir powder boosted with ritonavir and administered with an optimised NRTI background therapy, in HIV infected paediatric patients.

The RMP version 15.0 has also been submitted to reflect on the final data from these two paediatric studies. In addition, the MAH took the opportunity to introduce the new RMP template

Rev. 2."
Request for Supplementary Information adopted on 04.10.2018.

Toujeo - insulin glargine - EMEA/H/C/000309/II/0105/G
Sanofi-Aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 20.09.2018.

Tremfya - guselkumab - EMEA/H/C/004271/II/0005
Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.4 and 4.8 of the SmPC in order to add hypersensitivity and rash as adverse drug reactions with the frequency uncommon, together with a statement describing the characteristics of the serious hypersensitivity events. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted."

XGEVA - denosumab - EMEA/H/C/002173/II/0065
Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.8 of the SmPC to modify the frequency category of the ADR Atypical Femoral Fracture (AFF) from "rare" to "uncommon" and to add descriptive language regarding latency observed in clinical studies. The Package Leaflet has been updated accordingly. In addition, the MAH is taking the opportunity to remove the black triangle and corresponding text from the Annexes as Xgeva is no longer under additional monitoring, to implement editorial changes in the annexes and to update the contact details of the local representative in Ireland in the Package Leaflet.
An updated RMP (version 33) was provided as part of the application."

Xolair - omalizumab - EMEA/H/C/000606/II/0093
Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of section 4.6 of the SmPC based on the data from the Xolair Pregnancy Registry (EXPECT) and final study report Q2952g listed as

a category 3 study in the RMP; this is an observational study to evaluate pregnancy outcomes and estimate the incidence of spontaneous fetal loss in pregnant women exposed to omalizumab prenatally and to explore the potential risk to newborn infants exposed via breast milk. The Package Leaflet is proposed to be updated accordingly. The RMP version 14.0 has also been submitted."	
Zykadia - ceritinib - EMEA/H/C/003819/II/0026 Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin, "Update of section 4.5 of the SmPC in order to update the safety information based on final results from study CLDK378A2103, a Post Authorisation Measure Study (MEA 002) which evaluated the effects of ceritinib daily dosing on the pharmacokinetics of the probe drugs midazolam and warfarin, which are metabolised by CYP3A4 and CYP2C9 respectively, in patients with ALK-positive advanced tumors including NSCLC. The Package Leaflet is updated accordingly. The RMP version 14 has also been submitted."	
WS1461 **Glyxambi-EMEA/H/C/003833/WS1461/0017** **Jentadueto-EMEA/H/C/002279/WS1461/0047** **Trajenta-EMEA/H/C/002110/WS1461/0035** Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 , 4.8 and 5.1 of the SmPC to update the warnings related to acute pancreatitis and bullous pemphigoid and the efficacy and safety information based on final results from study listed as a category 3 in the RMP "A multicenter, international, randomized, parallel group, double blind, placebo-controlled CArdiovascular Safety & Renal Microvascular outcomE study with LINAgliptin, 5 mg once daily in patients with type 2 diabetes mellitus at high vascular risk (CARMELINA)". The RMP have also been updated accordingly for all products (Trajenta and Jentadueto version 12, Glyxambi version 4.0) and to be in accordance with the revision 2 of the	

RMP template."

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

B.5.4. PRAC assessed procedures

PRAC Led
alli - orlistat - EMEA/H/C/000854/II/0058
Glaxo Group Ltd, Informed Consent of Xenical, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Submission of the final report for non-interventional PASS study 204675 "Evaluating the effectiveness of the revised alli pack information in helping pharmacy staff within the EU supply alli appropriately" listed as a category 3 study in the RMP.
In addition, the MAH took the opportunity to update the RMP template in accordance to GVP module V Rev 2 (RMP version 17)."

PRAC Led
Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0148
Amgen Europe B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Update of annex IID to implement information on education material proposal to address the incorrect self-administration of Aranesp via the SureClick pre-filled pen and associated dosing errors. The RMP (version 9.1) is updated accordingly and aligned to the latest revision 2."

Request for Supplementary Information adopted on 04.10.2018.

PRAC Led

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

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

PRAC Led

Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/II/0063

Omrix Biopharmaceuticals N. V., , PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "C.I.11: Submission of an updated RMP version 14.2 in order to transition to RMP version 2, updated exposure data, updates following PRAC request in accordance to PSUSA/00010297 (removal of lack of efficacy as identified risk), reclassification and/or removal of risk from the safety specification."

Request for Supplementary Information adopted on 04.10.2018.

PRAC Led

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

Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Provision of final Study Report for non-interventional PASS Study RRA-21430; Acute Pancreatitis Retrospective Observational Epidemiology Cohort Study: Acute pancreatitis in patients with

T2DM who are new users of canagliflozin as compared with new users of other AHAs: a retrospective cohort study using large claims databases in the US."

