



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

07 November 2016
EMA/CHMP/682760/2016
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP) Draft agenda for the meeting on 07-10 November 2016

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

07 November 2016, 13:00 – 19:30, room 2A

08 November 2016, 08:30 – 19:30, room 2A

09 November 2016, 08:30 – 19:30, room 2A

10 November 2016, 08:30 – 16:00, room 2A

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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



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1. Introduction

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

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 07-10 November 2016. See November 2016 CHMP minutes (to be published post December 2016 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 07-10 November 2016

1.3. Adoption of the minutes

CHMP minutes for 10-13 October 2016.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. - pegfilgrastim - EMEA/H/C/004342

treatment of neutropenia

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday 09 November 2016 at time 11:00

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

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

treatment of neutropenia

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday 09 November 2016 at time 11:00

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

2.1.3. insulin aspart - EMEA/H/C/004046

treatment of diabetes mellitus in adults

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday 09 November 2016 at time 14:00

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

BWP report

2.1.4. [aceneuramic acid - Orphan - EMEA/H/C/004176](#)

Ultragenyx UK Limited; treatment of Hereditary Inclusion Body Myopathy (HIBM)

Scope: Oral explanation

Action: Oral explanation to be held on Tuesday 08 November 2016 at time 14:00

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

2.2. [Re-examination procedure oral explanations](#)

2.3. [Post-authorisation procedure oral explanations](#)

2.3.1. [Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0020 & EMEA/H/C/002720/R/0022](#)

MAH: PTC Therapeutics International Limited,

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

Scope: Oral explanation to be held on Tuesday 08 November 2016 at time 16:00

Type II variation

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

Oral explanation was held on 11 October 2016. Request for Supplementary Information adopted on 21.07.2016, 01.04.2016.

Renewal of Marketing Authorisation

Action: For adoption

Participation of patients' representatives

See 9.1.2

2.4. Referral procedure oral explanations

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. lonoctocog alfa - EMEA/H/C/004075

treatment of haemophilia A

Scope: Opinion

Action: For adoption

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

BWP report

3.1.2. - darunavir - EMEA/H/C/004068

treatment of HIV-1

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 15.09.2016, 26.05.2016. List of Questions adopted on 17.12.2015.

3.1.3. - brodalumab - EMEA/H/C/003959

moderate to severe plaque psoriasis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 01.04.2016.

BWP report

3.1.4. - insulin glargine - EMEA/H/C/004101

treatment of diabetes mellitus

Scope: Opinion

Action: For adoption

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

BWP report

3.1.5. - teriparatide - EMEA/H/C/004368

treatment of osteoporosis

Scope: Opinion

Action: For adoption

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

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

treatment of type 2 diabetes mellitus

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 13.10.2016. List of Questions adopted on 21.07.2016.

BWP report

3.1.7. - tadalafil - EMEA/H/C/004297

treatment of pulmonary arterial hypertension (PAH)

Scope: Opinion

Action: For adoption

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

3.1.8. - teriparatide - EMEA/H/C/003916

treatment of osteoporosis

Scope: Opinion

Action: For adoption

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

BWP report

3.1.9. tenofovir alafenamide - EMEA/H/C/004169

chronic hepatitis B in adults

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 23.06.2016.

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

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

Scope: Opinion

Action: For adoption

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

BWP report

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

3.2.1. - anamorelin - EMEA/H/C/003847

treatment of anorexia, cachexia or unintended weight loss in adult patients with non-small cell lung cancer (NSCLC)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 25.02.2016.

3.2.2. - daptomycin - EMEA/H/C/004310

treatment of complicated skin and soft-tissue infections

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.06.2016.

3.2.3. - sodium zirconium cyclosilicate - EMEA/H/C/004029

for the treatment of hyperkalaemia

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 28.04.2016.

3.2.4. - methotrexate - EMEA/H/C/003756

treatment of rheumatological and dermatological diseases

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.07.2015.

3.2.5. - pentosan polysulfate sodium - Orphan - EMEA/H/C/004246

bene-Arzneimittel GmbH; treatment of Interstitial Cystitis

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.06.2016.

3.2.6. - rolapitant - EMEA/H/C/004196

prevention of nausea and vomiting

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.07.2016.

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

3.3.1. - cladribine - EMEA/H/C/004230

treatment of highly active relapsing-remitting multiple sclerosis (MS)

Scope: Day 120 list of questions

Action: For adoption

3.3.2. - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/004250

treatment of HIV-1 infection

Scope: Day 120 list of questions

Action: For adoption

3.3.3. - sarilumab - EMEA/H/C/004254

treatment of active rheumatoid arthritis

Scope: Day 120 list of questions

Action: For adoption

BWP report

3.3.4. - etirinotecan pegol - EMEA/H/C/003874

Accelerated assessment

treatment of breast cancer with brain metastases

Scope: Day 120 list of questions

Action: For adoption

3.3.5. - edoxaban - EMEA/H/C/004339

prevention of stroke; embolism and treatment of venous thromboembolism

Scope: Opinion

Action: For adoption

3.3.6. adalimumab - EMEA/H/C/004279

treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

Scope: Day 120 list of questions

Action: For adoption

BWP report

3.3.7. telotristat ethyl - Orphan - EMEA/H/C/003937

Ipsen Pharma; treatment of carcinoid syndrome

Scope: Day 120 list of questions

Action: For adoption

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

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

GMP-Orphan SA; Wilson's disease

Scope: Response from PKWP on CHMP questions

Action: For adoption

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

3.4.2. eryaspase - Orphan - EMEA/H/C/004055

ERYTECH Pharma S.A.; treatment of leukaemia

Scope: Request for an extension to the clock stop to respond to the Day 180 List of Outstanding Issues adopted on 15.09.2016.

Action: For adoption

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

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

treatment of vulvovaginal atrophy

Scope: Request for an extension to the clock stop to respond to the Day 180 List of Outstanding Issues adopted on 13.10.2016.

Action: For adoption

List of Outstanding Issues adopted on 13.10.2016. List of Questions adopted on 26.05.2016.

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**

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. **Ruconest - conestat alfa - EMEA/H/C/001223/X/0034**

Pharming Group N.V

Rapporteur: Nithyanandan Nagercoil

Scope: "Addition of a new pharmaceutical form "powder and solvent for solution for injection" with self-administration kit."

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**

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

4.3.1. **Nexium Control - esomeprazole - EMEA/H/C/002618/X/0016**

Pfizer Consumer Healthcare Ltd

Rapporteur: Romaldas Mačiulaitis, Co-Rapporteur: Robert James Hemmings, PRAC
Rapporteur: Simona Kudeliene

Scope: "Extension application to introduce a new pharmaceutical form (Gastro-resistant capsule, hard)"

Action: For adoption

4.3.2. **Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/X/0047**

Merck Serono Europe Limited

Rapporteur: Nithyanandan Nagercoil

Scope: "Extension application to introduce a new pharmaceutical form (solution for injection)

associated with 3 strengths of (300 IU + 150 IU)/ 0.48 ml, (450 IU + 225 IU)/ 0.72 ml and (900 IU + 450 IU)/ 1.44 ml.”

Action: For adoption

4.3.3. **Revestive - teduglutide - Orphan - EMEA/H/C/002345/X/0029**

Shire Pharmaceuticals Ireland Ltd

Rapporteur: Sinan B. Sarac

Scope: “Extension application to add a new strength of 1.25mg (paediatric formulation).”

