13 December 2016
EMA/847927/2016 Rev.1
Inspections, Human Medicines Pharmacovigilance and Committees Division

# Committee for medicinal products for human use (CHMP)

## Draft agenda of the meeting on 12-15 December 2016

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

12 December 2016, 13:00 – 19:30, room 3A

13 December 2016, 08:30 – 19:30, room 3A

14 December 2016, 08:30 – 19:30, room 3A

15 December 2016, 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 12-15 December 2016. See December 2016 CHMP minutes (to be published post January 2017 CHMP meeting).

## 1.2. Adoption of agenda

CHMP agenda for 12-15 December 2016

## 1.3. Adoption of the minutes

CHMP minutes for 7-10 November 2016.

# 2. Oral Explanations

## 2.1. Pre-authorisation procedure oral explanations

## 2.2. Re-examination procedure oral explanations

## 2.3. Post-authorisation procedure oral explanations

## 2.4. Referral procedure oral explanations

# 3. Initial applications

## 3.1. Initial applications; Opinions

### 3.1.1. - alectinib - EMEA/H/C/004164

indicated for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive.

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 28.01.2016.

### 3.1.2. - chlormethine - Orphan - EMEA/H/C/002826

Actelion Registration Ltd.; treatment of mycosis fungoides-type cutaneous T-cell lymphoma (MF-type CTCL)

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 24.09.2015.

### 3.1.3. - baricitinib - EMEA/H/C/004085

treatment of moderate to severe active rheumatoid arthritis (RA)

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 13.10.2016. List of Questions adopted on 23.06.2016.

### 3.1.4. - pregabalin - EMEA/H/C/004277

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

Scope: Opinion

**Action**: For adoption

### 3.1.5. - rituximab - EMEA/H/C/004112

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

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 13.10.2016. List of Questions adopted on 25.02.2016.

BWP report

### 3.1.6. - simoctocog alfa - EMEA/H/C/004459

treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency)

Scope: Opinion

**Action**: For adoption

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

### 3.2.1. - abaloparatide - EMEA/H/C/004157

treatment of osteoporosis

Scope: Day 180 list of outstanding issue

**Action**: For adoption

List of Questions adopted on 01.04.2016.

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

treatment of haemophilia A

Scope: Day 180 list of outstanding issue

**Action**: For adoption

List of Questions adopted on 21.07.2016.

Scope: List of Experts to ad-hoc expert group meeting, adopted by written procedure on 28.11.2016.

**Action**: For information

BWP report

### 3.2.3. - adalimumab - EMEA/H/C/004212

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

Scope: Day 180 list of outstanding issue

**Action**: For adoption

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

BWP report

### 3.2.4. - fluciclovine (18F) - EMEA/H/C/004197

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

Scope: Day 180 list of outstanding issue

**Action**: For adoption

List of Questions adopted on 28.04.2016.

### 3.2.5. - ivabradine - EMEA/H/C/004241

treatment of angina pectoris

Scope: Day 180 list of outstanding issue

**Action**: For adoption

List of Questions adopted on 01.04.2016.

### 3.2.6. - pemetrexed - EMEA/H/C/004488

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

Scope: Day 180 list of outstanding issue

**Action**: For adoption

List of Questions adopted on 21.07.2016.

### 3.2.7. - vosaroxin - Orphan - EMEA/H/C/004118

Sunesis Europe Ltd; treatment acute myeloid leukaemia

Scope: Day 180 list of outstanding issue

**Action**: For adoption

List of Questions adopted on 28.04.2016.

### 3.2.8. - padeliporfin - EMEA/H/C/004182

treatment of prostate cancer

Scope: Day 180 list of outstanding issue

**Action**: For adoption

List of Questions adopted on 26.05.2016.

### 3.2.9. - tofacitinib - EMEA/H/C/004214

treatment of active rheumatoid arthritis

Scope: Day 180 list of outstanding issue

**Action**: For adoption

List of Questions adopted on 21.07.2016.

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

treatment of metastatic colorectal cancer

Scope: Day 180 list of outstanding issue

**Action**: For adoption

List of Questions adopted on 21.07.2016.

BWP report

### 3.2.11. - adalimumab - EMEA/H/C/004373

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

Scope: Day 180 list of outstanding issue

**Action**: For adoption

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

BWP report

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

### 3.3.1. - cerliponase alfa - Orphan - EMEA/H/C/004065

Accelerated assessment

BioMarin International Limited; treatment of neuronal ceroid lipofuscinosis type 2

Scope: Day 120 list of questions

**Action**: For adoption

BWP report

### 3.3.2. - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/004240

treatment of HIV-1 infection

Scope: Day 120 list of questions

**Action**: For adoption

### 3.3.3. - levamisole - Orphan - EMEA/H/C/004330

ACE Pharmaceuticals BV; treatment of Steroid Sensitive Nephrotic syndrome

Scope: Day 120 list of questions

**Action**: For adoption

### 3.3.4. - entecavir - EMEA/H/C/004458

treatment of chronic hepatitis B virus infection

Scope: Day 120 list of questions

**Action**: For adoption

### 3.3.5. - entecavir - EMEA/H/C/004377

treatment of chronic hepatitis B virus infection

Scope: Day 120 list of questions

**Action**: For adoption

### 3.3.6. - andexanet alfa - EMEA/H/C/004108

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

Scope: Day 120 list of questions

**Action**: For adoption

BWP report

### 3.3.7. - etanercept - EMEA/H/C/004167

treatment of arthritis, ankylosing spondylitis, plaque psoriasis and paediatric plaque psoriasis

Scope: Day 120 list of questions

**Action**: For adoption

### 3.3.8. - miglustat - EMEA/H/C/004366

treatment of Gaucher disease

Scope: Day 120 list of questions

Similarity Assessment Report

**Action**: For adoption

### 3.3.9. - neratinib - EMEA/H/C/004030

extended adjuvant treatment of adult patients with early-stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab based therapy

Scope: Day 120 list of questions

**Action**: For adoption

### 3.3.10. - trastuzumab - EMEA/H/C/004346

treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)

Scope: Day 120 list of questions

**Action**: For adoption

BWP report

### 3.3.11. - d-biotin - EMEA/H/C/004153

treatment of progressive multiple sclerosis (primary or secondary)

Scope: Day 120 list of questions

**Action**: For adoption

### 3.3.12. - midostaurin - Orphan - EMEA/H/C/004095

Accelerated assessment

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

Scope: Day 120 list of questions

**Action**: For adoption

### 3.3.13. - solithromycin - EMEA/H/C/004179

treatment of bacterial infections

Scope: Day 120 list of questions

**Action**: For adoption

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

### 3.4.1. - etanercept - EMEA/H/C/004192

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

Scope: Letter from the applicant requesting an extension of clock stop to respond to the List of Questions adopted on 1 April 2016.

**Action**: For adoption

List of Questions adopted on 01.04.2016.

### 3.4.2. - pegfilgrastim - EMEA/H/C/004262

treatment of neutropenia

Scope: Letter from the applicant dated 1 December 2016 requesting an extension of clock stop to respond to the List of Questions adopted on 13 October 2016.

**Action**: For adoption

List of Questions adopted on 13.10.2016

### 3.4.3. - ocrelizumab - EMEA/H/C/004043

treatment of multiple sclerosis

Scope: Letter from the applicant dated 23 November 2016 requesting an extension of clock stop to respond to the List of Questions adopted on 15 September 2016.

**Action**: For adoption

List of Questions adopted on 15.09.2016.

### 3.4.4. - nonacog beta pegol - Orphan - EMEA/H/C/004178

Novo Nordisk A/S; treatment of haemophilia B

Scope: List of Experts to ad-hoc expert group meeting , adopted by written procedure on 28.11.2016.

**Action**: For information

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

### 3.4.5. - atezolizumab - EMEA/H/C/004143

treatment of metastatic urothelial treatment of urothelial carcinoma and non-small cell lung cancer (NSCLC)

Scope: Letter from the applicant dated 30 November 2016 requesting an extension of clock stop to respond to the List of Questions adopted on 15 September 2016.

**Action**: For information

List of Questions adopted on 15.09.2016.

### 3.4.6. - miglustat - EMEA/H/C/004016

treatment of Gaucher disease

Scope: Similarity Assessment Report

**Action**: For adoption

List of Outstanding Issues adopted on 23.06.2016, 01.04.2016. List of Questions adopted on 23.07.2015.

### 3.4.7. - niraparib - Orphan - EMEA/H/C/004249

Tesaro UK Limited; Treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer

Scope: Similarity Assessment Report

**Action**: For adoption

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

## 3.6. Initial applications in the decision-making phase

## 3.7. Withdrawals of initial marketing authorisation application

### 3.7.1. - pegfilgrastim - EMEA/H/C/004342

treatment of neutropenia

Scope: Withdrawal

**Action**: For information

Oral explanation 10.11.2016, List of Outstanding Issues adopted on 13.10.2016, 21.07.2016. List of Questions adopted on 01.04.2016.

### 3.7.2. - pegfilgrastim - EMEA/H/C/004023

treatment of neutropenia

Scope: Withdrawal

**Action**: For information

Oral explanation 10.11.2016, List of Outstanding Issues adopted on 13.10.2016, 21.07.2016. List of Questions adopted on 01.04.2016.

# 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. Repatha - evolocumab - EMEA/H/C/003766/X/0002

Amgen Europe B.V.

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola

Scope: Opinion

“To add a new strength of 420 mg (120 mg/mL) for evolocumab solution for injection in cartridge, for subcutaneous (SC) administration by an automated mini-doser device.”

**Action**: For adoption

List of Outstanding Issues adopted 26.05.2016. List of Questions adopted on 25.02.2016.

### 4.1.2. Tivicay - dolutegravir - EMEA/H/C/002753/X/0018/G

ViiV Healthcare UK Limited

Rapporteur: Filip Josephson, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Julie Williams

Scope: "An extension application to add two new strengths (10mg and 25mg tablets) to support the extension (variation type II C.I.6) of the target population covered by the authorised therapeutic indication for Tivicay to treat paediatric patients from 6 years of age infected with HIV. Data from cohort I and II A of the clinical trial ING112578 are presented in support of the new therapeutic indication."

**Action**: For adoption

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

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

Roche Registration Limited

Rapporteur: Greg Markey, Co-Rapporteur: David Lyons, PRAC Rapporteur: Julie Williams

Scope: "Extension application to introduce a new pharmaceutical form associated with 3 new strengths (267mg, 534mg and 801mg film-coated tablets)

**Action:** For adoption

List of Questions adopted on 15.09.2016.

### 4.2.2. Ilaris - canakinumab - EMEA/H/C/001109/X/0045/G

Novartis Europharm Ltd

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Grouped application comprising an extension application covering an additional formulation (150 mg/ml solution for injection) and a type II variation (C.I.6.a) to add a new indication.
The proposed new indication is based on the results of the pivotal phase 3 study CACZ885N2301 and covers the treatment of adults and children of 2 years of age and older with one of the following Periodic Fever Syndromes:
- Tumour Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS);
- Hyperimmunoglobulin D Syndrome (HIDS) / Mevalonate Kinase Deficiency (MKD);
- Familial Mediterranean Fever (FMF) in patients in whom colchicine is contraindicated, is not tolerated, or does not provide an adequate response.
As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are proposed to be updated and the Package Leaflet is proposed to be updated accordingly. In addition, the annexes have been aligned with the latest QRD template v.10. A revised RMP version 11 was provided as part of the application."

**Action**: For adoption

List of Questions adopted on 15.09.2016.

## 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. Benepali - etanercept - EMEA/H/C/004007/X/0016

Samsung Bioepis UK Limited (SBUK)

Rapporteur: Andrea Laslop, PRAC Rapporteur: Rafe Suvarna

Scope: “To add a new strength of 25 mg solution for injection in pre-filled syringe.”

**Action**: For adoption

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

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

# 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. Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0024

Biofrontera Bioscience GmbH

Rapporteur: Harald Enzmann, Co-Rapporteur: Patrick Salmon, PRAC Rapporteur: Martin Huber

Scope: “Extension of Indication from "Treatment of actinic keratosis of mild to moderate severity on the face and scalp (Olsen grade 1 to 2; see section 5.1) and of field cancerization" to the following:
"Treatment of actinic keratosis of mild to moderate severity on the face and scalp (Olsen grade 1 to 2; see section 5.1) and of field cancerization in adults including the elderly. Treatment of non-aggressive basal cell carcinoma (primary superficial or nodular basal cell carcinoma or mixed types of both, with good or intermediate prognosis) on the face, scalp, neck, trunk and extremities in adults including the elderly."

Consequently, sections 4.1, 4.2, 4.4, 4.6, 4.8 and 5.1 of the SmPC are updated. Editorial changes have been proposed in sections 2, 4.5, 4.7, 5.2, 6.5 and 9 of the SmPC. The Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.”

**Action**: For adoption

Request for Supplementary Information adopted on 10.11.2016.

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

Roche Registration Limited

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

Scope: "Extension of Indication to include the use of Avastin in combination with paclitaxel and carboplatin for the treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer.
As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated with efficacy and safety information from study GOG-0213. The Package Leaflet is updated in accordance. An update RMP is also included (version 27)."

Similarity Assessment Report

**Action**: For adoption

BWP report

### 5.1.3. Benepali - etanercept - EMEA/H/C/004007/II/0019/G

Samsung Bioepis UK Limited (SBUK)

Rapporteur: Andrea Laslop, PRAC Rapporteur: Rafe Suvarna

Scope: "Extension of indication to include two new indications for the treatment of juvenile idiopathic arthritis and paediatric plaque psoriasis already approved for the reference medicinal product (Enbrel) for Benepali.

As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Annex II, the Package Leaflet and Labelling are updated in accordance. The RMP (version 4.2) is also updated accordingly. Furthermore, the PI is brought in line with the latest QRD template version 10."