PRAC Led

JETREA - ocriplasmin -

EMEA/H/C/002381/II/0042/G

Oxurion NV, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "C.I.13z: Submission of the final report from 'ORBIT study (TG-MV-018): Ocriplasmin Research to Better Inform Treatment (ORBIT)'. This is a multicenter, prospective, observational study which assesses clinical outcomes and safety of JETREA® administered in a real-world setting for the treatment of symptomatic VMA.

C.I.13z: Submission of the final report from 'Use of Intravitreal JETREA® in Clinical Practice: A European Prospective Drug Utilisation Study (TG-MV-017)' listed as a category 3 study in the RMP. This study is a European, multicentre, observational study. The study includes two parts, a drug utilisation study (DUS) and the Patient Educational Material Evaluation Survey (PEMES). The main objective of the DUS is to document JETREA utilisation patterns in real-life clinical practice. The objective of the PEMES is to assess the effectiveness of the risk minimisation measures (i.e. the patient educational material [PEM] provided to patients prior to the injection of JETREA).

C.I.13z: Submission of the final report from 'INJECT: INvestigation of JETREA® in Patients with Confirmed Vitreomacular Traction'. This is a non-interventional, multi-centre, worldwide study in patients treated with JETREA® (ocriplasmin) for the approved indication in their country. The aim of the study is to evaluate safety, clinical effectiveness, and HRQoL outcomes in a real world setting among a large population of patients exposed to ocriplasmin across different countries according to country's approved indications.

In addition, RMP V7.2 has been updated accordingly and the second revision of the RMP template has been implemented as well."

PRAC Led

MabThera - rituximab -

EMEA/H/C/000165/II/0152

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, “Submission of the final study report of the non-interventional drug utilisation study (DUS) BA28478 (MabThera drug utilisation study and patient alert card evaluation in non-oncology patients in Europe: an infusion centre-based approach). Consequently, update of sections 4.2 and 4.4 of the SmPC and Annex II.E to remove the patient alert card as an additional risk minimisation measure for the risks of PML and infections, for the non-oncology indications. The Package leaflet is updated in accordance. The RMP is laso updated (version 18). This submission is done in fulfilment of FUM-68.1 and FUM-71.”
Request for Supplementary Information adopted on 06.09.2018.

PRAC Led

Neulasta - pegfilgrastim - EMEA/H/C/000420/II/0099

Amgen Europe B.V., Rapporteur: Robert James Hemmings, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Robert James Hemmings, “Submission of an updated RMP version 5.1 in order to add study 20160176, a retrospective cohort study of female breast cancer patients aged 66 years and over selected from the US SEER-Medicare database to estimate the risk of acute myeloid leukemia/myelodysplastic syndrome for breast cancer patients, as a new Pharmacovigilance activity (category 3). In addition the MAH submitted the draft protocol for study 20160176.”
Request for Supplementary Information adopted on 12.07.2018.

PRAC Led

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

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

PRAC Led

Thalidomide Celgene - thalidomide - EMEA/H/C/000823/II/0056, Orphan

Celgene Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, “Update of the RMP version 19 in line with the updated Guideline on Good Pharmacovigilance Practices (GVP) Module V to propose the reclassification and/or renaming of known safety concerns associated with the use of thalidomide. Consequently, Annex IID, SmPC section 4.4 and 4.6 and PL have been updated accordingly.” Request for Supplementary Information adopted on 04.10.2018.

PRAC Led

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

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

PRAC Led

Volibris - ambrisentan - EMEA/H/C/000839/II/0055

GlaxoSmithKline (Ireland) Limited, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Concepcion Prieto Yerro, “C.I.11: Submission of an updated RMP (version 7.6) in order to remove the provision of the educational materials for healthcare professionals given the availability of the SmPC and the experience of using ambrisentan as requested by the PRAC in the PSUR procedure PSUSA/00000129/201706. The Annex II of the product information is updated accordingly. In addition, the MAH also took the opportunity to update the Annex II as requested by the Portuguese Agency following the approval of the last update to the educational materials (risks of decreases in haemoglobin or haematocrit, renal impairment, peripheral oedema and fluid retention, and hypersensitivity reaction) and to correct typographical errors in the Annex II of the product information.” Request for Supplementary Information adopted

on 12.07.2018.

PRAC Led

WS1357

Efficib-EMEA/H/C/000896/WS1357/0089

Janumet-EMEA/H/C/000861/WS1357/0089

Januvia-EMEA/H/C/000722/WS1357/0063

Ristaben-EMEA/H/C/001234/WS1357/0055

Ristfor-EMEA/H/C/001235/WS1357/0076

TESAVEL-EMEA/H/C/000910/WS1357/0063

Velmetia-EMEA/H/C/000862/WS1357/0092

Xelevia-EMEA/H/C/000762/WS1357/0067

Merck Sharp & Dohme B.V., Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP version 10 in order to remove “theoretic carcinogenic potential” form the list of safety concerns, currently classified as “missing information”.”