Action: For adoption

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

4.4.1. **Xtandi - enzalutamide - EMEA/H/C/002639/X/0029**

Astellas Pharma Europe B.V.

Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Eva A. Segovia

Scope: “To add new pharmaceutical form and strengths (film-coated tablets 40 mg and 80 mg) to the currently approved presentations for Xtandi.” Request for clock stop extension to respond to the List of questions adopted on 21.07.2016.

Action: For adoption

List of questions adopted on 21.07.2016

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

5.1.2. [Arzerra - ofatumumab - Orphan - EMEA/H/C/001131/II/0045/G](#)

Novartis Europharm Ltd

Rapporteur: Hanne Lomholt Larsen, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Doris Stenver

Scope: "Extension of indication to include the combination of Arzerra with fludarabine and cyclophosphamide or in combination with bendamustine for the treatment of adult patients with relapsed CLL.

As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2, 6.6 and 9 of the SmPC are updated. The Package Leaflet and the RMP (v.13) are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 23.06.2016.

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

5.1.4. [Caprelsa - vandetanib - EMEA/H/C/002315/II/0016](#)

Genzyme Europe BV

Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard

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

Further, the MAH requested one additional year of market protection for a new indication.

Action: For adoption

Request for Supplementary Information adopted on 13.10.2016, 23.06.2016, 01.04.2016, 19.11.2015.

5.1.5. [Humira - adalimumab - EMEA/H/C/000481/II/0154](#)

AbbVie Ltd.

Rapporteur: Kristina Dunder

Scope: "Extension of Indication to include adolescents from 12 years of age for the Humira hidradenitis suppurativa indication. As a consequence, sections 4.1, 4.2, 5.1 and 5.2, of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 21.07.2016.

5.1.6. [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

5.1.7. [Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0049](#)

Pfizer Limited

Rapporteur: Greg Markey, Co-Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Rafe Suvarna

Scope: "Extension of Indication to include a wider paediatric population starting from 6 weeks of age for Nimenrix. As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and the RMP are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016, 28.04.2016.

5.1.8. [Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0131](#)

Gilead Sciences International Ltd

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

Scope: "Extension of Indication to include treatment of HIV-1 infected adolescents, with NRTI resistance or toxicities precluding the use of first line agents, aged 12 to < 18 years for Truvada.

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 and the Risk Management plan (v.13) are updated in accordance."

Action: For adoption

5.1.9. [Vimpat - lacosamide - EMEA/H/C/000863/II/0060/G](#)

UCB Pharma S.A.

Rapporteur: Filip Josephson, Co-Rapporteur: Luca Pani, PRAC Rapporteur: Qun-Ying Yue

Scope: "C.I.6.a - Extension of Indication to add a new indication as monotherapy in the treatment of partial-onset seizures. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly.

In addition, the applicant took the opportunity to update the PI in line with the latest QRD template."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016, 28.04.2016.

5.1.10. [Vimpat - lacosamide - EMEA/H/C/000863/II/0065/G](#)

UCB Pharma S.A.

Rapporteur: Filip Josephson, Co-Rapporteur: Luca Pani, PRAC Rapporteur: Qun-Ying Yue

Scope: "This is a group of variations including extension of Indication to include monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in children from 4 to less than 16 years old with epilepsy. For the treatment initiation pack it is proposed to extend only adjunctive treatment to adolescents weighting more than 50 kg (not suitable for monotherapy and children and adolescents weighting less than 50 kg). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring Annex IIIA in line with the latest QRD template version 10 and to introduce combined SmPC for film coated tablets. Moreover, updated RMP version 12 has been submitted.

Furthermore, only for syrup presentation, in addition sections 6.3 and 6.5 of the SmPC are updated."

Action: For adoption

5.1.11. [Tafinlar Mekinist - dabrafenib trametinib - EMEA/H/C/WS0996](#)

Novartis Europharm Ltd

Lead Rapporteur: Filip Josephson, Lead Co-Rapporteur: Paula Boudewina van Hennik, PRAC

Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include the combination treatment with trametinib and dabrafenib of adult patients with advanced non-small cell lung cancer (NSCLC) with a BRAF V600 mutation. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the Mekinist and Tafinlar SmPC are updated. The Package Leaflet and RMP are updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to align the SmPCs of Mekinist and Tafinlar. Furthermore, the Product Information is brought in line with the latest QRD template version 10."

Action: For adoption

- 5.2. Update on on-going Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008**
- 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. - Ciclosporin – Orphan - EMEA/H/C/04411**

Santen Oy; Treatment of severe vernal keratoconjunctivitis in children and adolescents aged 4 to 18 years old

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

Note: Products requesting eligibility under PRIME scheme are listed in the Annex G.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

Note: Recommendation for PRIME are listed in the Annex G.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Helicobacter Test INFAL - 13C-urea - EMEA/H/C/000140/II/0019

MAH: INFAL GmbH

Re-examination Rapporteur: TBC,

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

Letter from the applicant dated 25 October 2016 requesting the re-examination of the CHMP Opinion adopted 13 October 2016, appointment of Re-examination Rapporteur

Action: For adoption

Opinion adopted on 13.10.2016. Request for Supplementary Information adopted on 15.09.2016, 21.07.2016, 23.06.2016, 01.04.2016, 28.01.2016.

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

MAH: PTC Therapeutics International Limited,

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

Scope: Oral explanation to be held on 08 November 2016 at time 16:00

Type II variation

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

Oral explanation was held on 11 October 2016. Request for Supplementary Information adopted on 21.07.2016, 01.04.2016.

Renewal of Marketing Authorisation

Action: For adoption

Participation of patients' representatives

See 2.3.1

9.1.3. Tyverb - lapatinib - EMEA/H/C/000795/II/0048/G

Novartis Europharm Ltd

Rapporteur: Filip Josephson, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Rapporteur: Ulla Wändel Liminga

Scope: "1) C.I.4 (type II): Update of sections 4.4, 4.8, and 5.1 of the SmPC in order to add a warning on QTc prolongation and update safety information following the submission of study report EGF114271 (A Phase IV placebo controlled single sequence crossover study to evaluate the effect of repeat oral doses of lapatinib on cardiac repolarization in patients with advanced cancer). The Package Leaflet is updated accordingly.