**Action**: For adoption

See Annex to Agenda B.5.3

### 5.1.4. Cinryze - c1-esterase inhibitor, human - EMEA/H/C/001207/II/0045

Shire Services BVBA

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include children with hereditary angioedema (HAE) in the treatment and pre-procedure prevention of angioedema attacks.
As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2, 6.5 and 6.5 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance.

In addition, an update of regional information in module 3.2.R due to the proposed dose recommendation for children is submitted."

**Action**: For adoption

Request for Supplementary Information adopted on 15.09.2016.

### 5.1.5. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/II/0002

Janssen-Cilag International NV

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Leonor Chambel

Scope: "Extension of Indication for Darzalex in the treatment of adult patients with multiple myeloma who have received at least 1 prior therapy.
As a consequence, sections 4.2, 4.4, 4.5, 5.1 and 5.2 of the SmPC are updated in order to update the information on posology, warnings, interactions, efficacy and pharmacokinetics. A new warning is introduced in section 4.4 regarding neutropenia/thrombocytopenia induced by background therapy.

Annex II is updated to remove all the specific obligations following submissions of the final results of studies MMY3003 and MMY3004.

The Package Leaflet and Risk Management Plan (RMP version 2) are updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Similarity Assessment Report

**Action**: For adoption

BWP report

### 5.1.6. Firazyr - icatibant - Orphan - EMEA/H/C/000899/II/0034/G

Shire Orphan Therapies GmbH

Rapporteur: Kristina Dunder, Co-Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Qun-Ying Yue

Scope: "A type II variation (C.I.6) to modify the existing marketing authorization to include a recommendation for use in children (study HGT-FIR-086) following completion of the PIP (EMEA-000408-PIP01-08-M05)
In addition, it is proposed to reflect the conduct of a juvenile toxicity study (JE049-0172) in SmPC section 5.3 in order to fulfill article 37 of regulation 1901/2006. Study JE049-0172 has previously been assessed by EMA.

Section 5.2. of the SmPC has been updated to reflect the effect on age (elderly), gender and race on PK of icatibant."

**Action**: For adoption

### 5.1.7. Inovelon - rufinamide - Orphan - EMEA/H/C/000660/II/0037

Eisai Ltd

Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard

Scope: "Extension of Indication to include treatment of seizures associated with Lennox-Gastaut Syndrome in paediatric patients 1 year of age and older, based on the results of study E2080-G000-303 (Study 303); a randomized, controlled, open-label study to evaluate the cognitive development effects and safety, and pharmacokinetics of adjunctive rufinamide treatment in paediatric subjects 1 to less than 4 years of age with inadequately controlled Lennox-Gastaut Syndrome. This study was conducted to fulfil the long-term (2 years) safety and efficacy objectives required as part of the Paediatric Investigation Plan

(PIP) EMEA-000709-PIP01-09. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are proposed to be updated and the Package Leaflet is proposed to be updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the annexes, to implement changes in line with the latest QRD template and to combine the SmPCs, labelling and Package Leaflets for the three authorised strengths of the tablet formulation in line with the current version of the QRD template. The application included an updated RMP version 9.0."

**Action**: For adoption

Request for Supplementary Information adopted on 15.09.2016.

### 5.1.8. Izba - travoprost - EMEA/H/C/002738/II/0005

Alcon Laboratories (UK) Ltd

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Almath Spooner

Scope: "Extension of Indication to include treatment of paediatric patients aged 2 months to < 18 years with ocular hypertension or paediatric glaucoma in order to decrease of elevated intraocular pressure. 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 has been updated accordingly. In addition, the marketing authorisation holder took the opportunity to introduce minor corrections in the SmPC and to update the list of local representatives in the PL. The RMP has updated to version 9.0"

**Action**: For adoption

### 5.1.9. Jardiance - empagliflozin - EMEA/H/C/002677/II/0014

Boehringer Ingelheim International GmbH

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

Scope: "Extension of indication to include a new indication on prevention of cardiovascular events, based on the final data of the cardiovascular safety phase III clinical trial EMPA-REG OUTCOME. As a consequence, section 4.1 of the SmPC is updated. The Package Leaflet is also updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to make some editorial changes."

**Action**: For adoption

Request for Supplementary Information adopted on 15.09.2016, 23.06.2016, 25.02.2016.

### 5.1.10. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0011

Merck Sharp & Dohme Limited

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to extend the existing indication for Keytruda 50mg to include previously untreated patients with locally advanced or metastatic Non-Small Cell Lung Cancer (NSCLC) whose tumors express PD-L1. 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. An updated RMP version 4.0 was provided as part of the application.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

**Action**: For adoption

Request for Supplementary Information adopted on 10.11.2016.

### 5.1.11. Opdivo - nivolumab - EMEA/H/C/003985/II/0019

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of Indication to include the treatment of locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy for OPDIVO.

As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the proposed indication, add a warning about the patient populations excluded from the clinical trial, and update the safety information. The Package Leaflet is updated in accordance.
Moreover, the updated RMP version 7.0 has been submitted"

**Action**: For adoption

### 5.1.12. Votubia - everolimus - Orphan - EMEA/H/C/002311/II/0041

Novartis Europharm Ltd

Rapporteur: Harald Enzmann, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Martin Huber

Scope: "Extension of Indication to include adjunctive treatment of patients aged 2 years and older with refractory seizures associated with tuberous sclerosis complex (TSC) for Votubia 2 mg, 3 mg and 5 mg dispersible tablets.
Sections 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated in parallel based on the results from the pivotal study. In addition, sections 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 are also updated for the 2.5 mg, 5 mg and 10 mg tablets to reflect on data relevant to these formulations.
The Package Leaflet is updated in accordance.
Furthermore, the PI is brought in line with the latest QRD template version 10."

**Action**: For adoption

Request for Supplementary Information adopted on 15.09.2016.

### 5.1.13. Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0053

Bial - Portela & Cª, S.A.

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

Scope: "Extension of indication to include the use of Zebinix as monotherapy in adults, in addition to the previously authorised indication as adjunctive therapy. 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. This submission includes an updated RMP (version 15.0). In

addition, the MAH is claiming an additional 1-year period of market protection under Article 14(11) of Regulation (EC) No 726/2004.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

**Action**: For adoption

Request for Supplementary Information adopted on 21.07.2016.

### 5.1.14. Trajenta Jentadueto - linagliptin linagliptin / metformin - EMEA/H/C/WS0915

Boehringer Ingelheim International GmbH

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

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

**Action**: For adoption

Request for Supplementary Information adopted on 13.10.2016, 26.05.2016.

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

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

# 6. Ancillary medicinal substances in medical devices

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

## 6.2. Update of Ancillary medicinal substances in medical devices

# 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)

# 8. Pre-submission issues

## 8.1. Pre-submission issue

### 8.1.1. – Glecaprevir/ Pibrentasvir - EMEA/H/C/04430

Treatment of chronic hepatitis C (CHC) in adults

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

**Action:** For adoption

### 8.1.2. Sofosbuvir, Velpatasvir, Voxilaprevir- EMEA/H/C/04350

Treatment of chronic hepatitis C (CHC) in adults

Scope: Briefing note and 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. Ranexa - ranolazine - EMEA/H/C/000805/II/0051

Menarini International Operations Luxembourg S.A., treatment of angina pectoris.

Rapporteur: Kristina Dunder

Scope: "Update of section 5.1 of the SmPC in order to include the data from the final CSR of study RIVER-PCI. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the details of local representative in Bulgaria in the Package Leaflet and to bring the Annex II in line with the latest QRD template version 9.1."

**Action**: For discussion

Request for Supplementary Information adopted on 21.07.2016, 14.04.2016.

See Annex to Agenda B.5.2

# 10. Referral procedures

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

### 10.1.1. Direct-acting antivirals (DAAV) indicated for the treatment of hepatitis C (interferon free): Daklinza - daclatasvir; Exviera - dasabuvir ; Viekirax - ombitasvir, paritaprevir, ritonavir ; Olysio – simeprevir; Sovaldi - sofosbuvir sofosbuvir, Harvoni - ledipasvir –EMEA/H/A-20/1438

Applicant: Bristol-Myers Squibb Pharma EEIG (Daklinza); AbbVie Ltd (Exviera, Viekirax); Janssen-Cilag International N.V. (Olysio); Gilead Sciences International Ltd (Harvoni, Sovaldi)

Rapporteur for the Article 20 referral:
PRAC Lead Rapporteur: Margarida Guimarães; PRAC Lead Co-rapporteur: Dolores Montero Corominas
CHMP Lead Rapporteur: Fátima Ventura; CHMP Lead Co-rapporteur: Aranzazu Sancho-Lopez

CHMP Rapporteurs: Rapporteur: Filip Josephson, Co-Rapporteur: Robert James Hemmings (Daklinza), Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege (Exviera, Viekirax), Rapporteur: Aranzazu Sancho-Lopez, Co-Rapporteur: Daniela Melchiorri (Olysio);

Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs (Sovaldi), Rapporteur: Filip Josephson, Co-Rapporteur: Joseph Emmerich (Harvoni)

Scope: Opinion

Review of the benefit-risk balance of DAAV following notification by the European Commission of a referral under Article 20 of Regulation (EC) No 726/2004 based on pharmacovigilance data

**Action:** For Adoption

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

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

## 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

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

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

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

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

Scope: List of Outstanding Issues

Harmonisation exercise for Etopophos and associated names

**Action:** For adoption

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

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

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

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

Scope: List of Outstanding Issues

Harmonisation exercise for Vepesid and associated names

**Action:** For adoption

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

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

Sanofi Aventis group of companies and associated companies

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

Scope: List of outstanding issues/Opinion

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

**Action:** For adoption

List of outstanding Issues adopted 13.10.2016, 28.04.2016. List of Questions adopted on 19.11.2015.

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

Lundbeck group of companies and associated companies

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

Scope: List of Outstanding Issues/Opinion

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

**Action:** For adoption

List of outstanding issues adopted on 13.10.2016, 23.06.2016, 01.04.2016. List of Questions adopted 17.12.2015

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

### 10.6.1. Dienogest/Ethinylestradiol containing products indicated in acne - Dienogest / Ethinylestradiol - EMEA/H/A-31/1435

Rapporteur: Martina Weise, Co-Rapporteur: Nithyanandan Nagercoil,

Scope: Opinion

**Action:** For adoption

List of Outstanding Issues adopted on 15.09.2016, 23 June 2016.

### 10.6.2. Micro Therapeutics Research Labs, India - EMEA/H/A-31/1450

Rapporteur: To be appointed, Co-Rapporteur: To be appointed

Scope: reliability of the data of bioequivalence studies

Appointment of (Co)Rapporteur, List of Questions and timetable

**Action:** For adoption

Letter from the Medicines Evaluation Board (MEB) in the Netherlands dated 1 December 2016, from the Norwegian Medicines Agency (NoMA) dated 2 December 2016, from the Croatian Agency for Medicinal Products and Medical Devices (HALMED) dated 2 December 2016, from the National Board of Health in Denmark dated 5 December 2016, from the

Medical Products Agency (MPA) in Sweden dated 5 December 2016, from Icelandic Medicines Agency dated 5 December 2016, from Medicines and Healthcare Products Regulatory Agency in United Kingdom dated 7 December 2016, from State Agency of Medicines in Estonia dated 7 December 2016, from Spanish Agency of Medicines and Medical Devices dated 7 December 2016, notifying of an official referral under Article 31 and its grounds.

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

Symbiopharm GmbH,

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

Scope: List of experts to Ad-hoc expert meeting, updated timetable

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

**Action:** For adoption

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

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

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

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

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

## 11. Pharmacovigilance issue

### 11.1. Early Notification System

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

**Action**: For information

## 12. Inspections

### 12.1. GMP inspections

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

## 12.2. GCP inspections

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

## 12.3. Pharmacovigilance inspections

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

## 12.4. GLP inspections

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

# 13. Innovation Task Force

## 13.1. Minutes of Innovation Task Force

**Action**: For information

## 13.2. Innovation Task Force briefing meetings

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

### 13.2.1. Completed ITF Briefing Meetings in 2016

**Action:** For information

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

## 13.4. Nanomedicines activities

Minutes of 6th TC of the IPRF Nano Working Group on 7 December 2016

**Action:** For information

# 14. Organisational, regulatory and methodological matters

## 14.1. Mandate and organisation of the CHMP

### 14.1.1. Co-opted membership of the CHMP

The mandate of Robert J. Hemmings as Co-opted member of the CHMP expires in February 2017

Scope: Agreement on the expertise required for 5$^{th}$ Co-opted membership

**Action:** For adoption

### 14.1.2. Updated policy on handling competing interests for scientific committees' members and experts

Scope: Policy 0044 - European Medicines Agency policy on the handling of competing interests of scientific committees' members and experts

**Action:** For information

### 14.1.3. EMA report on 10 years of experience with conditional marketing authorisations

Scope: Presentation of the main findings from the analysis

**Action:** For information

### 14.1.4. Best practice guide on measures improving predictability of submissions and adherence to communicated submission deadlines (EMA/760652/2016)

**Action:** For information

### 14.1.5. Presentation on Classification of Post-Authorisation Studies (CPAS)

**Action:** For information

### 14.1.6. Survey on initial marketing authorisation – Update

**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 28 November – 1 December 2016

**Action:** For information

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

Call for nomination of a CHMP representative to the ENCePP Steering Group. Nominations should be sent by 30th November 2016

**Action:** For adoption

### 14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 7-9 December 2016
**Action**: For information

### 14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 21-22 November 2016

**Action:** For information

### 14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at December 2016 PDCO

**Action:** For information

Report from the PDCO meeting held on 14-16 December 2016

**Action:** For information

### 14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 6-8 December 2016
**Action:** For information

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 12-14 December 2016

**Action:** For information

Notes regarding 'Specific scientific guidance for allergies with lower prevalence' (EMA/826761/2016)

**Action**: For discussion

Follow up from January 2016 CHMP

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

### 14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 28 November – 1 December 2016. Table of conclusions

**Action:** For information

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

Scope: Nomination of a replacement SAWP member and his alternate following retirement of Dr Jens Ersbøll. The required area of expertise is oncology