Request for Supplementary Information adopted on 06.09.2018, 12.04.2018.

PRAC Led

WS1364

Lyrica-EMEA/H/C/000546/WS1364/0092

Pregabalin

Pfizer-EMEA/H/C/003880/WS1364/0021

Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP version 12.0 in order to include the changes proposed by EMEA/H/C/PSUSA/00002511/201701, updating the safety specifications and risk minimisation measures. The pharmacovigilance plan has also been updated. The draft protocol for non-interventional non-imposed PASS (A0081359) titled “A population-based cohort study of Pregabalin to characterize pregnancy outcomes” has been submitted.

The MAH has taken the opportunity to include minor updates and to align the RMP to template revision 2.”

Request for Supplementary Information adopted

on 04.10.2018, 17.05.2018.

PRAC Led
WS1402
Bretaris
Genuair-EMEA/H/C/002706/WS1402/0038
Eklira
Genuair-EMEA/H/C/002211/WS1402/0038
AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of an updated RMP version 7.0 in order to proposed changes in categorisation of safety concerns and missing information in the RMP as per the guidance provide for the revision 2 of the RMP and to provide the RMP under the revision 2 template."
Request for Supplementary Information adopted on 06.09.2018.

PRAC Led
WS1403
Brimica
Genuair-EMEA/H/C/003969/WS1403/0023
Duaklir
Genuair-EMEA/H/C/003745/WS1403/0023
AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of an updated RMP version 4.0 in order to proposed changes in categorisation of safety concerns and missing information in the RMP as per the guidance provide for the revision 2 of the RMP and to provide the RMP under the revision 2 template."
Request for Supplementary Information adopted on 06.09.2018.

B.5.5. CHMP-CAT assessed procedures

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0027, ATMP
Amgen Europe B.V., Rapporteur: Olli Tenhunen, , "Update of section 4.8 of the SmPC in order to add granulomatous dermatitis as new adverse drug reaction with an uncommon frequency and to update the adverse reaction dyspnoea from

dyspnoea exertional to dyspnoea under common frequency."

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0001, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune Kjeken,

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

PRAC Led
Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0028, ATMP
Amgen Europe B.V., Rapporteur: Olli Tenhunen, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 4.0 in order to align the important identified and potential risks and missing information with the revised guideline Good Pharmacovigilance Practices Module V (Revision 2), resulting in the reclassification and removal of a number of identified and potential risks and missing information."

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

WS1445
Kisplyx-EMEA/H/C/004224/WS1445/0017
Lenvima-EMEA/H/C/003727/WS1445/0020
Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren
Request for Supplementary Information adopted on 11.10.2018.

WS1457/G
Fertavid-EMEA/H/C/001042/WS1457/0040/G
Puregon-EMEA/H/C/000086/WS1457/0098/G
Merck Sharp & Dohme B.V., Informed Consent of Puregon, Lead Rapporteur: Nithyanandan Nagercoil
Request for Supplementary Information adopted on 11.10.2018.

WS1460

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

Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, “To update Section 4.7 “Effects on the ability to drive and use machines “ of the current Viagra, Ververti and sildenafil Pfizer (sildenafil citrate) Summaries of Product Characteristics (SmPCs), to align the content of the SmPC with the requirement of the current European Union (EU) Quality Review of Documents (QRD) template. The package leaflet (PL) has already been updated accordingly.”

WS1466/G

Atripla-EMEA/H/C/000797/WS1466/0133/G

Biktarvy-EMEA/H/C/004449/WS1466/0002/G

Descovy-EMEA/H/C/004094/WS1466/0035/G

Emtriva-EMEA/H/C/000533/WS1466/0126/G

Eviplera-EMEA/H/C/002312/WS1466/0094/G

Genvoya-EMEA/H/C/004042/WS1466/0052/G

Odefsey-EMEA/H/C/004156/WS1466/0036/G

Stribild-EMEA/H/C/002574/WS1466/0098/G

Truvada-EMEA/H/C/000594/WS1466/0152/G

Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings

---

WS1471/G

Infanrix hexa-EMEA/H/C/000296/WS1471/0248/G

GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren,

---

WS1481

Mircera-EMEA/H/C/000739/WS1481/0071

NeoRecormon-EMEA/H/C/000116/WS1481/0100

Roche Registration GmbH, Lead Rapporteur: Martina Weise

WS1485/G

Competact-EMEA/H/C/000655/WS1485/0072/G

Glubrava-EMEA/H/C/000893/WS1485/00

58/G

Takeda Pharma A/S, Lead Rapporteur: Peter Kiely,

WS1487

Blitzima-EMEA/H/C/004723/WS1487/0017

Ritemvia-EMEA/H/C/004725/WS1487/0017

Rituzena-EMEA/H/C/004724/WS1487/0018

Truxima-EMEA/H/C/004112/WS1487/0019

Celltrion Healthcare Hungary Kft., Duplicate, Duplicate of Truxima, Lead Rapporteur: Sol Ruiz