2) C.I.4 (type II): Update of section 4.8 of the SmPC in order to further elaborate on the undesirable effect 'serious cutaneous reactions' based on the review of the Novartis safety database. The Package Leaflet is updated accordingly"

Action: For adoption

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)

CHMP Rapporteurs: Rapporteur: Filip Josephson, Co-Rapporteur: Robert James Hemmings (Daklinza), Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege (Exviera, Viekirax), Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Daniela Melchiorri (Olysio); Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs (Sovaldi), Rapporteur: Filip Josephson, Co-Rapporteur: Joseph Emmerich (Harvoni)

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

Scope: Minutes of the SAG HIV/Viral diseases meeting

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 information

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

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

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

Scope: LoOI/Opinion

Prescription status of desloratadine-containing products

Action: For adoption

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

10.4.1. Paracomb 500mg/150mg film coated tablets - Paracetamol/Ibuprofen 500 mg/150 mg Paracetamol and Ibuprofen - EMEA/H/1447

Vale Pharmaceutical Ltd

RMS: UK, CMS: AT, BE, DE, FR, HR, IE, LU, NL, PT, ES

Decentralised Procedure numbers: UK/H/6034-5/001/DC, UK/H/6176/001/DC

Scope: Start of procedure and appointment of Rapporteurs

Disagreement regarding justification for a fixed dose combination, the demonstration of an additional benefit and of an acceptable safety profile

Action: For adoption

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

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

Janssen-Cilag Group of companies and associated companies

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

Scope: Amended timetable

Action: For adoption

List of outstanding issues adopted 13.10.2016, 01.04.2016, 26.03.2015. List of Questions adopted on 26.06.2014

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

Janssen-Cilag Group of companies and associated companies

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

Scope: Amended timetable

Action: For adoption

List of outstanding issues adopted 13.10.2016, 01.04.2016, 26.03.2015. List of Questions adopted on 26.06.2014

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

10.6.1. Vancomycin containing products – (vancomycin) - EMEA/H/A-31/1440

Rapporteur: Concepcion Prieto-Yerro, Co-rapporteur: Alar Irs

Scope: LoOI/Opinion

Action: For adoption

Review of the benefit-risk balance following notification by the Spanish Agency of Medicines and Medical Devices of a referral under Article 31 of Directive 2001/83/EC.

Lists of Questions adopted on 21.07.2016, 01.04.2016.

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

Symbiopharm GmbH,

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

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

Letter from the MAH requesting an oral explanation in front of the CHMP.

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

November 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

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

13.4. Nanomedicines activities

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 5th Co-opted membership

Action: For adoption

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 24-27 October 2016

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 3-4 November 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 November 2016 PDCO

Action: For information

Report from the PDCO meeting held on 9-11 November 2016

Action: For information

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 3-4 November 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 7-9 November 2016

Action: For information

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

14.3.1. Scientific Advice Working Party (SAWP)

Chair: Robert J. Hemmings

Scope: Report from the SAWP meeting held on 24-27 October 2016. Table of conclusions

Action: For information

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

Scope: SA new initiative: Biosimilar Pilot

Action: For adoption

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

Action: For information

The letters of candidacy together with the CV of both member and alternate, as per the SAWP Mandate requirements [see Article 2(10)], should be sent, deadline 7 December 2016.

Scope: SAWP Chair election. The candidates should submit their brief résumés in support of their candidature, deadline 7 December 2016.

Action: For information

Scope: Scientific guidance on Post-Authorisation Efficacy Study (PAES)
(EMA/PDCO/CAT/CMDh/PRAC/CHMP/261500/2015)

Action: For adoption

14.3.2. Biosimilar Medicinal Product Working Party (BMWP)

Revision of the Guideline on non-clinical and clinical development of similar biological medicinal products containing low-molecular-weight-heparins
EMA/CHMP/BMWP/118264/2007 Rev. 1

Action: For adoption for 3-month public consultation

14.3.3. Biostatistics Working Party (BSWP)

Scope: Nomination of new core member following resignation of David Jonathan Wright
Nominations received:

- Current membership list

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

14.8. Planning and reporting

14.9. Others

15. Any other business

15.1. AOB topic

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

CHMP Rapporteur: Harald Enzmann

Scope: Updated guideline to be published for 3-month public consultation

Action: For adoption

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 *(section 5.3)*

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 Pharmacovigilance 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/



07 November 2016
EMA/CHMP/682759/2016

Annex to November 2016 CHMP Agenda

PRE SUBMISSION AND POST AUTHORISATIONS ISSUES

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A. PRE SUBMISSION ISSUES

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

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

Final Outcome of Rapporteurship allocation for
November 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

Atriance - nelarabine -

EMA/H/C/000752/S/0034, Orphan

MAH: Novartis Europharm Ltd, Rapporteur: Sinan

B. Sarac, PRAC Rapporteur: Torbjorn Callreus

IMVANEX - modified vaccinia Ankara virus -

EMA/H/C/002596/S/0022

MAH: Bavarian Nordic A/S, Rapporteur: Greg

Markey, PRAC Rapporteur: Rafe Suvarna

Lojuxta - lomitapide -

EMA/H/C/002578/S/0023

MAH: Aegerion Pharmaceuticals Limited,

Rapporteur: Johann Lodewijk Hillege, PRAC

Rapporteur: Menno van der Elst

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Bronchitol - mannitol -

EMA/H/C/001252/R/0028, Orphan

MAH: Pharmaxis Pharmaceuticals Limited,

Rapporteur: Nithyanandan Nagercoil,

Co-Rapporteur: Joseph Emmerich, PRAC

Rapporteur: Julie Williams

Capecitabine Accord - capecitabine -

EMA/H/C/002386/R/0021

MAH: Accord Healthcare Ltd, Generic, Generic of
Xeloda, Rapporteur: Filip Josephson, PRAC
Rapporteur: Martin Huber

**Capecitabine Teva - capecitabine -
EMA/H/C/002362/R/0025**

MAH: Teva B.V., Generic, Generic of Xeloda,
Rapporteur: Filip Josephson, PRAC Rapporteur:
Martin Huber

**Nimenrix - meningococcal group A, C, W135
and Y conjugate vaccine -
EMA/H/C/002226/R/0059**

MAH: Pfizer Limited, Rapporteur: Greg Markey,
Co-Rapporteur: Karsten Bruins Slot, PRAC
Rapporteur: Rafe Suvarna

**Riluzole Zentiva - riluzole -
EMA/H/C/002622/R/0021**

MAH: Aventis Pharma S.A., Rapporteur: Greg
Markey, Co-Rapporteur: Pierre Demolis, PRAC
Rapporteur: Julie Williams

**Sancuso - granisetron -
EMA/H/C/002296/R/0047**

MAH: Kyowa Kirin Limited, Rapporteur:
Romaldas Mačiulaitis, Co-Rapporteur: Bart Van
der Schueren, PRAC Rapporteur: Jolanta
Gulbinovic

**Vepacel - prepandemic influenza vaccine
(H5N1) (whole virion, inactivated, prepared
in cell culture) -**

EMA/H/C/002089/R/0015

MAH: Nanotherapeutics Bohumil Sro,
Rapporteur: Bart Van der Schueren,
Co-Rapporteur: Andrea Laslop, PRAC
Rapporteur: Jean-Michel Dogné

B.2.3. Renewals of Conditional Marketing Authorisations

**Caprelsa - vandetanib -
EMA/H/C/002315/R/0023**

MAH: Genzyme Europe BV, Rapporteur: Pierre
Demolis, PRAC Rapporteur: Claire Ferard

**Cometriq - cabozantinib -
EMA/H/C/002640/R/0022, Orphan**

MAH: Ipsen Pharma, Rapporteur: Paula
Boudewina van Hennik, PRAC Rapporteur:
Sabine Straus

**SIRTURO - bedaquiline -
EMA/H/C/002614/R/0017, Orphan**

MAH: Janssen-Cilag International N.V.,
Rapporteur: Filip Josephson, Co-Rapporteur:
Karsten Bruins Slot, PRAC Rapporteur: Qun-Ying
Yue

Translarna - ataluren -

See main part of agenda points 2.3.1 and 9.1.2.