**Action:** For adoption

Scope: SAWP Chair election
**Action:** For adoption

Mandate, objectives and rules of procedure of the Scientific advice working party (SAWP) (EMEA/CHMP/SAWP/69686/04) - revision

**Action:** For adoption

### 14.3.2. Quality Working Party (QWP)

Chair: Jean-Louis Robert

QWP Work Plan (EMA/CHMP/CVMP/QWP/601201/2016)

**Action:** For adoption

Question & answers on the removal of heavy metals tests from a specification (EMA/CHMP/CVMP/QWP/693784/2016)

**Action:** For adoption

Concept paper on the need for revision of Note for guidance on quality of water for pharmaceutical use (EMA/CHMP/CVMP/QWP/BWP/428135/2016)

**Action:** For adoption for 3-month consultation

Correction to the Reflection paper on the Requirements for selection and justification of starting materials for the manufacture of chemical active substances

**Action:** For adoption

Q3D implementation strategy

**Action:** For adoption

### 14.3.3. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 23 November 2016.

**Action:** For adoption

Potential for name-related confusion identified post-authorisation with a CAP and a NAP

Scope: Adoption of NRG advice

**Action:** For adoption

### 14.3.4. Biostatistics Working Party (BSWP)

Vice-Chair: Thomas Lang

Election of the BSWP Chair

**Action:** For adoption

Guideline on multiplicity issues in clinical trials (EMA/CHMP/720718/2016)

**Action:** For adoption for 3-months public consultation

### 14.3.5. Central Nervous System Working Party (CNSWP)

Chair: Karl Broich

CNSWP Work plan 2017 (EMA/CHMP/627427/2016)

**Action:** For adoption

Guideline on the clinical development of medicinal products intended for the treatment of pain (EMA/CHMP/970057/2011)

**Action:** For adoption

### 14.3.6. Pharmacogenomics Working Party (PGWP)

Chair: Krishna Prasad/Markus Paulmichl

PGWP Work plan 2017 (EMA/CHMP/389037/2016)

**Action:** For adoption

### 14.3.7. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink

PKWP Work plan 2017 (EMA/CHMP/643117/2016)

**Action:** For adoption

Q & A Question on requirements for bioequivalence studies under fasting and fed conditions (general) (EMA/CHMP/805455/2016)

**Action:** For discussion

Q & A PKWP clarification on Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/Corr**); Appendix II section on oral solutions

**Action:** For adoption

### 14.3.8. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus,

RIWP Work plan 2017 (EMA/646364/2016)

**Action:** For adoption

### 14.3.9. Vaccines Working Party (VWP)

Chair: Mair Powell,

Nomination of Darko Krnic (Croatia) as an observer to VWP

- current list of VWP members and observers

**Action:** For adoption

## 14.4. Cooperation within the EU regulatory network

## 14.5. Cooperation with International Regulators

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

## 14.7. CHMP work plan

### 14.7.1. CHMP 2017 Draft Work Plan

**Action:** For discussion

## 14.8. Planning and reporting

### 14.8.1. 2017 forecast of the Business Pipeline report for the human scientific committees

**Action:** For information

## 14.9. Others

# 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)*

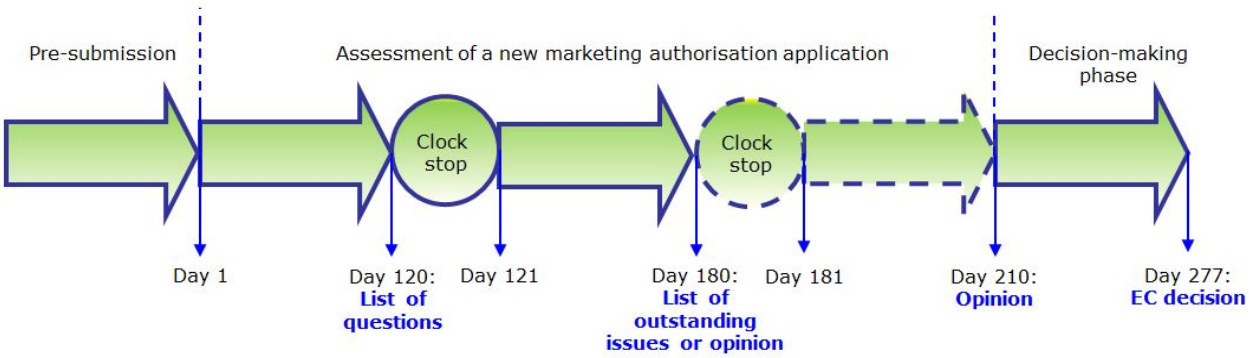
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 December 2016
EMA/CHMP/819197/2016

# Annex to December 2016 CHMP Agenda

PRE SUBMISSION AND POST AUTHORISATIONS ISSUES




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

## A. PRE SUBMISSION ISSUES

### A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for December 2016: **For adoption**

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

Final Outcome of Rapporteurship allocation for December 2016: **For adoption**

### A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

## B. POST-AUTHORISATION PROCEDURES OUTCOMES

### B.1. Annual re-assessment outcomes

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

**ATryn - antithrombin alfa - EMEA/H/C/000587/S/0028**
MAH: GTC Biotherapeutics UK Limited, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard

**Naglazyme - galsulfase - EMEA/H/C/000640/S/0065**
MAH: BioMarin Europe Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna

**Strensiq - asfotase alfa - EMEA/H/C/003794/S/0011, Orphan**
MAH: Alexion Europe SAS, Rapporteur: Greg Markey, PRAC Rapporteur: Almath Spooner

### B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

**Docetaxel Accord - docetaxel - EMEA/H/C/002539/R/0030**
MAH: Accord Healthcare Ltd, Generic, Generic of Taxotere, Rapporteur: Filip Josephson, PRAC Rapporteur: Claire Ferard

**Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/R/0059**
MAH: Pfizer Limited, Rapporteur: Greg Markey, Co-Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Rafe Suvarna
Request for Supplementary Information adopted on 10.11.2016.

**Revlimid - lenalidomide - EMEA/H/C/000717/R/0091, Orphan**
MAH: Celgene Europe Limited, Rapporteur: Pierre Demolis, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Claire Ferard

### B.2.2. Renewals of Marketing Authorisations for unlimited validity

**Docetaxel Kabi - docetaxel - EMEA/H/C/002325/R/0015**
MAH: FRESENIUS KABI ONCOLOGY PLC, Generic, Generic of Taxotere, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard

**Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/R/0050**
MAH: Merck Serono Europe Limited, Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Julie Williams

**Pioglitazone Teva - pioglitazone - EMEA/H/C/002297/R/0016**
MAH: Teva B.V., Generic, Generic of Actos, Glustin, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner
Request for Supplementary Information adopted on 13.10.2016.

**Pioglitazone Teva Pharma - pioglitazone - EMEA/H/C/002410/R/0013**
MAH: Teva B.V., Generic, Generic of Actos, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner
Request for Supplementary Information adopted on 13.10.2016.

### B.2.3. Renewals of Conditional Marketing Authorisations

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

**Caprelsa - vandetanib -**
**EMEA/H/C/002315/R/0023**
MAH: Genzyme Europe BV, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard
Request for Supplementary Information adopted on 10.11.2016.

## B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

**Signal detection**

PRAC recommendations on signals adopted at the PRAC meeting held on 28 November – 1 December 2016 PRAC:

**Proton pump inhibitors (PPIs): dexlansoprazole; esomeprazole; lansoprazole; omeprazole; pantoprazole; rabeprazole** –
**CONTROLOC control** EMEA/H/C/001097; pantoprazole
**PANTECTA control**; EMEA/H/C/001099; pantoprazole
**PANTOLOC control** EMEA/H/C/001100; pantoprazole
**PANTOZOL control** EMEA/H/C/001013; pantoprazole
**SOMAC control** – EMEA/H/C/001098; pantoprazole
CHMP Rapporteur: Greg Markey
PRAC Rapporteur: Rafe Suvarna

**NEXIUM control**; EMEA/H/C/002618; esomeprazole
CHMP Rapporteur: Romaldas Mačiulaitis
PRAC Rapporteur: Simona Kudeliene

Signal of gastric polyps

- PRAC recommendation on a variation:
  **For adoption**

**Vildagliptin; vildagliptin/metformin hydrochloride** –
**Galvus** EMEA/H/C/000771; vildagliptin
**Jalra** EMEA/H/C/001048; vildagliptin
**Xiliarx** EMEA/H/C/001051; vildagliptin
**Eucreas** EMEA/H/C/000807; vildagliptin/metformin hydrochloride
**Icandra** EMEA/H/C/001050; vildagliptin/metformin hydrochloride
**Zomarist** EMEA/H/C/001049; vildagliptin
CHMP Rapporteur: Kristina Dunder

PRAC Rapporteur: Qun-Ying Yue - Signal of pemphigoid

- PRAC recommendation on a variation: **For adoption**

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its November/December 2016 meeting:

**EMEA/H/C/PSUSA/00000226/201605**
(apixaban)
CAPS:
**Eliquis** (EMEA/H/C/002148) (apixaban), MAH: Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "18 May 2015 to 17 May 2016"

**EMEA/H/C/PSUSA/00002491/201604**
(pramipexole)
CAPS:
**Mirapexin** (EMEA/H/C/000134) (pramipexole), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen
**Sifrol** (EMEA/H/C/000133) (pramipexole), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen
NAPS:
**Calmolan 0,54 mg-Tabletten 1-30129 AT** - G.L. PHARMA GMBH
**Pramipexol - 1 A Pharma 0,54 mg Tabletten 77956.00.00 DE** - 1 A PHARMA GMBH
**Pramipexol G.L. 0,54 mg-Tabletten 1-30123 AT** - G.L. PHARMA GMBH
**Pramipexol HEXAL 0,54 mg Tabletten 77954.00.00 DE** - HEXAL AG
**Pramipexol Sandoz 0,54 mg Tabletten 77955.00.00 DE** - HEXAL AG
, PRAC Rapporteur: Doris Stenver, "07/04/2013 - 06/04/2016"

**EMEA/H/C/PSUSA/00009118/201605**
(decitabine)
CAPS:
**Dacogen** (EMEA/H/C/002221) (decitabine), MAH: Janssen-Cilag International NV, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, "02 May 2015 to 01 May 2016"

**EMEA/H/C/PSUSA/00010301/201605**
(ibrutinib)

CAPS:
**Imbruvica** (EMEA/H/C/003791) (ibrutinib), MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams, “13 November 2015 to 12 May 2016”

**EMEA/H/C/PSUSA/00010307/201605**
(aclidinium bromide / formoterol fumarate dihydrate)
CAPS:
**Brimica Genuair** (EMEA/H/C/003969) (aclidinium / formoterol fumarate dihydrate), MAH: AstraZeneca AB, Rapporteur: Nithyanandan Nagercoil
**Duaklir Genuair** (EMEA/H/C/003745) (aclidinium / formoterol fumarate dihydrate), MAH: AstraZeneca AB, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, “20 November 2015 - 19 May 2016”

**EMEA/H/C/PSUSA/00010316/201605**
(ketoconazole (centrally authorised product only))
CAPS:
**Ketoconazole HRA** (EMEA/H/C/003906) (ketoconazole), MAH: Laboratoire HRA Pharma, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Željana Margan Koletić, “20 November 2015 to 19 May 2016”

**EMEA/H/C/PSUSA/00010318/201605**
(nintedanib (oncology indications))
CAPS:
**Vargatef** (EMEA/H/C/002569) (nintedanib), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Leonidas Klironomos, “22 Nov 2015 to 21 May 2016”

## B.4. EPARs / WPARs

**Afstyla - lonoctocog alfa - EMEA/H/C/004075**
Applicant: CSL Behring GmbH, treatment of haemophilia A, New active substance (Article 8(3) of Directive No 2001/83/EC)

**Cavoley - pegfilgrastim - EMEA/H/C/004342**
Applicant: STADA Arzneimittel AG, treatment of neutropenia, Duplicate, Duplicate of Efgratin,

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

**Darunavir Mylan - darunavir - EMEA/H/C/004068**
Applicant: MYLAN S.A.S, treatment of HIV-1, Generic, Generic of Prezista, Generic application (Article 10(1) of Directive No 2001/83/EC)

**Efgratin - pegfilgrastim - EMEA/H/C/004023**
Applicant: Gedeon Richter Plc., treatment of neutropenia, Similar biological application (Article 10(4) of Directive No 2001/83/EC)
**WPAR**

**Fiasp - insulin aspart - EMEA/H/C/004046**
Applicant: Novo Nordisk A/S, treatment of diabetes mellitus in adults, Known active substance (Article 8(3) of Directive No 2001/83/EC)

**Kepnetic - aceneuramic acid - EMEA/H/C/004176, Orphan**
Applicant: Ultragenyx UK Limited, treatment of Hereditary Inclusion Body Myopathy (HIBM), New active substance (Article 8(3) of Directive No 2001/83/EC)
**WPAR**

**Lusduna - insulin glargine - EMEA/H/C/004101**
Applicant: Merck Sharp & Dohme Limited, treatment of diabetes mellitus, Similar biological application (Article 10(4) of Directive No 2001/83/EC)

**Movymia - teriparatide - EMEA/H/C/004368**
Applicant: STADA Arzneimittel AG, treatment of osteoporosis, Duplicate, Duplicate of Terrosa, Similar biological application (Article 10(4) of Directive No 2001/83/EC)

**Suliqua - insulin glargine / lixisenatide - EMEA/H/C/004243**
Applicant: sanofi-aventis groupe, treatment of type 2 diabetes mellitus, Fixed combination application (Article 10b of Directive No 2001/83/EC)