WS1492

Stribild-EMEA/H/C/002574/WS1492/0104

Truvada-EMEA/H/C/000594/WS1492/0155

Viread-EMEA/H/C/000419/WS1492/0195

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

WS1507

Abseamed-EMEA/H/C/000727/WS1507/0078

Binocrit-EMEA/H/C/000725/WS1507/007

8
Epoetin alfa
Hexal-EMEA/H/C/000726/WS1507/0077
Sandoz GmbH, Lead Rapporteur: Alexandre Moreau, “To align the Instruction For Use (IFU) to include additional information concerning myelodysplastic syndromes (MDS). The annexes are also brought in line with the QRD general principles regarding the SmPC information for a generic/hybrid/biosimilar product”

WS1514
HyQvia-EMEA/H/C/002491/WS1514/0044
Kiovig-EMEA/H/C/000628/WS1514/0084
Baxalta Innovations GmbH, Lead Rapporteur: Jan Mueller-Berghaus

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

MULTAQ - dronedarone - EMEA/H/C/001043/II/0041
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege
Request for Supplementary Information adopted on 13.09.2018.

Withdrawal of type II variation application

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

adalimumab - EMEA/H/C/004879
, treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa (HS), crohn’s disease, paediatric Crohn’s disease, ulcerative colitis, uveitis, paediatric uveitis, treatment of juvenile idiopathic arthritis, paediatric plaque psoriasis, paediatric Crohn's disease, adolescent hidradenitis suppurativa, paediatric uveitis, treatment of juvenile idiopathic arthritis, paediatric plaque psoriasis, paediatric Crohn's disease, paediatric uveitis

deferasirox - EMEA/H/C/005156
, treatment of chronic iron overload, Generic, Generic of EXJADE

adalimumab - EMEA/H/C/005253
, treatment of juvenile idiopathic arthritis,

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

imipenem / cilastatin / relebactam - EMEA/H/C/004808
, 4.1 Therapeutic indications
TRADEMARK is indicated for the treatment of bacterial infections due to gram-negative microorganisms

osilodrostat - EMEA/H/C/004821, Orphan
Novartis Europharm Limited, treatment of Cushing's syndrome

solriamfetol - EMEA/H/C/004893
, is indicated to improve wakefulness in patients with narcolepsy or obstructive sleep apnoea.

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

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

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

mecasermin - EMEA/H/C/000704/S/0055

susoctocog alfa - EMEA/H/C/002792/S/0023

cholic acid - EMEA/H/C/001250/S/0026, Orphan
Laboratoires CTRS

tocofersolan - EMEA/H/C/000920/S/0031

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

Natpar - parathyroid hormone - EMEA/H/C/003861/R/0016, Orphan
Shire Pharmaceuticals Ireland Limited,
Rapporteur: Bart Van der Schueren, PRAC
Rapporteur: Rhea Fitzgerald

Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (H5N1) (live attenuated, nasal) - EMEA/H/C/003963/R/0019
AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Daniela Philadelphy

Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/R/0063
ViiV Healthcare UK Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber

Zydelig - idelalisib - EMEA/H/C/003843/R/0043
Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

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

Imbruvica - ibrutinib - EMEA/H/C/003791/II/0046, Orphan
Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "Extension of Indication to include new indication for Imbruvica; to broaden the current indication and apply for an extension of indication with respect to include treatment of adult patients with Waldenström's macroglobulinaemia (WM) in combination with rituximab. This proposed broaden indication is supported by the final clinical study report results of phase 3 study PCYC-1127-CA. As a consequence, section 4.1 and 4.8 of the SmPC is updated update the safety information. No changes were required to the broaden indication for the Package Leaflet. In addition, the Marketing authorisation holder (MAH) took the opportunity to update in the SmPC and Package Leaflet with minor editorial/administrative changes.
An updated version of the IMBRUVICA EU Risk Management Plan (RMP) (version 12) is also included in this submission."