EMA/H/C/002720/R/0022, Orphan

MAH: PTC Therapeutics International Limited,
Rapporteur: Johann Lodewijk Hillege, PRAC
Rapporteur: Sabine Straus
Request for Supplementary Information adopted
on 28.04.2016.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

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

EMA/H/C/PSUSA/00001353/201604

(febuxostat)

CAPS:

Adenuric (EMA/H/C/000777) (febuxostat),

MAH: Menarini International Operations
Luxembourg S.A., Rapporteur: Andrea Laslop,
PRAC Rapporteur: Jan Neuhauser, "21/04/2015 -
20/04/2016"

EMA/H/C/PSUSA/00010272/201603

(insulin degludec / liraglutide)

CAPS:

Xultophy (EMA/H/C/002647) (insulin degludec

/ liraglutide), MAH: Novo Nordisk A/S,
Rapporteur: Kristina Dunder, PRAC Rapporteur:
Menno van der Elst, "01 Oct 2015 - 31 March
2016"

B.4. EPARs / WPARs

Cystadrops - mercaptamine -

EMA/H/C/003769, Orphan

Applicant: Orphan Europe S.A.R.L., treatment of
cystinosis, Known active substance (Article 8(3)
of Directive No 2001/83/EC)

Emtricitabine/Tenofovir disoproxil Krka -

emtricitabine / tenofovir disoproxil -

EMA/H/C/004215

Applicant: KRKA, d.d., Novo mesto, treatment of
HIV-1 infection, Generic, Generic of Truvada,
Generic application (Article 10(1) of Directive No
2001/83/EC)

**Emtricitabine/Tenofovir disoproxil Mylan -
emtricitabine / tenofovir disoproxil -
EMA/H/C/004050**

Applicant: MYLAN S.A.S, treatment of HIV,
Generic, Generic of Truvada, Generic application
(Article 10(1) of Directive No 2001/83/EC)

**Ocaliva - obeticholic acid -
EMA/H/C/004093, Orphan**

Applicant: Intercept Pharma Ltd, treatment of
primary biliary cirrhosis, New active substance
(Article 8(3) of Directive No 2001/83/EC)

**Pemetrexed ditromethamine Hospira -
Pemetrexed Ditromethamine -
EMA/H/C/004306**

Applicant: Hospira UK Limited, treatment of
malignant pleural mesothelioma and non-small
cell lung cancer, Generic application (Article
10(1) of Directive No 2001/83/EC)

**Rekovelte - follitropin delta -
EMA/H/C/003994**

Applicant: Ferring Pharmaceuticals A/S, indicated
for controlled ovarian stimulation, New active
substance (Article 8(3) of Directive No
2001/83/EC)

**SomaKit TOC - edotreotide -
EMA/H/C/004140, Orphan**

Applicant: Advanced Accelerator Applications,
Diagnosis of gastro-entero-pancreatic
neuroendocrine tumours, Well-established use
application (Article 10a of Directive No
2001/83/EC)

**Tenofovir disoproxil Mylan - tenofovir
disoproxil - EMA/H/C/004049**

Applicant: MYLAN S.A.S, treatment of HIV-1
infection and hepatitis B infection, Generic,
Generic of Viread, Generic application (Article
10(1) of Directive No 2001/83/EC)

**Venclyxto - venetoclax -
EMA/H/C/004106, Orphan**

Applicant: AbbVie Ltd., treatment of adult
patients with chronic lymphocytic leukaemia
(CLL), 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

Empliciti - elotuzumab -**EMA/H/C/003967/II/0001/G**

MAH: Bristol-Myers Squibb Pharma EEIG,
Rapporteur: Paula Boudewina van Hennik
Request for Supplementary Information adopted
on 15.09.2016.

Esbriet - pirfenidone -**EMA/H/C/002154/II/0039, Orphan**

MAH: Roche Registration Limited, Rapporteur:
Greg Markey
Request for Supplementary Information adopted
on 27.10.2016.

Weekly start timetable. The Committee adopted
a Request for Supplementary information
together with a specific timetable.

Eylea - aflibercept -**EMA/H/C/002392/II/0028**

MAH: Bayer Pharma AG, Rapporteur: Pierre
Demolis
Request for Supplementary Information adopted
on 15.09.2016, 14.04.2016.

Weekly start timetable.

Flixabi - infliximab -**EMA/H/C/004020/II/0003**

MAH: Samsung Bioepis UK Limited (SBUK),
Rapporteur: Jan Mueller-Berghaus
Request for Supplementary Information adopted
on 29.09.2016.

Weekly start timetable.

**Foclivia - influenza virus surface antigens
(inactivated) of strain****A/Vietnam/1194/2004 (H5N1) -****EMA/H/C/001208/II/0023/G**

MAH: Novartis Vaccines Influenza Srl,
Rapporteur: Daniela Melchiorri

Weekly start timetable.

Hemoblast - thrombin -**EMA/H/D/002769/II/0001/G**

MAH: BSI Group, Rapporteur: Daniela Melchiorri,
Co-Rapporteur: Robert James Hemmings
Request for Supplementary Information adopted
on 15.09.2016, 26.05.2016.

Hizentra - human normal immunoglobulin -**EMA/H/C/002127/II/0070**

MAH: CSL Behring GmbH, Rapporteur: Jan
Mueller-Berghaus

Weekly start timetable.

<p>IDELVION - albutrepenonacog alfa - EMA/H/C/003955/II/0001/G, Orphan MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 15.09.2016.</p>	Weekly start timetable.
<p>Kalydeco - ivacaftor - EMA/H/C/002494/II/0046, Orphan MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Concepcion Prieto Yerro, Request for Supplementary Information adopted on 15.09.2016, 12.05.2016.</p>	Weekly start timetable.
<p>Kanuma - sebelipase alfa - EMA/H/C/004004/II/0006/G, Orphan MAH: Alexion Europe SAS, Rapporteur: Bart Van der Schueren</p>	
<p>Memantine LEK - memantine - EMA/H/C/002630/II/0007/G MAH: Pharmathen S.A., Generic, Generic of Ebixa, Rapporteur: Martina Weise Request for Supplementary Information adopted on 15.09.2016.</p>	Weekly start timetable.
<p>NexoBrid - bromelain enriched proteolytic enzyme preparation from Ananas comosus - EMA/H/C/002246/II/0027/G, Orphan MAH: MediWound Germany GmbH, Rapporteur: Harald Enzmann Request for Supplementary Information adopted on 29.09.2016.</p>	Weekly start timetable.
<p>NovoSeven - eptacog alfa / eptacog alfa (activated) - EMA/H/C/000074/II/0093 MAH: Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 15.09.2016.</p>	Weekly start timetable.
<p>Orencia - abatacept - EMA/H/C/000701/II/0103/G MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 06.10.2016.</p>	Weekly start timetable.
<p>Pheburane - sodium phenylbutyrate - EMA/H/C/002500/II/0014 MAH: Lucane Pharma, Rapporteur: David Lyons</p>	Weekly start timetable.
<p>Prialt - ziconotide - EMA/H/C/000551/II/0050</p>	

MAH: Eisai Ltd, Rapporteur: Koenraad Norga
Request for Supplementary Information adopted
on 15.09.2016.

Rapilysin - reteplase - Weekly start timetable. The Committee adopted
EMA/H/C/000105/II/0062 a Request for Supplementary information
MAH: Actavis Group PTC ehf, Rapporteur: Harald together with a specific timetable.
Enzmann
Request for Supplementary Information adopted
on 20.10.2016.