**Tadalafil Generics - tadalafil - EMEA/H/C/004297**

| | |
|---|---|
| Applicant: MYLAN S.A.S, treatment of pulmonary arterial hypertension (PAH), Generic, Generic of Adcirca, Cialis, Generic application (Article 10(1) of Directive No 2001/83/EC) | |
| **Terrosa - teriparatide - EMEA/H/C/003916**<br>Applicant: Gedeon Richter Plc., treatment of osteoporosis, Similar biological application (Article 10(4) of Directive No 2001/83/EC) | |
| **Vemlidy - tenofovir alafenamide - EMEA/H/C/004169**<br>Applicant: Gilead Sciences International Ltd, treatment of chronic hepatitis B, New active substance (Article 8(3) of Directive No 2001/83/EC) | |
| **Zinplava - bezlotoxumab - EMEA/H/C/004136**<br>Applicant: Merck Sharp & Dohme Limited, indicated for the prevention of Clostridium difficile infection (CDI) recurrence, New active substance (Article 8(3) of Directive No 2001/83/EC) | |

### B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

#### B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

| | |
|---|---|
| **Aflunov - prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - EMEA/H/C/002094/II/0026/G**<br>MAH: Seqirus S.r.l, Rapporteur: Daniela Melchiorri<br>Request for Supplementary Information adopted on 21.07.2016, 03.03.2016, 03.12.2015. | Weekly start timetable. |
| **BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0138**<br>MAH: Pfizer Limited, Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 06.10.2016. | Weekly start timetable. |
| **Colobreathe - colistimethate sodium - EMEA/H/C/001225/II/0023**<br>MAH: Forest Laboratories UK Limited, Rapporteur: Nithyanandan Nagercoil<br>Request for Supplementary Information adopted | Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable. |

| | |
|---|---|
| on 17.11.2016, 12.05.2016, 03.03.2016. | |
| **Elocta - efmoroctocog alfa - EMEA/H/C/003964/II/0008/G**<br>MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 13.10.2016. | |
| **Empliciti - elotuzumab - EMEA/H/C/003967/II/0003**<br>MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik<br>Opinion adopted on 24.11.2016.<br>Request for Supplementary Information adopted on 13.10.2016. | Positive Opinion adopted by consensus on 24.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Esbriet - pirfenidone - EMEA/H/C/002154/II/0039, Orphan**<br>MAH: Roche Registration Limited, Rapporteur: Greg Markey<br>Request for Supplementary Information adopted on 27.10.2016. | Weekly start timetable. |
| **Foclivia - influenza virus surface antigens (inactivated) of strain A/Vietnam/1194/2004 (H5N1) - EMEA/H/C/001208/II/0023/G**<br>MAH: Seqirus S.r.l, Rapporteur: Daniela Melchiorri<br>Request for Supplementary Information adopted on 27.10.2016. | Weekly start timetable. |
| **Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0013/G, Orphan**<br>MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac<br>Request for Supplementary Information adopted on 13.10.2016. | Weekly start timetable. |
| **Ixiaro - japanese encephalitis vaccine (inactivated, adsorbed) - EMEA/H/C/000963/II/0083**<br>MAH: Valneva Austria GmbH, Rapporteur: Jan Mueller-Berghaus | Weekly start timetable. |
| **Nulojix - belatacept - EMEA/H/C/002098/II/0034/G**<br>MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson<br>Opinion adopted on 17.11.2016.<br>Request for Supplementary Information adopted on 15.09.2016, 09.06.2016. | Positive Opinion adopted by consensus on 17.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| **Opdivo - nivolumab - EMEA/H/C/003985/II/0020**<br>MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez<br>Request for Supplementary Information adopted on 17.11.2016. | Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable. |
| **Opdivo - nivolumab - EMEA/H/C/003985/II/0022/G**<br>MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez<br>Request for Supplementary Information adopted on 01.12.2016. | Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable. |
| **Pixuvri - pixantrone - EMEA/H/C/002055/II/0032/G**<br>MAH: CTI Life Sciences Limited, Rapporteur: Greg Markey | Weekly start timetable. |
| **Praluent - alirocumab - EMEA/H/C/003882/II/0014/G**<br>MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege | Weekly start timetable. |
| **Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0147/G**<br>MAH: Pfizer Limited, Rapporteur: Kristina Dunder | Weekly start timetable. |
| **Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0110**<br>MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus | |
| **Rapilysin - reteplase - EMEA/H/C/000105/II/0062**<br>MAH: Actavis Group PTC ehf, Rapporteur: Harald Enzmann<br>Request for Supplementary Information adopted on 20.10.2016. | Weekly start timetable. |
| **Repatha - evolocumab - EMEA/H/C/003766/II/0012**<br>MAH: Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege | Weekly start timetable. |
| **Savene - dexrazoxane - EMEA/H/C/000682/II/0031, Orphan**<br>MAH: Clinigen Healthcare Ltd, Rapporteur: Pierre Demolis | Weekly start timetable. |
| **Simponi - golimumab - EMEA/H/C/000992/II/0071/G** | Weekly start timetable. |

| | |
|---|---|
| MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder | |
| **Soliris - eculizumab - EMEA/H/C/000791/II/0088/G, Orphan** MAH: Alexion Europe SAS, Rapporteur: Aranzazu Sancho-Lopez | Weekly start timetable. |
| **Soliris - eculizumab - EMEA/H/C/000791/II/0089, Orphan** MAH: Alexion Europe SAS, Rapporteur: Aranzazu Sancho-Lopez | Weekly start timetable |
| **Stelara - ustekinumab - EMEA/H/C/000958/II/0051/G** MAH: Janssen-Cilag International NV, Rapporteur: Greg Markey Opinion adopted on 24.11.2016. Request for Supplementary Information adopted on 20.10.2016. | Positive Opinion adopted by consensus on 24.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0110** MAH: GSK Biologicals SA, Rapporteur: Kristina Dunder Opinion adopted on 17.11.2016. | Positive Opinion adopted by consensus on 17.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Tysabri - natalizumab - EMEA/H/C/000603/II/0098/G** MAH: Biogen Idec Ltd, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 24.11.2016. | Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable. |
| **Vimpat - lacosamide - EMEA/H/C/000863/II/0064/G** MAH: UCB Pharma S.A., Rapporteur: Filip Josephson Opinion adopted on 01.12.2016. Request for Supplementary Information adopted on 29.09.2016. | Positive Opinion adopted by consensus on 01.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0058** MAH: Bial - Portela & Cª, S.A., Rapporteur: Martina Weise Request for Supplementary Information adopted on 15.09.2016. | |
| **WS0922/G Hexacima- EMEA/H/C/002702/WS0922/0052/G Hexaxim-** | |

| | |
|---|---|
| **EMEA/H/W/002495/WS0922/0059/G**<br>**Hexyon-**<br>**EMEA/H/C/002796/WS0922/0055/G**<br>MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 13.10.2016. | |
| **WS0969**<br>**Infanrix hexa-**<br>**EMEA/H/C/000296/WS0969/0204**<br>MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren<br>Opinion adopted on 24.11.2016.<br>Request for Supplementary Information adopted on 13.10.2016. | Positive Opinion adopted by consensus on 24.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS0976/G**<br>**Infanrix hexa-**<br>**EMEA/H/C/000296/WS0976/0205/G**<br>MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren<br>Request for Supplementary Information adopted on 13.10.2016. | |
| **WS1003**<br>**HyQvia-EMEA/H/C/002491/WS1003/0031**<br>**Kiovig-EMEA/H/C/000628/WS1003/0075**<br>MAH: Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus | |
| **WS1043/G**<br>**Helixate NexGen-**<br>**EMEA/H/C/000276/WS1043/0182/G**<br>**KOGENATE Bayer-**<br>**EMEA/H/C/000275/WS1043/0189/G**<br>MAH: Bayer Pharma AG, Lead Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 24.11.2016. | Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable. |
| **WS1061/G**<br>**Humalog-**<br>**EMEA/H/C/000088/WS1061/0151/G**<br>**Liprolog-**<br>**EMEA/H/C/000393/WS1061/0115/G**<br>MAH: Eli Lilly Nederland B.V., Lead Rapporteur: Robert James Hemmings | |

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

| | |
|---|---|
| **Arzerra - ofatumumab -**<br>**EMEA/H/C/001131/II/0048, Orphan** | |

| | |
|---|---|
| MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, “Submission of final clinical study of the study OMB115991: 'A Phase II, Multi-Centre Study Investigating the Safety and Efficacy of Ofatumumab Plus Bendamustine in Patients with Untreated or Relapsed CLL'. With the present submission, no changes to the product information are proposed.” | |
| **Cerdelga - eliglustat - EMEA/H/C/003724/II/0008, Orphan**<br>MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, “Update of SmPC section 5.1 to include 2, 3 and 4 years composite stability endpoint data based on the final results of the ENCORE study.”<br>Request for Supplementary Information adopted on 13.10.2016. | |
| **Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0081**<br>MAH: GSK Biologicals SA, Rapporteur: Bart Van der Schueren, “To submit the final effectiveness results of clinical study HPV-040, a community randomized study conducted in Finland to evaluate the effectiveness of two vaccination strategies for 12 -15 year old early adolescents using Cervarix, i.e., to vaccinate female adolescents only, or to vaccinate female and male adolescents.”<br>Request for Supplementary Information adopted on 15.09.2016. | |
| **Effentora - fentanyl - EMEA/H/C/000833/II/0044**<br>MAH: Teva B.V., Rapporteur: Martina Weise, “Update of sections 4.4, 4.6 and 4.8 as applicable of the SmPC in order to add a warning on adrenal insufficiency, androgen deficiency and Neonatal withdrawal syndrome following a request from FDA to introduce a class label safety warning. The PL was updated accordingly.<br><br>In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0 and to apply a combined SmPC”<br>Request for Supplementary Information adopted on 10.11.2016. | Weekly start timetable. |
| **Eperzan - albiglutide -** | Weekly start timetable. The Committee |

| | |
|---|---|
| **EMEA/H/C/002735/II/0027/G**<br>MAH: GlaxoSmithKline Trading Services, Rapporteur: Kristina Dunder, “Submission of the final study reports for non-clinical toxicity studies:<br>2015N232567 - Investigation of blood brain barrier penetration of albiglutide in mice and 2016N269355 - Subcutaneous juvenile toxicity study in mice.”<br>Request for Supplementary Information adopted on 17.11.2016. | adopted a Request for Supplementary information together with a specific timetable: |
| **Fycompa - perampanel - EMEA/H/C/002434/II/0034/G**<br>MAH: Eisai Europe Ltd., Rapporteur: Robert James Hemmings, “Update of sections 4.5 and 5.1 of the SmPC in order to add information on the conversion of patients to Fycompa monotherapy (E2007-G000-504, hereby Study 504) and to include the effect of withdrawal of concomitant enzyme-inducing antiepileptic drugs (EIAEDs) on plasma concentrations of perampanel (A supportive analysis, CPMS-E2007-0013R).<br><br>In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.” | Weekly start timetable. |
| **Incruse - umeclidinium bromide - EMEA/H/C/002809/II/0013**<br>MAH: Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, “Update of section 4.8 of the SmPC and relevant section of the PL to add hypersensitivity reactions including rash, urticaria, pruritus as uncommon and anaphylaxis and angioedema as rare adverse reactions.<br>The MAH is taking the opportunity to update the Local representative section in the PL.” | Weekly start timetable. |
| **Intuniv - guanfacine - EMEA/H/C/003759/II/0004**<br>MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.2 (Posology and Method of Administration), 4.4 (Special Warnings and Precautions for Use), and 4.8 (Undesirable Effects) of the SmPC in order to include a warning and update the safety information as a result of a post-marketing case of hypertensive encephalopathy upon abrupt discontinuation of Intuniv (guanfacine hydrochloride). | |

| | |
|---|---|
| The Package Leaflet is updated accordingly."<br>Request for Supplementary Information adopted on 13.10.2016, 23.06.2016. | |
| **Ivemend - fosaprepitant - EMEA/H/C/000743/II/0034/G**<br>MAH: Merck Sharp & Dohme Limited, Rapporteur: Filip Josephson, "C.I.4 - Update of sections 5.1 and 5.2 of the SmPC in order to include pharmacodynamic and pharmacokinetic data relevant to the paediatric population.<br>C.I.4 - Update of sections 5.3 of the SmPC in order to include non-clinical data relevant to the paediatric population.<br>The Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0." | Weekly start timetable. |
| **Jevtana - cabazitaxel - EMEA/H/C/002018/II/0035**<br>MAH: Sanofi-Aventis Groupe, Rapporteur: Pierre Demolis, "Update of sections 4.2, 5.1 and 5.2 of the SmPC in order to add information on study TED12689 a phase 1-2 dose finding, safety and efficacy study of cabazitaxel in pediatric patients with refractory solid tumors including tumors of the central nervous system."<br>Request for Supplementary Information adopted on 10.11.2016. | |
| **Keppra - levetiracetam - EMEA/H/C/000277/II/0162**<br>MAH: UCB Pharma S.A., Rapporteur: Koenraad Norga, PRAC Rapporteur: Laurence de Fays, "Update of the RMP to include an additional epidemiological study (EPD172) to further characterise the risk of acute kidney injury with levetiracetam and other AEDs (RMP version 7.0)."<br>Request for Supplementary Information adopted on 15.09.2016. | Weekly start timetable. |
| **Keytruda - pembrolizumab - EMEA/H/C/003820/II/0013**<br>MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, "Update of section 4.4 of the SmPC with information regarding the possible occurrence of simultaneous immune-related adverse reactions. The Package Leaflet has been updated accordingly."<br>Request for Supplementary Information adopted | Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable. |