Imbruvica - ibrutinib - EMEA/H/C/003791/II/0047, Orphan
Janssen-Cilag International NV, Rapporteur: Filip

Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, “Extension of Indication to include new indication for Imbruvica (ibrutinib); to extend the existing chronic lymphocytic leukaemia (CLL) indication to include combination use with obinutuzumab for the treatment of adult patients with previously untreated CLL. This proposed indication is supported by the data from the phase 3 study PCYC-1130-CA. As a consequence, section 4.1, 4.8 and 5.1 of the SmPC is updated, in 4.1 to include the extended indication, in 4.8 to update the safety information to include long terms safety (supported by results of study 3038-1) and section 5 to update the existing CLL label studies with long term efficacy data for CLL (supported by long term efficacy results of study PCYC-1112-CA and PCYC-1116-CA).
The Package Leaflet is/are updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update in the SmPC and Package Leaflet with minor editorial/administrative changes.
An updated version of the IMBRUVICA EU Risk Management Plan (RMP) (version 12) is also included in this submission.”

Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0013

Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné, “Extension of Indication for Trumenba to include active immunisation of children 1-9 years old. Sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated in parallel based on the results from the two pivotal studies B1971017 and B1971035.
The Package Leaflet is updated in accordance.
The RMP version 2.0 has also been submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to submit a corrected version of the final report of study B1971016, which was included in the initial marketing authorisation application.”

Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0041

Pfizer Ireland Pharmaceuticals, Rapporteur: Alar Irs, PRAC Rapporteur: Maia Uusküla, “Extension of Indication to include paediatric patients from birth to less than 2 months old for Zinforo; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC based on results from study

D3720C00009 (C2661002) an open-label, multicentre study to evaluate the safety, tolerability, pharmacokinetics, and efficacy of ceftaroline in neonates and young infants with late-onset sepsis. The Package Leaflet is updated in accordance. The RMP (v 17.0) has also been submitted."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0061, Orphan
Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik

Aldurazyme - laronidase - EMEA/H/C/000477/II/0071/G
Genzyme Europe BV, Rapporteur: Greg Markey

Fasenra - benralizumab - EMEA/H/C/004433/II/0010
AstraZeneca AB, Rapporteur: Bruno Sepodes

Flixabi - infliximab - EMEA/H/C/004020/II/0034
Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus

Hulio - adalimumab - EMEA/H/C/004429/II/0001
Mylan S.A.S, Rapporteur: Bart Van der Schueren

Kevzara - sarilumab - EMEA/H/C/004254/II/0011/G
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

Nulojix - belatacept - EMEA/H/C/002098/II/0051
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson

Nulojix - belatacept - EMEA/H/C/002098/II/0052/G
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson

Nulojix - belatacept - EMEA/H/C/002098/II/0053
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson

Nulojix - belatacept - EMEA/H/C/002098/II/0054/G

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson

Semglee - insulin glargine - EMEA/H/C/004280/II/0009
Mylan S.A.S, Rapporteur: Martina Weise

Stocrin - efavirenz - EMEA/H/C/000250/II/0116/G
Merck Sharp & Dohme B.V., Duplicate, Duplicate of Sustiva, Rapporteur: Bruno Sepodes

WS1475
Infanrix hexa-EMEA/H/C/000296/WS1475/0249
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1500/G
HyQvia-EMEA/H/C/002491/WS1500/0045/G
Kiovig-EMEA/H/C/000628/WS1500/0086/G
Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus

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

ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0003
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, “Update to the section 5.1 of the SmPC to revise information on perioperative management including the number of surgical procedures, dosing and haemostatic efficacy based on the results from the final clinical study report for the surgery study 261204.”

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 take for minor editorial amendments to be made in the SmPC, Labelling and Package Leaflet.”

Firdapse - amifampridine - EMEA/H/C/001032/II/0060, Orphan

BioMarin International Limited, Rapporteur: Kristina Dunder, “Update section 5.1 of the SmPC to include results from study LMS-003: a double-blind, placebo-controlled, paralell group study to evaluate the efficacy and safety of amifampridine in patients with Lambert-Eaton Myasthenic Syndrome (LEMS).”

Firdapse - amifampridine - EMEA/H/C/001032/II/0061, Orphan

BioMarin International Limited, Rapporteur: Kristina Dunder, “Submission of the final reports from non-clinical studies (vpt 5604,vpt5336, vpt5401 and 100034669) on dependence and off-target effectsas agreed during the last Annual Re-assessment.”

Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0028

MSD Vaccins, Rapporteur: Kristina Dunder, “Update of section 5.1 of the SmPC in order to consolidate the existing information following a request of the CHMP (EMEA/H/C/003852/II/0024/G).
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.”

Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0102

CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, “Update of section 2 of the SmPC in order to update the IgG subclass values according to performed analyses. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the package leaflet.”

Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0008

Roche Registration GmbH, Rapporteur: Mark Ainsworth, “Submission of the final report for Study 15-3109, an 8-week immunotoxicity study of ocrelizumab by intravenous injection in juvenile cynomolgus monkeys with a 9-month recovery period, to address a CHMP recommendation.”