Ratiograstim - filgrastim - Weekly start timetable.
EMA/H/C/000825/II/0052
MAH: ratiopharm GmbH, Rapporteur: Outi
Mäki-Ikola

Senshio - ospemifene - Weekly start timetable.
EMA/H/C/002780/II/0010
MAH: Shionogi Limited, Rapporteur: Paula
Boudewina van Hennik
Request for Supplementary Information adopted
on 04.08.2016.

Stelara - ustekinumab - Weekly start timetable. The Committee adopted
EMA/H/C/000958/II/0051/G a Request for Supplementary information
MAH: Janssen-Cilag International N.V., together with a specific timetable.
Rapporteur: Greg Markey
Request for Supplementary Information adopted
on 20.10.2016.

Surgiflo Haemostatic Matrix Kit -Ferrosan - Weekly start timetable.
human thrombin -
EMA/H/D/002301/II/0015/G
MAH: Presafe Denmark A/S, Rapporteur: Jan
Mueller-Berghaus
Request for Supplementary Information adopted
on 15.09.2016.

Tevagrastim - filgrastim - Weekly start timetable.
EMA/H/C/000827/II/0061
MAH: TEVA GmbH, Duplicate, Duplicate of
Biograstim, Rapporteur: Outi Mäki-Ikola

Vimizim - elosulfase alfa - Weekly start timetable.
EMA/H/C/002779/II/0015, Orphan
MAH: BioMarin Europe Ltd, Rapporteur: Johann
Lodewijk Hillege,

Voncento - human coagulation factor VIII / Weekly start timetable.
human von willebrand factor -
EMA/H/C/002493/II/0021/G
MAH: CSL Behring GmbH, Rapporteur: Paula
Boudewina van Hennik

Request for Supplementary Information adopted on 15.09.2016.

Zaltrap - aflibercept -

Weekly start timetable.

EMA/H/C/002532/II/0025/G

MAH: Sanofi-Aventis Groupe, Rapporteur: Filip Josephson

Request for Supplementary Information adopted on 04.08.2016, 19.05.2016.

WS0950

Weekly start timetable.

Leganto-EMA/H/C/002380/WS0950/0021

Neupro-EMA/H/C/000626/WS0950/0071

MAH: UCB Manufacturing Ireland Ltd., Lead

Rapporteur: Bruno Sepodes

Request for Supplementary Information adopted on 04.08.2016.

WS0954

Filgrastim

Hexal-EMA/H/C/000918/WS0954/0033

Zarzio-EMA/H/C/000917/WS0954/0034

MAH: SANDOZ GmbH, Lead Rapporteur: Greg Markey

Hexacima-EMA/H/C/002702/WS0964/0051/G

Hexaxim-EMA/H/W/002495/WS0964/0058/G

Hexyon-EMA/H/C/002796/WS0964/0054/G

MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus

Request for Supplementary Information adopted on 15.09.2016.

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

Ambirix - hepatitis A (inactivated) and hepatitis B(rDNA) (HAB) vaccine (adsorbed) - EMA/H/C/000426/II/0077

MAH: GSK Biologicals SA, Rapporteur: Robert James Hemmings, "Update of section 6.6 of the SmPC in order to update the re-suspension instructions, based on user testing results. The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 9.1, to include some corrections and to align the wording across combined hepatitis A and hepatitis B

vaccines (i.e. Twinrix Adult, Twinrix Paediatric and Ambirix).”
Request for Supplementary Information adopted on 21.07.2016.

Bydureon - exenatide -

Weekly start timetable.

EMA/H/C/002020/II/0038

MAH: AstraZeneca AB, Rapporteur: Kristina Dunder, , “Submission of the final results of study 2993LAR-105 to examine the effects of exenatide once weekly on glucose control and safety in subjects with type II diabetes mellitus managed with diet modification and exercise and/or oral anti-diabetic medications.”
Request for Supplementary Information adopted on 15.09.2016.

Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMA/H/C/000721/II/0080

MAH: GSK Biologicals SA, Rapporteur: Bart Van der Schueren, “Submission of final Study report for study HPV-060. Study HPV-060 is an extension of the study HPV-014 (EXT 014 Y5-10). Study HPV-014 with 4 years post-vaccination data was submitted as a commitment in November 2009 (EMA/H/C/721/FU2 20.5)
The purpose of this variation is to fulfil the Post-Authorization Measure (PAM) (MEA-082) with the long term follow up (10 years post-vaccination) data from study HPV-060. GlaxoSmithKline Biologicals (GSK Biologicals) considers that there is no need to change the SmPC at this stage.”
Request for Supplementary Information adopted on 15.09.2016.

Effentora - fentanyl -

EMA/H/C/000833/II/0044

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.
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”

Fycompa - perampanel -

Positive Opinion adopted by consensus on

EMA/H/C/002434/II/0030

20.10.2016. The Icelandic and Norwegian CHMP

MAH: Eisai Europe Ltd., Rapporteur: Robert James Hemmings, "Update of sections 5.1 and 5.2 of the SmPC to reflect the results from study E2007-G000-235."

Opinion adopted on 20.10.2016.

Request for Supplementary Information adopted on 28.07.2016, 16.06.2016.

Members were in agreement with the CHMP recommendation.

Giotrif - afatinib -

EMA/H/C/002280/II/0020

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to add the results of the primary analysis of the LUX-Lung 7 study, a global, randomised, open-label, Phase IIb trial that prospectively compared the efficacy and safety of afatinib to the reversible EGFR tyrosine kinase inhibitor (TKI) gefitinib for the first-line treatment of patients with EGFR mutation positive NSCLC."

Request for Supplementary Information adopted on 15.09.2016.

Weekly start timetable.

Glivec - imatinib -

EMA/H/C/000406/II/0106

MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, "Update of section 4.8 of the SmPC to add the new ADR 'musculoskeletal pain upon treatment discontinuation' with a frequency of very common. The Package Leaflet has been updated accordingly. Further, the MAH has taken the opportunity to merge the SmPCs of the different strengths of the same pharmaceutical form i.e. 50 mg and 100 mg hard capsules, and 100 mg and 400 mg film coated tablets, respectively, and to align the annexes with version 10 of the QRD template."

Weekly start timetable.

Harvoni - sofosbuvir / ledipasvir -

EMA/H/C/003850/II/0035

MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to add emerging clinical data available from studies SOLAR-1 and SOLAR-2."

Invirase - saquinavir -

EMA/H/C/000113/II/0120

MAH: Roche Registration Limited, Rapporteur: Milena Stain, "Update of sections 4.4 and 4.5 of the SmPC in order to add a warning regarding the co-administration of Invirase/ritonavir with cobicistat and other pharmaco-enhancers and to

Weekly start timetable.

correct an error in the fold increase in exposure of maraviroc in the interaction table. The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10, to correct minor typographical errors and to amend Annex A."

Request for Supplementary Information adopted on 15.09.2016.

Invokana - canagliflozin -

EMA/H/C/002649/II/0020

MAH: Janssen-Cilag International N.V.,

Rapporteur: Martina Weise, PRAC Rapporteur:

Valerie Strassmann, "Submission of a revise RMP in order to update the following information:

Article 20 procedure on DKA including updates to reflect discussions with PRAC on renal impairment/renal failure; hypersensitivity and DKA, update the information related to revisions to proposed dates for completion of clinical studies and to include additional studies requested as part of the Article 20 DKA review procedure."