| | |
|---|---|
| on 17.11.2016. | |
| **Levemir - insulin detemir - EMEA/H/C/000528/II/0082**<br>MAH: Novo Nordisk A/S, Rapporteur: Hanne Lomholt Larsen, “Update of sections 4.4 of the SmPC with additional information regarding avoidance of accidental mix-ups and medication errors.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 9.1 and 10.0 and to correct a mistake in the recommendation for use of the first of the two titration algorithms in section 4.2 of the SmPC.” | Weekly start timetable. |
| **NovoMix - insulin aspart - EMEA/H/C/000308/II/0087**<br>MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, “Update of section 4.4 f the SmPC to include a warning on the risk of medication errors. The package leaflet has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.” | |
| **NovoSeven - eptacog alfa / eptacog alfa (activated) - EMEA/H/C/000074/II/0092**<br>MAH: Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik, “Update of section 4.4 of the SmPC in order to delete sucrose warning. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes/corrections in the SmPC and Package Leaflet and to bring the PI in line with the latest QRD template version 10 (combined SmPC has been introduced).”<br>Request for Supplementary Information adopted on 06.10.2016, 04.08.2016. | Weekly start timetable. |
| **Orfadin - nitisinone - EMEA/H/C/000555/II/0056**<br>MAH: Swedish Orphan Biovitrum International AB, Rapporteur: Luca Pani, “Update of section 5.1 of the SmPC in order to present the efficacy data based on a complementary analysis of the pivotal study for Orfadin (NTBC study).<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the Product Information in line with the latest QRD template version 10.” | Weekly start timetable. |

| | |
|---|---|
| Request for Supplementary Information adopted on 15.09.2016. | |
| **Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0014**<br>MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil, "Update of section 5.3 of the SmPC in order to revise the ivacaftor animal:human exposure ratio. The Package Leaflet is updated accordingly." | Weekly start timetable. |
| **Otezla - apremilast - EMEA/H/C/003746/II/0011**<br>MAH: Celgene Europe Limited, Rapporteur: Patrick Salmon, "Submission of study report CC-10004-PSOR-010; a Phase 3b, multicenter, randomized, placebo-controlled, double-blind, double-dummy, study of the efficacy and safety of apremilast (CC-10004), etanercept, and placebo, in subjects with moderate to severe plaque psoriasis. The submission of this clinical study report fulfils PAM EMEA/H/C/003746/MEA/003." | |
| **Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0097**<br>MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen, "Submission of final study report of study 1160.173 "A prospective, open label study to evaluate the pharmacokinetics of dabigatran in non-valvular atrial fibrillation (NVAF) patients with severely impaired renal function on dabigatran etexilate 75 mg BID therapy"."<br>Request for Supplementary Information adopted on 01.12.2016. | Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable. |
| **Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0145**<br>MAH: Pfizer Limited, Rapporteur: Kristina Dunder, "Update of the SmPC section 5.1 with information on Prevenar 13 effects on invasive pneumococcal disease, antimicrobial resistance and otitis media caused by nontypeable H. influenzae. Editorial changes have also been proposed throughout the SmPC."<br>Request for Supplementary Information adopted on 13.10.2016. | |
| **Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-** | Positive Opinion adopted by consensus on 17.11.2016. The Icelandic and Norwegian CHMP |

| | |
|---|---|
| **valent, adsorbed) - EMEA/H/C/001104/II/0146**<br>MAH: Pfizer Limited, Rapporteur: Kristina Dunder, "Update of the SmPC section 4.5 to include information on Prevenar 13 co-administration with the tetanus toxoid conjugated meningococcal polysaccharide serogroups A, C, W and Y vaccine based on the results of study MenACWY-TT-104. Minor editorial changes have been introduced throughout the PI. Additionally the MAH took the opportunity to align the PI with the latest QRD template version 10.0."<br>Opinion adopted on 17.11.2016. | Members were in agreement with the CHMP recommendation. |
| **Ranexa - ranolazine - EMEA/H/C/000805/II/0051**<br>MAH: Menarini International Operations Luxembourg S.A., Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to include the data from the final CSR of study RIVER-PCI. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the details of local representative in Bulgaria in the Package Leaflet and to bring the Annex II in line with the latest QRD template version 9.1."<br>Request for Supplementary Information adopted on 21.07.2016, 14.04.2016. | Weekly start timetable. |
| **Rapamune - sirolimus - EMEA/H/C/000273/II/0163/G**<br>MAH: Pfizer Limited, Rapporteur: Kristina Dunder, "Update of section 4.4 of the SmPC to update the current warning on angioedema to include a possible dose-dependent effect between sirolimus and angioedema based on post-marketing data. Update of section 4.8 of the SmPC to include neuroendocrine carcinoma of the skin and malignant carcinoma as new ADRs and to include squamous cell carcinoma of the skin and basal cell carcinoma as part of the ADR 'skin cancer' based on post-marketing data. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to combine the 0.5 mg, 1 mg and 2 mg tablets SmPC, to fully detail all components of the Rapamune printing ink in section 6.1 of the SmPC and in the Package Leaflet, to align the wording in section 4 of the Package Leaflet with section 4.8 of the SmPC regarding Clostridium | Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable. |

| | |
|---|---|
| difficile, to update the list of local representatives for the Czech republic, Norway and Sweden in the Package Leaflet and to bring the PI in line with the latest QRD template version 10."<br>Request for Supplementary Information adopted on 01.12.2016. | |
| **Revestive - teduglutide - EMEA/H/C/002345/II/0032, Orphan**<br>MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Sinan B. Sarac, "Update of sections 4.3, 4.4, and 4.8 of the SmPC in order to update the safety information in line with updated CCDS following review of the MAH's safety database. The Package Leaflet is updated accordingly.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in section 5.1 of the SmPC." | |
| **Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0037/G**<br>MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, "Update of SmPC section 4.8 to add a new ADR 'skin discolouration' with the frequency 'not known'. The PL has been updated accordingly. Additionally, minor editorial changes have been introduced throughout the PI. The MAH took also the opportunity to align the PI with the latest version of the QRD template 10.0."<br>Opinion adopted on 24.11.2016. | Positive Opinion adopted by consensus on 24.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Rotarix - human rotavirus, live attenuated - EMEA/H/C/000639/II/0086**<br>MAH: GlaxoSmithKline Biologicals S.A., Rapporteur: Bart Van der Schueren, "Final study report of EPI-ROTA-052 BOD EU SUPP (201433) in which the strain surveillance data of the European Rotavirus Network (EuroRotaNet) during the rotavirus seasons from September 2006 to August 2015 is described. The study is listed in the Rotarix RMP as an outstanding additional pharmacovigilance activity. This is a category 3 study, but not a Post-Authorisation Safety Study (PASS)."<br>Request for Supplementary Information adopted on 15.09.2016. | Weekly start timetable. |
| **Saxenda - liraglutide - EMEA/H/C/003780/II/0010**<br>MAH: Novo Nordisk A/S, Rapporteur: Johann | Positive Opinion adopted by consensus on 01.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

| | |
|---|---|
| Lodewijk Hillege, “Update of sections 4.2 and 5.1 of the SmPC in order to update the documented treatment effect currently limited to 1 year. The proposed update of the current labelling for long-term efficacy, safety and tolerable use in the management of obesity is based on 3-year data from trial 1839.<br><br>In addition, the Marketing authorisation holder took the opportunity to bring the PI in line with the latest QRD template version 10 and implement minor linguistic updates.”<br>Opinion adopted on 01.12.2016.<br>Request for Supplementary Information adopted on 29.09.2016. | recommendation. |
| **Stivarga - regorafenib - EMEA/H/C/002573/II/0018**<br>MAH: Bayer Pharma AG, Rapporteur: Paula Boudewina van Hennik, “Update the SmPC section 4.2 and 5.2 based on results from phase 1 study which evaluated the pharmacokinetics and safety of regorafenib in cancer subjets with severe renal impairment compared to cancer subjects without or mild renal impairment. The package leaflet is updated accordingly.”<br>Request for Supplementary Information adopted on 13.10.2016. | |
| **Strensiq - asfotase alfa - EMEA/H/C/003794/II/0008, Orphan**<br>MAH: Alexion Europe SAS, Rapporteur: Greg Markey, PRAC Rapporteur: Almath Spooner, “Update of sections 4.4 and 4.8 of the SmPC in order to reinforce the wording on the risk of anaphylaxis. The Package Leaflet is updated accordingly. The MAH took th eopportunity to include the Pharmacotherapeutic group in section 5.1.”<br>Request for Supplementary Information adopted on 13.10.2016, 21.07.2016. | |
| **Tamiflu - oseltamivir - EMEA/H/C/000402/II/0122**<br>MAH: Roche Registration Limited, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, “Update of section 5.1 of the SmPC and RMP to reflect the results of study IRIS (NV20237) a prospective, multicenter, information-gathering study, comprising virological surveillance and assessment of clinical outcomes, which enrolled patients over a 7-year period. | |

| | |
|---|---|
| In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version."<br>Request for Supplementary Information adopted on 21.07.2016. | |
| **Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0034**<br>MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, "To update Section 5.3 (Preclinical Safety Data) of the Summary of Product Characteristics (SmPC) to reflect that exposure margins have been re-calculated based on the area under the concentration-time curve (AUC) rather than based on body surface area (mg/m2)."<br>Opinion adopted on 17.11.2016. | Positive Opinion adopted by consensus on 17.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0025**<br>MAH: AbbVie Ltd., Rapporteur: Filip Josephson, "Update of sections 4.3 and 4.5 of the SmPC to add three additional contraindication medications with dronedarone, lurasidone and ranolazine. The Package Leaflet is updated accordingly." | |
| **Vimpat - lacosamide - EMEA/H/C/000863/II/0066/G**<br>MAH: UCB Pharma S.A., Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC in order to update the safety information regarding the use of lacosamide in patients with hepatic impairment, section 4.8 to add a new adverse drug reaction (hepatic enzyme increased (> 2x ULN)) and section 4.9 regarding lacosamide overdose based on postmarketing reports. The Package Leaflet is updated accordingly.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to make minor editorial change in the SmPC." | |
| **Zydelig - idelalisib - EMEA/H/C/003843/II/0029**<br>MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, "Submission of the final study report for the clinical study 101-07 "A Phase I Study To Investigate the Safety and Clinical Activity of Idelalisib in Combination with Chemotherapeutic Agents, Immunomodulatory Agents and Anti-CD-20 mAb in Subjects with | Weekly start timetable. |

| | |
|---|---|
| Relapsed or Refractory Indolent B-cell Non-Hodgkin Lymphoma, Mantle Celle Lymphoma or Chronic Lymphocytic Leukemia", in order to fulfil of the Post Approval Measure (PAM) MEA 009 for Zydelig." | |
| **WS1019**<br>**Clopidogrel Zentiva-EMEA/H/C/000975/WS1019/0055**<br>**Clopidogrel/Acetylsalicylic acid Zentiva-EMEA/H/C/001144/WS1019/0047**<br>**DuoPlavin-EMEA/H/C/001143/WS1019/0046**<br>**Iscover-EMEA/H/C/000175/WS1019/0128**<br>**Plavix-EMEA/H/C/000174/WS1019/0124**<br>MAH: Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC in order to add Kounis syndrome as a new ADR. The Package Leaflet is updated accordingly. In addition the Worksharing applicant (WSA) took the opportunity to make minor amendments to Annex II for Clopidogrel Zentiva, Iscover and Plavix, to update the contact details of the Bulgarian local representative in the Package Leaflet for all the products involved and the Italian, Hungarian and Lithuanian local representatives for Clopidogrel Zentiva, Iscover and Plavix, to combine the two strengths SmPCs for all the products involved in this Worksharing application, to combine the two strengths Package Leaflet for DuoPlavin and Clopidogrel/Acetylsalicylic acid Zentiva. Furthermore, the PI is brought in line with the latest QRD template version 10." | Weekly start timetable. |
| **WS1020**<br>**Clopidogrel/Acetylsalicylic acid Zentiva-EMEA/H/C/001144/WS1020/0046**<br>**DuoPlavin-EMEA/H/C/001143/WS1020/0045**<br>MAH: Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, "Update of sections 4.4 and 4.5 of the SmPC in order to add a new drug-drug interaction between nicorandil and NSAIDs including acetylsalicylic acid (ASA) and lysine-acetylsalicylate (LAS) and its increased risk for severe complications including gastrointestinal ulceration, perforation and haemorrhage. The Package Leaflet is updated accordingly. In addition the Worksharing applicant (WSA) took the opportunity to make a minor correction in | Weekly start timetable. |

| | |
|---|---|
| Annex II (typographical change)." | |
| **WS1034**<br>**Descovy-**<br>**EMEA/H/C/004094/WS1034/0007**<br>**Genvoya-**<br>**EMEA/H/C/004042/WS1034/0021**<br>**Odefsey-**<br>**EMEA/H/C/004156/WS1034/0005**<br>MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, "Update of section 4.5 of the SmPC with new pharmacology date from the final Study GS-US-311-1790." | |
| **WS1045**<br>**Entresto-**<br>**EMEA/H/C/004062/WS1045/0008**<br>**Neparvis-**<br>**EMEA/H/C/004343/WS1045/0006**<br>MAH: Novartis Europharm Ltd, Lead Rapporteur: Johann Lodewijk Hillege, "Submission of study no. 1570187: Effect of LBQ657 on cloned hERG potassium channels expressed in human embryonic kidney cells. No changes to PI have been proposed."<br>Opinion adopted on 01.12.2016. | Positive Opinion adopted by consensus on 01.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

### B.5.3. CHMP-PRAC assessed procedures

| | |
|---|---|
| **Aluvia - lopinavir / ritonavir -**<br>**EMEA/H/W/000764/II/0100**<br>MAH: AbbVie Ltd., Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard, "Update of sections 4.2 and 5.1 of the SmPC in order to update information following analysis of the published 48-week study results for "A Kaletra ONCE daily randomised Trial of the pharmacokinetics, safety and efficacy of twice-daily versus once-daily lopinavir/ritonavir tablets dosed by weight as part of combination antiretroviral therapy in HIV-1–infected children"(PENTA 18/KONCERT) in fulfilment of a Post Authorisation Measure MEA (Additional PhV activity in the Risk Management Plan).<br><br>In addition, the SOH takes the opportunity to remove the Missing Information safety concern of Limited Information of the Kaletra 100 mg/25 mg film-coated tablets in the paediatric population as part of the submitted RMP version | |

8."