PREVYMIS - letermovir - EMEA/H/C/004536/II/0009, Orphan

Merck Sharp & Dohme B.V., Rapporteur: Filip

Josephson, “Update of section 4.5 of the SmPC in order to update the information on drug-drug interaction between letermovir and fluconazole based on the interim results from study MK-8228-037; this is an open-label, 3-period, fixed-sequence trial to evaluate the effect of single-dose administration of letermovir on the single-dose PK of fluconazole, and the effect of single dose administration of fluconazole on the single-dose PK of letermovir in healthy females. In addition, the Marketing authorisation holder (MAH) took the opportunity include minor editorial changes in the product information.”	
Ryzodeg - insulin aspart / insulin degludec - EMEA/H/C/002499/II/0030/G Novo Nordisk A/S, Rapporteur: Kristina Dunder, “Update of sections 4.2 and section 5.1 of the SmPC in order to update the information on dosing and administration interval of Ryzodeg (insulin aspart/insulin degludec) based on data from 2 trials: • NN5401-4266, a 38 week trial comparing effect and safety of insulin degludec/insulin aspart vs. insulin glargine plus insulin aspart in subjects with type 2 diabetes treated with basal insulin with or without oral antidiabetic treatment in need of treatment intensification. • NN5401-3996, a 26-week trial comparing efficacy and safety of insulin degludec/insulin aspart BID and insulin degludec OD plus insulin aspart in subjects with type 2 Diabetes Mellitus treated with basal insulin in need of treatment intensification with mealtime insulin. In addition, the MAH took the opportunity to make editorial changes in the SmPC.”	
Symkevi - tezacaftor / ivacaftor - EMEA/H/C/004682/II/0002/G, Orphan Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Johann Lodewijk Hillege, “Update of section 4.5 of the SmPC with the results of the following 4 non-clinical drug-drug interaction (DDI) studies : Results from Study O092: Evaluation of VRT-1189001 as an Inducer of CYP1A2 and CYP2B6 using Primary Cryopreserved Human Hepatocytes Results from O093: Evaluation of VRT-0996107 as an Inducer of CYP2B6 using Primary Cryopreserved Human Hepatocytes Results from OPT-2018-041: Assessment of	

VRT-0893661, VRT-0996107, VRT-1189001 and VRT-1074233 as inhibitors of human OCT1, MATE1, MATE2-K, and BSEP mediated transport Results fOPT-2018-040: Assessment of VRT-0813077, VRT-0837018 and VRT-0842917 as substrates of human BCRP mediated transport.
The MAH took the oportunity to introduce some additional minor updates in the Product information."

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."

Veltassa - patiromer - EMEA/H/C/004180/II/0007

Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Jayne Crowe, "Update of section 4.2, 4.5 and 5.1 of the SmPC to reflect the results of study RLY5016-401;an Open-Label, Randomized, Parallel Group Phase 4 Study of the Efficacy and Safety of Patiromer for Oral Suspension With or Without Food for the Treatment of Hyperkalemia (TOURMALINE). The PL has been updated accordingly."

Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0196

Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, "Submission of the final abbreviated clinical study report from the post-authorisation safety study (PASS) GS-EU-174-1403, a pharmacoepidemiology study to define the long-term safety profile of tenofovir disoproxil fumarate (TDF) and describe the management of TDF-associated renal and bone toxicity in Chronic Hepatitis B (CHB)-infected adolescents aged 12 to <18 years in Europe, listed in the Viread RMP as a category 3 study. This submission fulfils this

additional pharmacovigilance activity and fulfils the post-authorisation measures MEA 255.1, MEA 255.2 and MEA 265.8."

B.6.10. CHMP-PRAC assessed procedures

CYLTEZO - adalimumab - EMEA/H/C/004319/II/0006

Boehringer Ingelheim International GmbH, Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study 1297.12: Efficacy, Safety and Immunogenicity of BI 695501 versus Humira in Patients with Moderate to Severe Chronic Plaque Psoriasis: A Randomized, Double-Blind, Parallel-Arm, Multiple-Dose, Active Comparator Trial; listed as a category 3 study in the RMP. The RMP version 3.0 has been updated accordingly."

Daklinza - daclatasvir - EMEA/H/C/003768/II/0031

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of section 5.1 of the SmPC in order to add information on long-term efficacy and drug resistance based on final results from study AI444046, listed as a category 3 study in the RMP. This is a phase 3 non-randomized, open-label, long-term follow-up and observational study of durability of efficacy, resistance and characterization of progression of liver disease in subjects with chronic hepatitis C previously treated with daclatasvir and/or asunaprevir.
In addition, the Marketing authorisation holder (MAH) took the opportunity to postpone (from Q2 2021 to Q2 2023) the due date of the safety study AI444427 evaluating recurrence of hepatocellular carcinoma. Annex II is updated in accordance.
The RMP version 6.0 has also been submitted."