Request for Supplementary Information adopted on 15.09.2016.

Jevtana - cabazitaxel -

EMA/H/C/002018/II/0035

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."

Kentera - oxybutynin -

Weekly start timetable.

EMA/H/C/000532/II/0041

MAH: Nicobrand Limited, Rapporteur: Bart Van der Schueren, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to implement the adopted wording from the final PRAC recommendation on the signal on psychiatric disorders. The Marketing authorisation holder (MAH) also proposes additional update of section 4.8 related to the adverse reactions known to be associated with anticholinergic therapy. The Package Leaflet is updated accordingly.

In addition, the MAH took the opportunity to update the SmPC (Annex I), Labelling (Annexe

IIIA) and Package leaflet (Annexe IIIB) in accordance with EDQM standards terms.”
Request for Supplementary Information adopted on 15.09.2016.

Lynparza - olaparib -

EMA/H/C/003726/II/0009/G, Orphan

MAH: AstraZeneca AB, Rapporteur: Pierre Demolis, PRAC Rapporteur: Carmela Macchiarulo“Update section 4.2 and section 5.2 of the SmPC to include information related to hepatic impairment based on the results of study D0816C00005 (MEA 005).

In addition section 4.4 and section 4.5 is updated to include information related to moderate CYP3A inducers based on the addendum to the Simcyp modelling report.

The package leaflet and risk management plan has also been updated to reflect the study results.

The requested group of variations proposed amendments to the Summary of Product Characteristics, Labelling and Package Leaflet and to the Risk Management Plan (RMP).”

Request for Supplementary Information adopted on 15.09.2016.

Nucala - mepolizumab -

EMA/H/C/003860/II/0005

MAH: GlaxoSmithKline Trading Services, Rapporteur: Nithyanandan Nagercoil, “Update of sections 4.4 and 4.8 of the SmPC in order to include “anaphylaxis” as an adverse reaction. The Package Leaflet is updated accordingly. Minor amendments to section 6.6 of the SmPC and to the Instructions for use and handling, reconstitution, and administration for the HCP are also introduced. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI (Product Information) in line with the latest QRD template version 10.”

Opinion adopted on 27.10.2016.

Positive Opinion adopted by consensus on 27.10.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Portrazza - necitumumab -

EMA/H/C/003886/II/0002

MAH: Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, “Submission of study I4X-MC-JFCL, investigating necitumumab in combination with paclitaxel and carboplatin chemotherapy versus paclitaxel and carboplatin chemotherapy alone as

the first line therapy in patients with Stage IV metastatic squamous non-small cell lung cancer (NSCLC). This variation leads to amendments of the Product Information: sections 4.4 and 5.1 of the SmPC were updated to reflect the findings of the study submitted. The update is being reflected in the PL."

Request for Supplementary Information adopted on 21.07.2016.

**Rotarix - human rotavirus, live attenuated - Weekly start timetable.
EMA/H/C/000639/II/0089**

MAH: GlaxoSmithKline Biologicals S.A.,
Rapporteur: Bart Van der Schueren, "Update of section 5.1 to introduce effectiveness data following completion of ecological observational study EPI-ROTA-025 VE AU DB (114910) - An ecological study to assess impact of rotavirus vaccination on hospitalisations for rotavirus gastroenteritis (RV GE) in children <5 years of age in Australia.

In addition, the marketing authorisation holder took the opportunity to introduce clarifications in the SmPC."

Twinrix Adult - hepatitis A (inactivated) and hepatitis B(rDNA) (HAB) vaccine (adsorbed) - EMA/H/C/000112/II/0110

MAH: GSK Biologicals SA, Rapporteur: Robert James Hemmings, "Update of section 6.6 of the SmPC in order to update the re-suspension instructions based on user testing results. The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 9.1, to include some corrections, to align the wording across combined hepatitis A and B vaccines (i.e. Twinrix Adult, Twinrix Paediatric and Ambirix) and to combine the SmPC of the vial and pre-filled syringe presentations."

Request for Supplementary Information adopted on 21.07.2016.

Twinrix Paediatric - hepatitis A (inactivated) and hepatitis B(rDNA) (HAB) vaccine (adsorbed) -

EMA/H/C/000129/II/0111

MAH: GSK Biologicals SA, Duplicate, Duplicate of Twinrix Adult, Rapporteur: Robert James Hemmings, "Update of section 6.6 of the SmPC in order to update the re-suspension instructions

based on user testing results. The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 9.1, to include some corrections, to align the wording across combined hepatitis A and B vaccines (i.e. Twinrix Adult, Twinrix Paediatric and Ambirix) and to combine the SmPC of the vial and pre-filled syringe presentations."

Request for Supplementary Information adopted on 21.07.2016.

**Vokanamet - canagliflozin / metformin -
EMA/H/C/002656/II/0016**

MAH: Janssen-Cilag International N.V.,
Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, "Submission of a revise RMP in order to update the following information: Article 20 procedure on DKA including updates to reflect discussions with PRAC on renal impairment/renal failure; hypersensitivity and DKA, update the information related to revisions to proposed dates for completion of clinical studies and to include additional studies requested as part of the Article 20 DKA review procedure."

Request for Supplementary Information adopted on 15.09.2016.

Votrient - pazopanib -

Weekly start timetable.

EMA/H/C/001141/II/0039

MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, "Update of section 4.8 to add the adverse reaction Polycythaemia. This variation, based on cumulative review of all cases, is provided following the PRAC request on the signal assessment report EPITT no 18660. The Package Leaflet is updated accordingly."

Xeplion - paliperidone -

Weekly start timetable.

EMA/H/C/002105/II/0030

MAH: Janssen-Cilag International N.V.,
Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to update the safety information after assessment of study R092670-SCA-3004. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to Align the Product information of Xeplion with safety updates implemented for TREVICTA Product Information (for which XEPLION is the

reference medicinal product) through variation EMEA/H/C/004066/X/0007/G.”
Request for Supplementary Information adopted on 15.09.2016.

Zoely - norgestrol / estradiol - Weekly start timetable.

EMEA/H/C/001213/II/0037

MAH: Teva B.V., Rapporteur: Joseph Emmerich, “Update of section 4.2 of the SmPC concerning reduced efficacy with regard to concomitant medications and section 4.5 of the SmPC concerning hepatic metabolism and HIV/HCV interactions. The Package Leaflet has been updated accordingly.”

Zoely - norgestrol / estradiol - Weekly start timetable.

EMEA/H/C/001213/II/0038

MAH: Teva B.V., Rapporteur: Joseph Emmerich, “Update of sections 4.4 and 4.5 of the SmPC concerning Hepatitis C and the risk of elevated ALT due to treatment with the HCV combination regimen ombitasvir/paritaprevir/ritonavir co-administered with ethinylestradiol-containing products. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and Package Leaflet.”

Zydelig - idelalisib - Weekly start timetable.

EMEA/H/C/003843/II/0025

MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, “Submission of the final report for a study of mechanisms of resistance to idelalisib in patients with chronic lymphocytic leukemia (CLL) in fulfilment of post-authorization measure (PAM) 013 for Zydelig.”

Request for Supplementary Information adopted on 15.09.2016.