**Amyvid - florbetapir (18F) - EMEA/H/C/002422/II/0022**

MAH: Eli Lilly Nederland B.V., Rapporteur: Harald Enzmann, PRAC Rapporteur: Valerie Strassmann, "Update of sections 4.4 and 5.1 of the SmPC in order to introduce quantitative read as an adjunct to visual read of florbetapir (18F) PET scans.
In addition, the Marketing authorisation holder (MAH) took the opportunity bring the PI in line with the latest QRD template version 10.0.
The updated RMP version 2.0 has been submitted"
Request for Supplementary Information adopted on 10.11.2016, 15.09.2016.

**Benepali - etanercept - EMEA/H/C/004007/II/0019/G**

MAH: Samsung Bioepis UK Limited (SBUK), Rapporteur: Andrea Laslop, PRAC Rapporteur: Rafe Suvarna, "Extension of indication to include two new indications for the treatment of juvenile idiopathic arthritis and paediatric plaque psoriasis already approved for the reference medicinal product (Enbrel) for Benepali.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Annex II, the Package Leaflet and Labelling are updated in accordance. The RMP (version 4.2) is also updated accordingly. Furthermore, the PI is brought in line with the latest QRD template version 10."
Request for Supplementary Information adopted on 10.11.2016.

**Bronchitol - mannitol - EMEA/H/C/001252/II/0027, Orphan**

MAH: Pharmaxis Pharmaceuticals Limited, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, "To submit the Clinical Study Report (CSR) for a study to investigate the efficacy and safety of Bronchitol in children and adolescents with cystic fibrosis (Study DPM-CF-204)."
Request for Supplementary Information adopted on 15.09.2016.

**Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0085**

MAH: GSK Biologicals SA, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné, “Submission of Study EPI-HPV-069, a meta-analysis assessing the risk of three autoimmune diseases following vaccination with Cervarix: autoimmune thyroiditis (AIT), Guillain-Barre Syndrome (GBS) and Inflammatory Bowel Disease (IBD). The EPI-HPV-069 study is a post-licensure commitment to the EMA (PASS register number EUPAS13332).

As part of this submission, an updated RMP (version 18) is provided, including changes related to the EPI-HPV-069 meta-analysis submitted and minor updates related to other studies.”

**Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0054**

MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Final clinical study report for study AS001 is submitted.
Sections 4.8 and 5.1 of the Summary of Product Characteristics (SmPC) are revised in order to update the efficacy and safety information (Week 204) for study AS001. The package leaflet remains unchanged.
A revised RMP (version 11.0) is also submitted.”
Request for Supplementary Information adopted on 13.10.2016.

**Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0055**

MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Final clinical study report for study PsA001 is submitted to provide data on long-term use of Cimzia in psoriatic arthritis subjects up to 216 weeks of treatment.
Sections 4.8 and 5.1 of the Summary of Product Characteristics (SmPC) are revised in order to update the efficacy and safety information (Week 216) for study PsA001. The package leaflet remains unchanged.
A revised RMP (veriosn 11) is also submitted.
This corresponds to MEA 027”
Request for Supplementary Information adopted on 13.10.2016.

**Epclusa - sofosbuvir / velpatasvir - EMEA/H/C/004210/II/0003**

MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.4, 4.5 and 5.1 of the SmPC in order to reflect on emerging clinical data from study GS-US-342-1202 investigating efficacy and safety in subjects with chronic hepatitis C virus (HCV) and human immunodeficiency virus (HIV)-1 coinfection.
In addition, minor administrative changes are implemented throughout the Product Information."

**Feraccru - iron - EMEA/H/C/002733/II/0002/G**

MAH: Shield TX (UK) Ltd, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Adam Przybylkowski, "Submission of two final study reports for in vitro studies conducted as part of post-authorisation measures MEA 001 and MEA 002 :
- One drug-drug interaction study to investigate drug interactions with Feraccru
- One drug-drug interaction study to identify UGT isoenzyme(s) that are responsible for metabolism of ferric maltol.
Consequential changes have been made to the RMP to reflect the completion of the studies."
Request for Supplementary Information adopted on 10.11.2016, 15.09.2016.

**Flixabi - infliximab - EMEA/H/C/004020/II/0009**

MAH: Samsung Bioepis UK Limited (SBUK), Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final study report of study SB2-G31-RA: A Randomised, Double-blind, Parallel Group, Multicentre Clinical Study to Evaluate the Efficacy, Safety, Pharmacokinetics and Immunogenicity of SB2 Compared to Remicade® in Subjects with Moderate to Severe Rheumatoid Arthritis despite Methotrexate Therapy.

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

| | |
|---|---|
| (Ankylosing Spondylitis) and CD (Crohn's Disease) patients.” | |
| **Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0061**<br>MAH: MedImmune LLC, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, “Update of sections 4.3 and 4.8 of the SmPC to reflect that Fluenz Tetra is contraindicated only in children with severe hypersensitivity to eggs (instead of all children with egg allergy), and to update the safety information (update of the number of children and adolescents in the safety database). The PIL is amended accordingly.<br><br>The RMP is updated to implement administrative changes to the high level description on Enhanced Safety Surveillance, and to change the milestones for study MA-VA-MEDI3250-1116.” | |
| **Iclusig - ponatinib - EMEA/H/C/002695/II/0032/G, Orphan**<br>MAH: Incyte Biosciences UK Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna, “Update of sections 4.2, 4.4, 4.8, 5.1 of the SmPC based on data from the ongoing Study AP24534-07-101 with a median duration of follow-up of approximately 48 months for the CP-CML patients and 3.6 months for the advanced phase Ph+ leukemia patients, as well as 48-month follow-up data from the ongoing Study AP24534-10-201 (PACE). The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and to align the annexes with the latest QRD template v.10.<br><br>An updated RMP version 14.1 was provided as part of the application in order to:<br>- include the 48-month follow up data from the phase 2 study (PACE);<br>- address the commitments made in the framework of the PSUR 4 assessment.<br>In addition, the MAH took the opportunity to update the RMP to include two additional potential risks that have been identified in the post-marketing setting:<br>- posterior reversible encephalopathy syndrome (PRES), for which data were included in the | |

PSUR 5 (PSUSA/00010128/201512);
- class effect of hepatitis B reactivation (EPITT ref. No. 18405 - SDA 013 and EMEA/H/C/002695/IA/TBC)."
Request for Supplementary Information adopted on 10.11.2016, 21.07.2016.

**Imbruvica - ibrutinib - EMEA/H/C/003791/II/0027/G, Orphan**
MAH: Janssen-Cilag International NV,
Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams, "1. C.I.4 - Update of sections 4.8 in order to include Stevens-Johnson Syndrome (SJS) and Onychoclasis as post-marketing adverse drug reactions (ADRs).
In addition the applicant has taken the opportunity to make minor editorial amendments to the SmPC, including an editorial amendment to section 4.8 to mark the existing ADR terms of tumor lysis syndrome (added in variation EMEA/H/C/003791/II/0004), erythema, angioedema, and urticaria (added in variation EMEA/H/C/003791/0008/G) with an "a" referring to the existing ADR table footnote that indicates that they originated from spontaneous post-marketing reports.

2. C.I.4 – Update of section 4.4 to include Hypertension as one of the risk factors for atrial fibrillation/flutter.

The Package Leaflet is updated accordingly.
Updated version 6.2 of the RMP has been submitted."
Request for Supplementary Information adopted on 10.11.2016.

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

**Jakavi - ruxolitinib - EMEA/H/C/002464/II/0031**

MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, “Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information for melofibrosis following the completion of two 5-year follow up studies INCB 18424-351 and INC424A2352, thereby addressing one of the outstanding Obligations in Annex II.”
Request for Supplementary Information adopted on 13.10.2016.

**Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0027/G**

MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, “C.I.4 (Type II): Submission of the final study report for the study TDM4997g/BO25734 (TH3RESA tudy) to address the safety concerns in Left Ventricular Dysfunction and Safety in Elderly patients. The RMP and Annex II.D are updated.
C.I.11.z (Type IB): To update the RMP following the submission of the third annual report of study H4621g.

The MAH takes the opportunity to implement the following administrative changes to the RMP:
- Inclusion of standard post-authorization data based on PSUR number 4 (reporting period from 22 February 2015 to 21 February 2016).
- Change of Herceptin picture in the Kadcyla Educational Material to align the picture with the recently approved version of the Herceptin vial label and carton.”

**Kaletra - lopinavir / ritonavir - EMEA/H/C/000368/II/0160**

MAH: AbbVie Ltd., Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard, “Update of sections 4.2 and 5.1 of the SmPC in order to update information following analysis of the published 48-week study results for “A Kaletra ONCE daily randomised Trial of the pharmacokinetics, safety and efficacy of twice-daily versus once-daily lopinavir/ritonavir tablets dosed by weight as part of combination antiretroviral therapy in HIV-1–infected children”(PENTA 18/KONCERT) in fulfilment of a Post Authorisation Measure MEA (Additional PhV activity in the Risk Management Plan).

In addition, the MAH takes the opportunity to remove the Missing Information safety concern of Limited Information of the Kaletra 100 mg/25 mg film-coated tablets in the paediatric population as part of the submitted RMP version 8."

**Lyxumia - lixisenatide - EMEA/H/C/002445/II/0020**

MAH: Sanofi-Aventis Groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Submission of the final clinical study report for study EFC12382, a randomized double-blind, placebo-controlled, 2 arm parallel group, multicentre study with a 24-week treatment period to assess the efficacy and safety of lixisenatide in patients with T2DM insufficiently controlled with basal insulin or without metformin, in order to fulfil MEA 004. In addition the MAH took the opportunity to update the RMP (version 4.0) accordingly."

**Opdivo - nivolumab - EMEA/H/C/003985/II/0018**

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update the safety information for toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), myositis, myocarditis and rhabdomyolysis based on findings from routine pharmacovigilance activities. The Package Leaflet is updated accordingly.
In addition, the RMP is updated to version 4.5 to reflect this new safety information."
Request for Supplementary Information adopted on 10.11.2016, 13.10.2016.

**Orfadin - nitisinone - EMEA/H/C/000555/II/0057**

MAH: Swedish Orphan Biovitrum International AB, Rapporteur: Luca Pani, PRAC Rapporteur: Carmela Macchiarulo, "Update of sections 4.2 and 5.1 of the SmPC in order to amend the dosing frequency further to the results of a clinical pharmacology study NTBC-003.
The Package Leaflet is updated accordingly."
Request for Supplementary Information adopted on 15.09.2016.

**Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0031/G**

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

**Prolia - denosumab - EMEA/H/C/001120/II/0057**

MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.6 of the SmPC in order to delete references to the Pregnancy and Lactation Surveillance programs. The Package Leaflet is updated accordingly.

The RMP has been revised to remove all references to the Pregnancy and Lactation Program.

In addition, the Marketing authorisation holder took the opportunity to make minor editorial updates to the SmPC and Package Leaflet."
Request for Supplementary Information adopted on 13.10.2016.

**Prolia - denosumab - EMEA/H/C/001120/II/0062**

MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the product information (SmPC sections 4.4, 4.8 and PL sections 3 and 4) as well as the Risk Management Plan (RMP) to update the safety information and reflect the multiple vertebral fractures (MVF) following discontinuation of Prolia treatement as a new important risk. This variation follows a concluded analysis of osteoporosis-related fracture data in subjects who discontinued investigational product and remained on study in either the Prolia phase 3 pivotal fracture study (Study 20030216) or its study extension (Study 20060289) to better understand the incidence of fracture following treatment discontinuation. The results of this analysis conclude that multiple vertebral fractures may occur following discontinuation of Prolia

treatment, particularly in patients with a history of vertebral fracture.
In addition, the applicant took the opportunity to update the PI in line with the QRD template latest version, amend the PI previous version typographical errors from previous version, and implement minor changes in the Package leaflet local representatives."

**Prolia - denosumab - EMEA/H/C/001120/II/0063**

MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the SmPC section 5.1 to provide information on the clinical study data experience in patients in treatment transition from an oral Bisphosphonate to desunomab, information resulting from the assessment on data of study report 20110153 and a discussion on the issue of long term antiresorptive treatment, in particular when long-term bisphosphonate treatment is followed by denosumab."

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

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard, "Scope C.I.4
Update of section 4.6 of the SmPC in order to update the safety information on lactation to indicate that atazanavir has been detected in human milk. The Package Leaflet and the RMP are updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.

Scope C.I.11.b
This type II variation aims to update the RMP in order to add "IRIS" and "angioedema" to Important Identified Risks and to update the epidemiology/exposure sections. The MAH also took the opportunity to make some reformatting changes to align the RMP with the current approved EMA template."

**Senshio - ospemifene - EMEA/H/C/002780/II/0012/G**

MAH: Shionogi Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Julie Williams, "-Update of section 4.5 of the SmPC in order to add the CYP3A4 in the drug interaction studies as a result of the submission of study

E1508I0242. The following post authorisation measure is fulfilled:
PAM 8: The Applicant is requested to investigate the CYP induction potential of ospemifene at clinically relevant intestinal concentrations to exclude potential CYP3A4 induction in the intestine. No CYP induction is expected for ospemifene and M-1 at clinically relevant systemic concentrations.

-Update of section 5.2 of the SmPC in order to update the elimination section of the SmPC as a result of the submission of study E1508I0242 to fulfil the following post authorisation measures:
PAM 13: The applicant committed to evaluate and the conversion of the Z-enantiomer of ospemifene to its E-enantiomer post marketing.
PAM 14: The applicant committed to evaluate the metabolism and excretion of ospemifene and its metabolites using the commercial ospemifene 60 mg under fed conditions in a postauthorization study.