Esmya - ulipristal acetate - EMEA/H/C/002041/II/0045/G

Gedeon Richter Plc., Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Submission of the final study reports from the 5 mechanistic in vitro studies following Esmya Article 20 referral procedure (EMEA/H/A-20/1460/C/2041/0043). These are

3083-N03-050 (PAM MEA 020), 3083-N04-050 (PAM MEA 021), 3083-N05-050 (PAM MEA 022), 3083-N01-050 (PAM REC) and 3083-N02-050 (PAM REC). In addition, the MAH submitted updated RMP version 16.1, as part of this application."

Hepsera - adefovir dipivoxil - EMEA/H/C/000485/II/0081

Gilead Sciences Ireland UC, , PRAC Rapporteur: Adrien Inoubli, "Submission of an updated RMP version 2.1 in order to bring it to the new revision 2 template. As a result, the safety concerns are being updated."

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. In addition, the MAH took the opportunity to remove the product information texts from Annex 6 of the RMP and would like to only keep the text for patient alert card in the RMP as additional risk minimisation measures."

Yervoy - ipilimumab - EMEA/H/C/002213/II/0063

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 and 4.8 of the SmPC and of annex II in order to add safety information regarding Graft Versus Host Disease (GVHD) in allogeneic hematopoietic stem cell transplant (HSCT) recipients after treatment with ipilimumab. The update is based on a review of post-marketing data. The Package Leaflet and the RMP (version 25.0) is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the PI and RMP and to include some changes in the RMP due to previous procedures."

B.6.11. PRAC assessed procedures

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 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 provided as part of the application.”

PRAC Led

Cayston - aztreonam -

EMEA/H/C/000996/II/0075, Orphan

Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP (version 7.1) for Cayston in order to comply with Revision 2 of the EU-RMP template, in accordance with the revised guidance in the Guideline on good pharmacovigilance practices (GVP) Module V (EMA/838713/2011; Revision 2).”

PRAC Led

Cimzia - certolizumab pegol -

EMEA/H/C/001037/II/0074/G

UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “Submission of the final report from studies (RA0021 and RA005) listed as a category 3 studies in the RMP. Study RA0021 (ARTIS registry) is to provide short- and long-term safety data from the use of certolizumab pegol (CZP) in Sweden for rheumatoid arthritis (RA) patients. Study RA005 (NBD registry) is to obtain safety and outcome data on RA patients receiving CZP and other RA treatments. In addition, the MAH submitted interim results for two ongoing registries studies (RA0020/RABBIT and

RA0022/BSRBR). Study RA0020/RABBIT is a German long-term observation of biologics/ DMARD in RA. Study RA0022/BSRBR is a longitudinal observational study of patients with RA treated with biologic agents, and prospective surveillance study for adverse events."

PRAC Led

Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0043

Merck Sharp & Dohme B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "C.I.11.b (type II): Submission of an updated RMP version 8.1 in order to implement revision 2 of the RMP template and to include data following completion of study P017, a phase III follow-up trial to collect outcome and safety of frozen-thawed embryo transfer (FTET) cycles performed with the embryos cryopreserved in studies P016 and P031, as requested as part of the assessment of PSUSA/00000875/201407 and to delete the important potential risks 'hypersensitivity' and 'lack of effect due to immunogenicity' from the list of safety concerns as requested as part of PSUSA/00000875/201707. In addition the MAH has taken the opportunity to include some data from the ongoing study P043, a multi-centre, open label, single-group trial to investigate the efficacy and safety of corifollitropin alfa in combination with hCG for initiation or restoration of puberty assessed by increased testicular volume in adolescent males 14 to < 18 years old with HH."

PRAC Led

Eviplera - emtricitabine / rilpivirine / tenofovir disoproxil - EMEA/H/C/002312/II/0098

Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 13.1 in order to 1) implement Revision 2 of the EU-RMP template, 2) remove certain safety concerns in line with the new RMP guidance and based on exposure data from clinical studies and post-marketing use and 3) change the Marketing Authorisation Holder name from Gilead Sciences International Ltd., Cambridge, UK (GSIL) to Gilead Sciences Ireland UC, Cork, Ireland

(GSIUC)."

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."

PRAC Led

Invokana - canagliflozin -

EMEA/H/C/002649/II/0040

Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Provision of the final CSR for Study RRA-21651; a retrospective, observational, new-user cohort study using 4 administrative claims databases in the US, undertaken to investigate the incidence of diabetic ketoacidosis among patients with type 2 diabetes mellitus treated with SGLT2 inhibitors or other antihyperglycemic agents."