WS0919

Exviera-EMEA/H/C/003837/WS0919/0015

Viekirax-EMEA/H/C/003839/WS0919/0015

MAH: AbbVie Ltd., Lead Rapporteur: Filip Josephson, “Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to reflect the findings of study M14-226 in patients with HCV infection and several renal impairment or End Stage Renal Disease.”

Request for Supplementary Information adopted on 15.09.2016, 01.04.2016.

WS0998

Weekly start timetable.

OFEV-EMEA/H/C/003821/WS0998/0011**Vargatef-EMEA/H/C/002569/WS0998/001****3**

MAH: Boehringer Ingelheim International GmbH,
Lead Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to include 'thrombocytopenia' as new ADR with a 'common' frequency for Vargated and an 'uncommon' frequency for Ofev. The Package Leaflet is updated accordingly.

In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor corrections to the English, Croatian and Slovak Annexes for Vargated and to the Slovak Annexes for Ofev and to bring the Product Information in line with the latest QRD template version 10."

WS1004

Weekly start timetable.

Ultibro**Breezhaler-EMEA/H/C/002679/WS1004/0****012****Ulunar****Breezhaler-EMEA/H/C/003875/WS1004/0****012****Xoterna****Breezhaler-EMEA/H/C/003755/WS1004/0****014**

MAH: Novartis Europharm Ltd, Lead Rapporteur: Hanne Lomholt Larsen, "Update of section 5.1 of the summary of product characteristics (SmPC) to reflect the final results of study CQVA149A2318 "A 52-week treatment, multi-center, randomised, double-blind, double dummy, parallel-group, active controlled study to compare the effect of QVA149 (indacaterol maleate/glycopyrronium bromide) with salmeterol/fluticasone (salm/flut) on the rate of exacerbations in subjects with moderate to very severe COPD".

In addition, the MAH took this opportunity to more accurately reflect the mean pre-dose values at week 64 from clinical study CQVA149A2304 report, included in the original marketing authorisation application."

Request for Supplementary Information adopted on 15.09.2016.

WS1010**Descovy-EMEA/H/C/004094/WS1010/000****6****Genvoya-EMEA/H/C/004042/WS1010/001**

7

Odefsey-EMEA/H/C/004156/WS1010/000

4

MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, "Update of section 5.2 of the SmPC in order to provide the final results from Study GS-US-320-1615 "A Phase 1, Open-Label, Parallel-Group, Single Dose Study to Evaluate the Pharmacokinetics of Tenofovir Alafenamide (TAF) in Subjects with Normal Hepatic Function and Subjects with Severe Hepatic Impairment".

In addition, the Worksharing applicant (WSA) took the opportunity to update section 4.2 of the SmPC for Descovy to allow dosing in patients with severe hepatic impairment.

The information from the CSR for Study GS-US-320-1615 does lead to the addition or deletion of a safety concern in the corresponding RMPs."

B.5.3. CHMP-PRAC assessed procedures

Aldara - imiquimod -

EMEA/H/C/000179/II/0067

MAH: Meda AB, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Rafe Suvarna, "Update of sections 4.2 and 5.1 of the SmPC in order to add data on the results of study X-03016-3284 (LEIDA 2) and a meta-analysis of X-03016-3271 and X-03016-3284. The RMP is updated (version 3)."

Request for Supplementary Information adopted on 15.09.2016, 26.05.2016.

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 15.09.2016.

EVARREST - human fibrinogen / human

thrombin - EMEA/H/C/002515/II/0027/G

MAH: Omrix Biopharmaceuticals N. V.,

Rapporteur: Jan Mueller-Berghaus, PRAC

Rapporteur: Brigitte Keller-Stanislawski "Group of variations consisting of:

- 1) Submission of the final results for study BIOS-13-005 updating the efficacy and safety information
- 2) Submission of the final results for study BIOS-13-004 updating the efficacy and safety information
- 3) Submission of the final results for study 400-12-002 updating the efficacy and safety information
- 4) Submission of the final results for study 400-12-005 updating the safety information
- 5) Update of section 5.1 of the SmPC to include further information on main existing efficacy studies

Sections 4.8, 5.1 of the SmPC are affected by this group of variations. In addition, the Product Information has been updated in accordance with the QRD template, version 10 and Guideline on core SmPC for plasma-derived fibrin/sealant/haemostatic products (EMA/CHMP/BPWP/598816/2010 rev.1). Section 4.2 has been updated regarding the paediatric information for children under the aged of 1 month, according to the EMA waiver. A revised RMP (version 3) is also introduced, including consequential and routine changes."

Exjade - deferasirox -**EMEA/H/C/000670/II/0052, Orphan**

MAH: Novartis Europharm Ltd, Rapporteur:

Pierre Demolis, Co-Rapporteur: Luca Pani, PRAC

Rapporteur: Claire Ferard, "Update of sections

4.4 and 5.1 of the SmPC to include final results of study ICL670F2201: 'a randomized, open-label, multicentre, two-arm phase II study to evaluate the safety of deferasirox film-coated tablet (FCT) formulation and deferasirox dispersable tablet (DT) formulation in patients with transfusion dependent thalassemia or myelodysplastic syndrome (MDS) at very low, low or intermediate risk requiring chelation therapy due to iron overload' and consequent warnings (in order to fulfil ANX 047). The MAH took the opportunity to update Annex II and the RMP (version 14) are updated accordingly."

Feraccru - iron -**EMA/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 15.09.2016.

Firdapse - amifampridine -**EMA/H/C/001032/II/0043, Orphan**

MAH: BioMarin Europe Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "Update of sections 4.4 and 5.3 of the SmPC respectively in order to delete the statements that amifampridine has not been fully tested in carcinogenicity models and to provide the findings from the carcinogenicity reports required for the completion of SOB 004.

The RMP (v.9) is proposed to be updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to request the removal of the requirement to complete carcinogenicity testing in an appropriate model in section E of the Annex II."

Request for Supplementary Information adopted on 15.09.2016.

Iclusig - ponatinib -**EMA/H/C/002695/II/0032/G, Orphan**

MAH: ARIAD Pharma 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.

An updated RMP version 14.1 was provided as part of the application in order to:

- include the 48-month follow up data from the phase 2 study (PACE);
- address the commitments made in the framework of the PSUR 4 assessment.

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:

- 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 21.07.2016.

Imbruvica - ibrutinib -

EMEA/H/C/003791/II/0025, Orphan

MAH: Janssen-Cilag International NV,
Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams, "Update of the SmPC section 4.4 to remove the warning and precaution regarding the effect of Ibrutinib on the QT interval and section 5.1 to provide additional information regarding the pharmacodynamic effect of Ibrutinib on QT/QTc intervals and cardiac electrophysiology. No changes to the Annex III Package Leaflet are proposed."

Request for Supplementary Information adopted on 15.09.2016.

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 Onychoclasia 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.”

**Jetrea - ocriplasmin -
EMA/H/C/002381/II/0026**

MAH: ThromboGenics NV, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, “Update of sections 4.4, 4.8 and 5.1 of the SmPC to reflect new long-term safety and efficacy data based on the final CSR for study TG-MV-014 in fulfilment of the post-authorisation measure MEA 002. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the annexes, to align the annexes with the latest QRD templates (v9.1 and 10) and to update the contact details of the local representative in Spain in the Package Leaflet. An updated RMP version 7 was included as part of the application.” Request for Supplementary Information adopted on 13.10.2016, 26.05.2016.