-Update of section 5.2 of the SmPC in order to update the distribution section as a result of the submission of study OSP-PF-046-N and OSP-PF-047-N to fulfil the following post authorisation measures:
PAM 6: The in vitro plasma protein binding data of M-1 in the non-clinical species will be provided post-authorisation for interspecies comparison between non-clinical species and humans. However the protocol should be adapted; the Applicant is requested to investigate a concentration range, e.g. 50 to 200 ng/mL for M1.
PAM 7: The blood-to-plasma ratio data for ospemifene in monkey and rat and the blood-to plasma ratio for M-1 in rat, monkey and human will be provided post-authorisation.
However the protocol should be adapted; the Applicant is requested to investigate a concentration range, e.g. 500 to 1200 ng/mL for ospemifene and 50 to 200 ng/mL for M 1.

-Update of section 5.2 of the SmPC in order to update the biotransformation section as a result of the submission of study OSP-PF-041-N to fulfil the following post authorisation measure:
PAM 9: The Applicant will provide BSEP transporter studies post-marketing.

As a consequence, an updated RMP version 1.2

is provided accordingly."
Request for Supplementary Information adopted on 10.11.2016.
Clockstop extension of 2 months requested to respond to RSI, responses expected 04.01.2017. For adoption.

**Soliris - eculizumab - EMEA/H/C/000791/II/0086/G, Orphan**

MAH: Alexion Europe SAS, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Eva A. Segovia, "Type II (C.I.4): Update of section 4.8 of the SmPC with the ADR frequencies to reflect overall exposure to eculizumab in clinical trials. The Package Leaflet (section 4) is updated accordingly.
Type II (C.I.3.b): update of section 4.4 of the SmPC with warning and precautions on meningococcal vaccination timing as recommended by PRAC. The Package Leaflet (sections 2 and 3) Annex II.D and the RMP (ver. 13) are updated accordingly.
In addition, the MAH took the opportunity of this RMP update to implement the PRAC recommendation suggesting to remove the off label use from the missing information, to provide the exposure data from PSUR 13 and to update the epidemiology sections with more complete and recent scientific literature data.
Moreover, the MAH took the opportunity of this submission to add editorial changes and to bring the PI in line with the latest QRD template."
Request for Supplementary Information adopted on 15.09.2016.

**Stivarga - regorafenib - EMEA/H/C/002573/II/0019**

MAH: Bayer Pharma AG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "The Marketing authorisation holder (MAH) took the opportunity to update Annex II to remove condition relating to the ceased COAST trial (15983).
In addition, section 5.1 of the SmPC has been updated in order to remove the information on KRAS mutation status and regorafenib efficacy."
Request for Supplementary Information adopted on 10.11.2016.

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

MAH: AstraZeneca AB, Rapporteur: Aranzazu

Sancho-Lopez, PRAC Rapporteur: Sabine Straus, “Update of SmPC sections 4.2, 4.4, 4.8, 5.1 and 5.2 based on the results from study D5160C00003 (AURA3) and the updated CSRs for studies D5160C00001 (AURAex) and D5160C00002 (AURA2). The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make editorial changes in the SmPC and Package Leaflet. The application included an updated RMP version 6.0.

The provision of the CSR from study AURA3 addresses the Specific Obligation for Tagrisso and hence the MAH requests the conversion from a Conditional Marketing Authorisation to a Marketing Authorisation not subject to Specific Obligations.”

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

MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, “Submission of the final CSR from the clinical drug-drug interaction study CAMN107A2132. An updated RMP version 17 was included as part of the application.”

**Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0035**

MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, “To update section 4.8 (Undesirable effects) of the SmPC under the sub-heading 'Tabulated summary of adverse reactions', to include 'liver function abnormalities' as an adverse event, observed in the post-marketing setting, and under the sub-heading 'Hepatic transaminases' to clarify events not observed in placebo-controlled studies. The package leaflet has been updated accordingly (section 4 under heading 'Possible side effects'). The MAH has also taken the opportunity to make minor administrative changes in the package leaflet and to review and update the status timelines of clinical and nonclinical study reports in the Risk Management Plan (v8).”

**Torisel - temsirolimus - EMEA/H/C/000799/II/0064, Orphan**

MAH: Pfizer Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, “Update of section 4.5 of the SmPC in order to

| | |
|---|---|
| add drug-drug interaction information based upon the PK analysis of Study 3066K1-148-US and supportive literature. The Package Leaflet is updated accordingly." | |
| **Translarna - ataluren - EMEA/H/C/002720/II/0016/G, Orphan**<br>MAH: PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus, "Update of section 4.4 to remove precautions for use relating to the co-administration of ataluren with substrates or inducers of UGT1A9 and section 4.5 of the SmPC to remove statements relating to the potential effect of co-administration of ataluren with inducers or substrates of UGT1A9 and to add results from studies PTC124-GD-026-HV and PTC124-GD-027-HV (MEA 011 and MEA 012). The Package Leaflet is updated accordingly.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the SmPC. Moreover, the updated RMP version 4.2 has been submitted."<br>Request for Supplementary Information adopted on 10.11.2016, 15.09.2016, 23.06.2016, 28.04.2016, 28.01.2016. | |
| **Translarna - ataluren - EMEA/H/C/002720/II/0020, Orphan**<br>MAH: PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus, "Update of sections 4.4, 4.8, 5.1 and 5.3 of the SmPC in order to reflect the results from the submitted study TC124-GD-020-DMD object of the specific obligation (SOB 001) for the conditional marketing authorisation. The Package Leaflet and the RMP are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some minor editorial changes throughout the Product information."<br>Opinion adopted on 23.11.2016.<br>Request for Supplementary Information adopted on 13.10.2016, 21.07.2016, 23.06.2016, 01.04.2016.<br>SAG meeting held on 29.09.2016, 16.06.2016. | Positive Opinion adopted by consensus on 23.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Xgeva - denosumab - EMEA/H/C/002173/II/0046**<br>MAH: Amgen Europe B.V., Rapporteur: Kristina | |

Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Update of section 4.6 of the SmPC in order to delete references to the Pregnancy and Lactation Surveillance programs. The Package Leaflet is updated accordingly.

The RMP has been revised to remove all references to the Pregnancy and Lactation Program.

In addition, the Marketing authorisation holder took the opportunity to make minor editorial updates to the SmPC and Package Leaflet.” Request for Supplementary Information adopted on 13.10.2016.

**Zelboraf - vemurafenib - EMEA/H/C/002409/II/0037**

MAH: Roche Registration Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, “Update of section 4.5 of the SmPC in order to include information on Drug-drug interaction with rifampicin.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the RMP and to request modification of MEA 011 part 2 “Study GO29475: Two-part steady-state interaction study with and rifampin (3YP3A4 inducer). Furthermore the MAH is requesting change of due dates for category 3 final study reports for studies GO29475 (MEA011), MO25515 (MEA006) and GP28492 (MEA010). The MAH is also including request for deletion from the RMP of the study “Phase I dose-escalation with efficacy tail extension study of vemurafenib in pediatric patients with surgically incurable and unresectable Stage IIIC or Stage IV melanoma harboring BRAFV600 mutations (MEA 005)” to reflect the Paediatric Product Specific Waiver for treatment of melanoma as agreed with the PDCO on 24 April 2016.”

**WS0971**
**Jardiance- EMEA/H/C/002677/WS0971/0022**
**Synjardy- EMEA/H/C/003770/WS0971/0021**

MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Dolores Montero Corominas, “Submission of the final clinical report for study 1245.28 (4-year data) 'A phase

III randomised, double-blind, active controlled parallel group efficacy and safety study of BI 10773 compared to glimepiride administered orally during 104 weeks with a 104-week extension period in patients with type 2 diabetes mellitus and insufficient glycaemic control despite metformin treatment' ."
Request for Supplementary Information adopted on 15.09.2016.

---

**WS1026**
**Rasilez-EMEA/H/C/000780/WS1026/0110**
**Rasilez HCT-EMEA/H/C/000964/WS1026/0080**
MAH: Novartis Europharm Ltd, Lead Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur: Carmela Macchiarulo, "Update of section 5.1 of the SmPC in order to reflect the results of study SPP100F2301 (ATMOSPHERE) a multicenter, randomized, doubleblind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (NYHA Class II - IV).

The RMP (v 13) has also been updated to reflect the study results."

---

### B.5.4. PRAC assessed procedures

---

PRAC Led
**ATryn - antithrombin alfa - EMEA/H/C/000587/II/0027**
MAH: GTC Biotherapeutics UK Limited, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, , "Introduction of the first version of the RMP following request in 6th Annual Re-assessment EMEA/H/C/000587/S/0021 and second renewal EMEA/H/C/000587/R/0024"
Request for Supplementary Information adopted on 15.09.2016.

---

PRAC Led
**Eperzan - albiglutide - EMEA/H/C/002735/II/0028/G**
MAH: GlaxoSmithKline Trading Services, PRAC Rapporteur: Julie Williams, , "II: C.I.11.b - Submission of a revised RMP in order to introduce the additional risk minimisation

---

measures addressing the important potential risk of medication errors. Annex II of the Product Information is updated accordingly.

II: C.I.11.b – Update of the RMP to add a new category 3 study as an additional pharmacovigilance activity - Study 204879: A Randomized, Open-label, Active-Controlled, Parallel-Group, Exploratory Study on the Effects of Repeated Doses of Albiglutide compared to Exenatide on Gastric Myoelectrical Activity and Gastric Emptying in Subjects with Type 2 Diabetes Mellitus

II: C.I.11.b - Update of the RMP to add a new category 3 study as an additional pharmacovigilance activity – Study 201840 - An Exploratory Randomized, 2-Part, Single-blind, 2-Period Crossover Study Comparing the Effect of Albiglutide with Exenatide on Regional Brain Activity Related to Nausea in Healthy Volunteers

II: C.I.11.b – Update of the RMP to add a new category 3 study as an additional pharmacovigilance activity – Cross-sectional survey to assess the effectiveness of the proposed additional educational materials using Patient Connect"

PRAC Led

**Halaven - eribulin -**

**EMEA/H/C/002084/II/0033**

MAH: Eisai Europe Ltd., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, , "Update of the RMP version 4.2 following the revision of the protocol for a post-authorisation study to capture data on the frequency of resolution and time to resolution of eribulin-induced or aggravated peripheral neuropathy from a phase 3 study, E7389-A001-303 (ACCRU) to an observational study, E7389-M044-504 (IRENE). The submission of the corresponding study report to the EMA / PRAC remains unchanged and is planned during 2019."

PRAC Led

**Inflectra - infliximab -**

**EMEA/H/C/002778/II/0047**

MAH: Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna, , "Update of the RMP (v 7.0) to merge the RMPs for Remsima and

Inflectra."

PRAC Led

**Lyxumia - lixisenatide -**

**EMEA/H/C/002445/II/0019**

MAH: Sanofi-Aventis Groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, , "Submission of the final clinical study report for a non-interventional PASS: a retrospective database study of GLP-1 receptor agonists and risk of acute pancreatitis, pancreatic cancer and thyroid cancer in particular medullary thyroid cancer, a category 3 study in order to fulfil MEA 007.2"

PRAC Led

**Pradaxa - dabigatran etexilate -**

**EMEA/H/C/000829/II/0093**

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Torbjorn Callreus, , "Submission of the final clinical trial report of study 1160.149 (Post-authorisation study to evaluate the effectiveness of the risk minimisation activities in the treatment of SPAF) in order to address part of follow-up measure FUM 026.
The risk management plan (RMP) (Ver. 31.6) has been updated with results from the clinical study 1160.149."
Request for Supplementary Information adopted on 15.09.2016, 26.05.2016.

PRAC Led

**Rapiscan - regadenoson -**

**EMEA/H/C/001176/II/0023**

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

PRAC Led

**Remsima - infliximab -**

**EMEA/H/C/002576/II/0039**

MAH: Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna, , "Update of the RMP (v 7.0) to merge the RMPs for Remsima and Inflectra."

PRAC Led

**Thymanax - agomelatine -**
**EMEA/H/C/000916/II/0031**

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

---

PRAC Led

**Thyrogen - thyrotropin alfa -**
**EMEA/H/C/000220/II/0088**

MAH: Genzyme Europe BV, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner, , “To transfer the RMP to the latest RMP template. As a consequence, gastrointestinal symptoms, constitutional symptoms, and injection site reactions have been downgraded to identified risks, not categorized as important and therefore have been deleted. In addition, “perceived lower TSH elevation after thyrotropin alfa administration” does not correspond to a safety risk for the patients treated with Thyrogen and was also deleted from the list of important potential risks.
Finally, study results and completion date of T4 study have been included and as a consequence, "Use of Thyrogen for remnant ablation in patients originally diagnosed with T4N0-1M0-1 thyroid cancer" was removed from the missing information section.
RMP version 9.0 is being submitted.”

---

PRAC Led

**Valdoxan - agomelatine -**
**EMEA/H/C/000915/II/0033**

MAH: Les Laboratoires Servier, Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Kristin Thorseng Kvande, , “Submission of the final study report for study CLE-20098-095: ‘HLA alleles as genetic risk factors for elevation of aminotransferase levels in patients treated with agomelatine’.
The product information and RMP are not impacted by this change.”

---

PRAC Led

---

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

---

PRAC Led
**WS0953**
**Jardiance-**
**EMEA/H/C/002677/WS0953/0019**
**Synjardy-**
**EMEA/H/C/003770/WS0953/0019**
MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Dolores Montero Corominas, , “To update the RMP with risk of DKA under the treatment of SGLT2 inhibitors for empagliflozin.
The PRAC had considered that “diabetic ketoacidosis with atypical presentation” should be included as important identified risk in the RMP for all SGLT2 inhibitors. In addition, ongoing and planned activities are being included in the RMP.”
Request for Supplementary Information adopted on 15.09.2016.

---

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

---

In addition, the due date for study 205052 is amended in the RMP version 8.2 submitted."

PRAC Led

**WS1063**

**Exviera-EMEA/H/C/003837/WS1063/0022**

**Viekirax-**

**EMEA/H/C/003839/WS1063/0027**

MAH: AbbVie Ltd., Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Dolores Montero Corominas, , "To update the RMP for Exviera and Viekirax with the following chnages:

1. The addition of information on cases of hepatic decompensation observed in patients with Child-Pugh B hepatic impairment, and the revision of the SmPC to change the dose recommendation of these patients to "not recommended", as well as the addition of statements recommending the monitoring of hepatic function in these patients as approved on 25 January 2016 ( (Ref: EMEA/H/C/WS/0873).