PRAC Led

Perjeta - pertuzumab -

EMEA/H/C/002547/II/0041

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final report from the pregnancy registry (H4621g/GE28099; MotHER; listed as a category 3 study in the RMP). This is a an observational study of pregnancy and pregnancy outcomes in women with breast cancer treated with Herceptin (trastuzumab), Perjeta (pertuzumab) in combination with Herceptin, or Kadcyla (ado-trastuzumab emtansine) during pregnancy or within 7 months prior to conception. In addition, the MAH submitted updated RMP version 11, as part of this application."

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 25 in order to align with the revised guideline GVP module 5 and addition of two category 3 studies:

- Addition of a new category 3 study (20170534), which is an open-label extension of the currently ongoing Study 20130173, a RMP category 3, involving pediatric subjects with osteogenesis imperfecta. This is based on the MAH commitment arising from Prolia approved Pediatric Investigation Plan (EMEA-000145-PIP02-12); open-label, prospective, extension study
- Addition of a new category 3 study to further characterize potential increased risk of cerebrovascular events (stroke) and other serious cardiovascular events in subjects with osteoporosis as per Pharmacovigilance Risk Assessment Committee (PRAC) recommendation during Prolia procedure EMEA/H/C/PSUSA/000954/201709. PRAC recommendation was to include the study in the RMP as a category 3 at the next regulatory opportunity; retrospective cohort database study."

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 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."

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)."

PRAC Led

Sutent - sunitinib -

EMEA/H/C/000687/II/0073

Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "C.I.11: Submission of an updated RMP version 17 in order to review the list of safety concerns to make it more risk proportionate based on any available safety data. The updates are in line with the new GVP Module V (Rev 2) guidelines and new RMP template."

PRAC Led

Vokanamet - canagliflozin / metformin -

EMEA/H/C/002656/II/0041

Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Provision of the final CSR for Study RRA-21651; a retrospective, observational, new-user cohort study using 4 administrative claims databases in the US, undertaken to investigate the incidence of diabetic ketoacidosis among patients with type 2 diabetes mellitus treated with SGLT2 inhibitors or other antihyperglycemic agents."

PRAC Led

WS1509

Atripla-EMEA/H/C/000797/WS1509/0138

Truvada-EMEA/H/C/000594/WS1509/015

8

Gilead Sciences Ireland UC, Lead Rapporteur:

Bruno Sepodes, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Greg Markey, “Submission of updated RMPs version 17.1 for Atripla and version 15.5 for Truvada, in order to 1) implement Revision 2 of the EU-RMP template and amend the safety concerns accordingly, 2) remove the additional risk minimisation measures for tenofovir disoproxil fumarate in the form of education materials regarding renal toxicity and bone events, with the resulting amendment of Annex II of the product information, 3) add clinical data from study GS-US-104-0352 (A Phase III, Randomized, Open-Label Study Comparing the Safety and Efficacy of Switching Stavudine or Zidovudine to Tenofovir Disoproxil Fumarate Versus Continuing Stavudine or Zidovudine in Virologically Suppressed HIV-Infected Children Taking Highly Active Antiretroviral Therapy), 4) revise the due dates for two category 3 studies, GS-US-276-0103 (A Prospective, Observational Study of Individuals Who Seroconvert While Taking Truvada for Pre Exposure Prophylaxis (PrEP)) and GS-EU-276-4027 (A Cross-Sectional Post Authorization Safety Study to Assess Healthcare Provider’s Level of Awareness of Risk Minimisation Materials for Truvada for Pre Exposure Prophylaxis in the European Union) and 5) implement already approved administrative changes.”

B.6.12. CHMP-CAT assessed procedures

autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - EMEA/H/C/003854/II/0016, Orphan, ATMP

Orchard Therapeutics (Netherlands) BV

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS1512
M-M-RVAXPRO-EMEA/H/C/000604/WS1512/0092
ProQuad-EMEA/H/C/000622/WS1512/0129
Zostavax-EMEA/H/C/000674/WS1512/0123
MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus

WS1513
Eucreas-EMEA/H/C/000807/WS1513/0072
Galvus-EMEA/H/C/000771/WS1513/0062
Icandra-EMEA/H/C/001050/WS1513/0074
Jalra-EMEA/H/C/001048/WS1513/0063
Xiliarx-EMEA/H/C/001051/WS1513/0061
Zomarist-EMEA/H/C/001049/WS1513/0074
Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder

WS1537/G
Humalog-EMEA/H/C/000088/WS1537/0167/G
Liprolog-EMEA/H/C/000393/WS1537/0128/G
Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

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

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

G. ANNEX G

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

Information related to Scientific Advice cannot be released at the present time as these contain

commercially confidential information.

Qualification of Biomarkers:

HTA:

G.2. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 10-13 December 2018 CHMP plenary:

G.3.2. List of procedures starting in December 2018 for January 2019 CHMP adoption of outcomes

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