2. Addition of a reference to nine drug-drug interaction studies as approved on 28 April 2016 (Ref: EMEA/H/C/WS0896/G).

3. Reference to the completion of rat 2 year carcinogenicity studies on dasabuvir (Exviera) and ombitasvir (Viekirax) as approved on 24 September 2015 (Ref: EMEA/H/C/003837/II/0006 and EMEA/H/C/003839/II/0004).

4. Update of section 4.2 of SmPC for Virkirax to recommend a decrease in treatment duration of 12 weeks in GT4 cirrhotic patients, with a consequential change to sections 4.4 and 5.1 as approved on 18 August 2016 (Ref: EMEA/H/C/003839/II/0022/G).

5. Removal of the nonclinical PAMS 1-3 in the initial RMP, (Ref: EMEA/H/C/03837/MEA/003, EMEA/H/C/038397/MEA/002, EMEA/H/C/03839/MEA/003)."

### B.5.5. CHMP-CAT assessed procedures

### B.5.6. CHMP-PRAC-CAT assessed procedures

### B.5.7. PRAC assessed ATMP procedures

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

| | |
|---|---|
| **WS0989**<br>**M-M-RVAXPRO-EMEA/H/C/000604/WS0989/0077**<br>**ProQuad-EMEA/H/C/000622/WS0989/0111**<br>MAH: Sanofi Pasteur MSD SNC, Lead Rapporteur: Jan Mueller-Berghaus | Weekly start timetable. |
| **WS1007**<br>**Ambirix-EMEA/H/C/000426/WS1007/0081**<br>**Fendrix-EMEA/H/C/000550/WS1007/0056**<br>**Infanrix hexa-EMEA/H/C/000296/WS1007/0209**<br>**Twinrix Adult-EMEA/H/C/000112/WS1007/0115**<br>**Twinrix Paediatric-EMEA/H/C/000129/WS1007/0116**<br>MAH: GlaxoSmithKline Biologicals, Lead Rapporteur: Bart Van der Schueren, | Weekly start timetable. |
| **WS1016/G**<br>**Aclasta-EMEA/H/C/000595/WS1016/0067/G**<br>**Zometa-EMEA/H/C/000336/WS1016/0076/G**<br>MAH: Novartis Europharm Ltd, Lead Rapporteur: Sinan B. Sarac | Weekly start timetable. |
| **WS1018**<br>**Helixate NexGen-EMEA/H/C/000276/WS1018/0179**<br>**KOGENATE Bayer-EMEA/H/C/000275/WS1018/0186**<br>MAH: Bayer Pharma AG, Duplicate, Duplicate of KOGENATE Bayer, Lead Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 24.11.2016.<br>Request for Supplementary Information adopted on 29.09.2016. | Positive Opinion adopted by consensus on 24.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1021**<br>**Genvoya-EMEA/H/C/004042/WS1021/0018**<br>**Stribild-EMEA/H/C/002574/WS1021/0070**<br>**Vitekta-EMEA/H/C/002577/WS1021/0025** | Positive Opinion adopted by consensus on 17.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

| | |
|---|---|
| MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings<br>Opinion adopted on 17.11.2016. | |
| **WS1024**<br>**Humalog-**<br>**EMEA/H/C/000088/WS1024/0147**<br>**Liprolog-**<br>**EMEA/H/C/000393/WS1024/0111**<br>MAH: Eli Lilly Nederland B.V., Informed Consent of Humalog, Lead Rapporteur: Robert James Hemmings<br>Request for Supplementary Information adopted on 20.10.2016. | Weekly start timetable. |
| **WS1027**<br>**Genvoya-**<br>**EMEA/H/C/004042/WS1027/0019**<br>**Stribild-EMEA/H/C/002574/WS1027/0071**<br>**Tybost-EMEA/H/C/002572/WS1027/0030**<br>MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings<br>Request for Supplementary Information adopted on 17.11.2016. | Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable. |
| **WS1042/G**<br>**Tivicay-**<br>**EMEA/H/C/002753/WS1042/0024/G**<br>**Triumeq-**<br>**EMEA/H/C/002754/WS1042/0033/G**<br>MAH: ViiV Healthcare UK Limited, Lead Rapporteur: Filip Josephson<br>Opinion adopted on 24.11.2016. | Positive Opinion adopted by consensus on 24.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1052**<br>**Entresto-**<br>**EMEA/H/C/004062/WS1052/0009**<br>**Neparvis-**<br>**EMEA/H/C/004343/WS1052/0007**<br>MAH: Novartis Europharm Ltd, Lead Rapporteur: Johann Lodewijk Hillege | |
| **WS1064**<br>**Comtess-**<br>**EMEA/H/C/000170/WS1064/0054**<br>**Entacapone Orion-**<br>**EMEA/H/C/002440/WS1064/0013**<br>MAH: Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola | |

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

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

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

## B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

### 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

**Ceplene - histamine dihydrochloride -**
**EMEA/H/C/000796/S/0030, Orphan**
MAH: Meda AB, Rapporteur: David Lyons, PRAC Rapporteur: Almath Spooner

**Kolbam - cholic acid -**
**EMEA/H/C/002081/S/0020, Orphan**
MAH: Retrophin Europe Ltd, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Rafe Suvarna

**Vyndaqel - tafamidis -**
**EMEA/H/C/002294/S/0036, Orphan**
MAH: Pfizer Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard

**Xagrid - anagrelide -**
**EMEA/H/C/000480/S/0077, Orphan**
MAH: Shire Pharmaceutical Contracts Ltd., Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard

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

**Darzalex - daratumumab - EMEA/H/C/004077/R/0003, Orphan**
MAH: Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Ana Sofia Diniz Martins,

**NovoThirteen - catridecacog - EMEA/H/C/002284/R/0020**
MAH: Novo Nordisk A/S, Rapporteur: Joseph Emmerich, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Claire Ferard

**Pandemic influenza vaccine H5N1 MedImmune - pandemic influenza vaccine (H5N1) (live attenuated, nasal) - EMEA/H/C/003963/R/0003**
MAH: MedImmune LLC, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jan Neuhauser

**Zoledronic acid Mylan - zoledronic acid - EMEA/H/C/002482/R/0013**
MAH: MYLAN S.A.S, Generic, Generic of Zometa, Rapporteur: Milena Stain, PRAC Rapporteur: Doris Stenver

**Zoledronic acid Teva - zoledronic acid - EMEA/H/C/002439/R/0018**
MAH: Teva B.V., Generic, Generic of Zometa, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

**Zoledronic acid Teva Pharma - zoledronic acid - EMEA/H/C/002437/R/0014**
MAH: Teva B.V., Generic, Generic of Aclasta, Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver

### B.6.6. VARIATIONS – START OF THE PROCEDURE

**Timetables for adoption** provided that the validation has been completed.

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

**RoActemra - tocilizumab - EMEA/H/C/000955/II/0066**
MAH: Roche Registration Limited, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Extension of indication to include an indication in adult patients for the treatment

of giant cell arteritis for the subcutaneous formulation of RoActemra. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated to reflect information relevant to this indication. The Package Leaflet is updated in accordance."

### B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

**HBVAXPRO - hepatitis B vaccine (rDNA) - EMEA/H/C/000373/II/0055**
MAH: Sanofi Pasteur MSD SNC, Rapporteur: Jan Mueller-Berghaus

**Lantus - insulin glargine - EMEA/H/C/000284/II/0107/G**
MAH: Sanofi-aventis Deutschland GmbH, Rapporteur: Johann Lodewijk Hillege

**Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0062**
MAH: Pfizer Limited, Rapporteur: Greg Markey

**Orencia - abatacept - EMEA/H/C/000701/II/0106/G**
MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola

**Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0111**
MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

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

**GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0136**
MAH: Merck Serono Europe Limited, Rapporteur: Nithyanandan Nagercoil, "Update of the SmPC sections 4.4 and 4.8 to revise the frequency of thromboembolic events from 'very rare' to 'rare'. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.0."

**Simponi - golimumab - EMEA/H/C/000992/II/0072**
MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Update of section 4.4 of the

SmPC in order to include reports of Merkel cell carcinoma in patients treated with TNF blocking agents including Simponi. The frequency of this ADR has been reclassified from “not known” to “rare”. Package Leaflet is updated accordingly.”

**Zeffix - lamivudine -**
**EMEA/H/C/000242/II/0068**
MAH: Glaxo Group Ltd, Duplicate, Duplicate of Epivir, Rapporteur: Joseph Emmerich, “Update of sections 4.4 and 4.6 of the SmPC to reflect pregnancy clinical outcome data from the Antiretroviral Pregnancy Registry (APR). In addition, an introductory paragraph for pregnancy has been added to section 4.6 of the SmPC in line with Epivir (lamivudine for Human Immunodeficiency Virus Indication) (variation II/84).”

**WS1077/G**
**Aluvia-**
**EMEA/H/W/000764/WS1077/0101/G**
**Kaletra-**
**EMEA/H/C/000368/WS1077/0163/G**
**Norvir-**
**EMEA/H/C/000127/WS1077/0143/G**
MAH: AbbVie Ltd., Lead Rapporteur: Joseph Emmerich, “Update of sections 4.3 and 4.5 of the SmPC in order to add information regarding the interaction of lopinavir/ritonavir and ritonavir with lurasidone and ranolazine. In addition, sections 4.4 and 4.5 of the SmPC are updated to add information regarding the interaction with injectable triamcinolone. The Labelling is updated accordingly.”

### B.6.10. CHMP-PRAC assessed procedures

**Levemir - insulin detemir -**
**EMEA/H/C/000528/II/0084**
MAH: Novo Nordisk A/S, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Doris Stenver, “Submission of the summary analysis report on the incidence of neoplasms with the combination of liraglutide and insulin detemir from the cardiovascular outcome trial for Victoza®, trial EX2211-3748 (LEADER®). As a consequence the following important potential risk “Potential risk of malignant neoplasms following combination treatment with insulin detemir + liraglutide + metformin” is deleted

from the updated RMP version 18."

**Saxenda - liraglutide -**
**EMEA/H/C/003780/II/0011**
MAH: Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Based on submission of the LEADER clinical study results (EX2211-3748: liraglutide effect on and action in diabetes, evaluation of cardiovascular outcome results), changes to sections 4.4, and 5.1 of the SmPC are being proposed in order to update the safety information and include a description of the clinical study outcomes. The Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement minor editorial changes throughout the product information.

The LEADER study was included in the liraglutide RMP as a required pharmacovigilance activity (category 3) to specifically address the important potential risk of cardiovascular disorders in patients with Type 2 Diabetes Mellitus. Updates to the liraglutide RMP based on the study results are also proposed: this variation application fulfils two post-approval commitments in relation to the cardiovascular outcomes trial (MEA 002), as well as to provide additional information on the breast cancer cases found in LEADER (MEA 005). RMP Version 27 was submitted with the application. These liraglutide RMP modifications are in line with the proposed updates to the Saxenda Product Information described above."

### B.6.11. PRAC assessed procedures

PRAC Led
**Mimpara - cinacalcet -**
**EMEA/H/C/000570/II/0056**
MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report for Study 20090686, a study designed to determine the efficacy of cinacalcet compared with vitamin D therapy for management of secondary HPT (hyperparathyroidism) in haemodialysis subjects.

This variation fulfils LEG 031."

PRAC Led
**Zaltrap - aflibercept -**
**EMEA/H/C/002532/II/0034**
MAH: Sanofi-Aventis Groupe, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of the final results of the Drug Utilisation Study monitoring the use of Zaltrap in cancer patients including potential off-label use and evaluating the potential for intravitreal use. This fulfils the post authorisation commitment MEA 03."

PRAC Led
**WS1088**
**Eucreas-**
**EMEA/H/C/000807/WS1088/0057**
**Galvus-EMEA/H/C/000771/WS1088/0048**
**Icandra-**
**EMEA/H/C/001050/WS1088/0058**
**Jalra-EMEA/H/C/001048/WS1088/0048**
**Xiliarx-EMEA/H/C/001051/WS1088/0047**
**Zomarist-**
**EMEA/H/C/001049/WS1088/0058**
MAH: Novartis Europharm Ltd, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Kristina Dunder, "Following the outcome of an Article 31 referral procedure for metformin and metformin-containing products (Procedure EMEA/H/A-31/1432), the Applicant was requested toupdate the Risk Management Plan (RMP) for galvus, Jalra, Xiliarx, Eucreas, Icandra and Zomarist to implement a targeted questionnaire for cases of lactic acidosis."

### B.6.12. CHMP-CAT assessed procedures

### B.6.13. CHMP-PRAC-CAT assessed procedures

### B.6.14. PRAC assessed ATMP procedures

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

**WS1090/G**
**OFEV-**
**EMEA/H/C/003821/WS1090/0012/G**
**Vargatef-**

**EMEA/H/C/002569/WS1090/0014/G**
MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Sinan B. Sarac

**WS1093**
**Genvoya-**
**EMEA/H/C/004042/WS1093/0025**
**Stribild-EMEA/H/C/002574/WS1093/0076**
**Tybost-EMEA/H/C/002572/WS1093/0033**
MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings

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

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

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

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

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

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

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

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

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

## E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

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

**E.1. PMF Certification Dossiers:**

**E.1.1. Annual Update**

**E.1.2. Variations:**

**E.1.3. Initial PMF Certification:**

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

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

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

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

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

**G. ANNEX G**

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

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

**Qualification of Biomarkers:**

**HTA:**

**G.2. Ongoing procedures**

**G.3. PRIME**

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

**G.3.1. List of procedures concluding at 12-15 December 2016 CHMP plenary:**

**G.3.2. List of procedures starting in November 2016 for January 2017 CHMP adoption of outcomes**

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