**Jevtana - cabazitaxel -
EMA/H/C/002018/II/0034**

MAH: Sanofi-Aventis Groupe, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, “Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to add information from completed study EFC11785 (Randomized, open-label multicenter study comparing cabazitaxel at 20 mg/m² and at 25 mg/m² every 3 weeks in combination with prednisone for the treatment of metastatic castration-resistant prostate cancer previously treated with a docetaxel-containing regimen). In addition, the MAH is proposing to modify the wording in section 4.1 of the indication from “hormone refractory” to “castration resistant” prostate cancer to reflect current terminology of the disease in the clinical practice. The RMP is updated accordingly and in accordance with the request from the latest PSUR procedure (EMA/C/H/002018/PSUSA/000476/201506)” Request for Supplementary Information adopted on 15.09.2016.

Kalydeco - ivacaftor -**EMA/H/C/002494/II/0049, Orphan**

MAH: Vertex Pharmaceuticals (Europe) Ltd.,
Rapporteur: Concepcion Prieto Yerro, PRAC
Rapporteur: Dolores Montero Corominas,
"Submission of the final Clinical Study Report (CSR) for Study VX11-770-109 (Study 109) to fulfil the RMP commitment to address the following safety concerns: hepatotoxicity, cataracts, cardiac arrhythmias, use in children between 2 to 5 years old, long-term safety. An updated RMP (v5.1 updated from v4.9) is included in this submission to include the final data from Study 109."

Request for Supplementary Information adopted on 15.09.2016.

Kyprolis - carfilzomib -**EMA/H/C/003790/II/0007/G, Orphan**

MAH: Amgen Europe B.V., Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Nikica Mirošević Skvrce "Update of sections 4.2 and 5.2 of the SmPC to revise the guidance on use in patients with renal and hepatic impairment with the submission of studies relating to renal impairment (CFZ001) and hepatic impairment (CFZ002).

In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make editorial changes to the Product information, which includes a correction of a typographical omission in section 4.4 to align the statement on sodium content with that in section 2 and the package leaflet by specifying levels given are per mL of reconstituted product.

The RMP has been updated accordingly."

Request for Supplementary Information adopted on 15.09.2016.

Levetiracetam Hospira - levetiracetam -**EMA/H/C/002783/II/0012**

MAH: Hospira UK Limited, Generic, Generic of Keppra, Rapporteur: Juris Pokrotnieks, PRAC Rapporteur: Laurence de Fays, "Update the product information (SmPC and PIL) for Levetiracetam in line with company core safety information (CSI) version 1.0.

A signal detection finding was included in the Levetiracetam CSI, to include an adverse effect Rhabdomyolysis & Blood creatine phosphokinase increased. Subsequently, the SmPC and PIL have been updated with this new information."

Request for Supplementary Information adopted on 15.09.2016.

**Odomzo - sonidegib -
EMA/H/C/002839/II/0005**

MAH: Novartis Europharm Ltd, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Julie Williams, "To submit the results from the pivotal registration study CLDE225A2201 and related analyses (correlative analysis of Gli1 data and molecular analysis in tumor material) with the aim to resolve two post-authorisation measures (PAES) listed in the Annex II.D of the Marketing Authorisation. Sections 4.8 and 5.1 of the SmPC and the Annex II are updated accordingly. Also the RMP is updated (version 4.0) to reflect the most recent 30-month data."

Request for Supplementary Information adopted on 13.10.2016.

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

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

In addition, the RMP is updated to version 4.5 to reflect this new safety information."

Request for Supplementary Information adopted on 13.10.2016.

**Senshio - ospemifene -
EMA/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 E150810242. 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."

**Sivextro - tedizolid phosphate -
EMA/H/C/002846/II/0009**

MAH: Merck Sharp & Dohme Limited,

Rapporteur: Bruno Sepodes, PRAC Rapporteur:

Dolores Montero Corominas, "Update of sections

4.4, 4.5 and 5.2 of the SmPC based on the

completed Drug-Drug Interaction study

MK-1986-004. The Package Leaflet has been

updated accordingly. In addition the MAH took the opportunity to implement editorial changes in the annexes and to update the annexes in line with the latest QRD template version 10.

The application included a revised RMP version 2.0 thereby removing the missing information for potential risks for drug-drug interactions mediated by CYP3A4, as well as:

- Addressing the identified risk for drug-drug interactions mediated via inhibition of Breast Cancer Resistance Protein (BCRP).
- Adding updates made to timelines for ongoing and planned studies for long term safety and Asian population experience."

Request for Supplementary Information adopted on 21.07.2016, 26.05.2016.

Stivarga - regorafenib -

EMA/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."

Tagrisso - osimertinib -

EMA/H/C/004124/II/0004

MAH: AstraZeneca AB, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Sabine Straus, "Update of section 5.2 of the SmPC to reflect the results of study 20 which was performed to assess the absolute bioavailability and to evaluate the PK parameters of Tagrisso in plasma following a single oral dose and a radio-labelled intravenous (IV) microdose of [14C] Tagrisso in healthy male subjects. In addition, the MAH took the opportunity to make a minor correction in SmPC section 6.5 and the Package Leaflet, where blister strips have been amended to blisters. Further, the MAH provided an updated RMP version 5.0 as part of the application."

Request for Supplementary Information adopted on 15.09.2016.

Translarna - ataluren -

EMA/H/C/002720/II/0016/G, Orphan

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. 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." Request for Supplementary Information adopted on 15.09.2016, 23.06.2016, 28.04.2016, 28.01.2016.

Translarna - ataluren -

See main part of agenda point 2.3.1 and 9.1.2.

EMA/H/C/002720/II/0020, Orphan

MAH: PTC Therapeutics International Limited,
Rapporteur: Johann Lodewijk Hillege, PRAC
Rapporteur: Sabine Straus, "Update of sections 4.4, 4.6, 4.7, 4.8, and 5.1 of the SmPC and Annex II in order to reflect the result from the submitted study TC124-GD-020-DMD object of SOB 001. The Package Leaflet and the RMP are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some minor editorial changes throughout the Product information." Request for Supplementary Information adopted on 13.10.2016, 21.07.2016, 23.06.2016, 01.04.2016.
SAG meeting held on 29.09.2016, 16.06.2016.

Translarna - ataluren -

EMA/H/C/002720/II/0026, Orphan

MAH: PTC Therapeutics International Limited,
Rapporteur: Johann Lodewijk Hillege, PRAC
Rapporteur: Sabine Straus, "Update of sections 4.4 and 4.5 of the SmPC to remove the interaction with inhibitors of breast cancer resistant protein (BCRP) based on the results of a drug-drug interaction study of the co-administration of ataluren and inhibitors of BCRP" Request for Supplementary Information adopted on 15.09.2016.

Tysabri - natalizumab -

EMA/H/C/000603/II/0095

MAH: Biogen Idec Ltd, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section sections 4.2, 4.3, 4.8, 5.1 and 5.2 of the SmPC based on the results of paediatric studies 101MS028 and 101MS328, in accordance with paediatric investigation plan (EMA-001095-PIP-12). An updated RMP version 21 was provided as part of the application." Request for Supplementary Information adopted on 15.09.2016, 23.06.2016.

**Tyverb - lapatinib -
EMA/H/C/000795/II/0048/G**

MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga"1) C.I.4 (type II): Update of sections 4.4, 4.8, and 5.1 of the SmPC in order to add a warning on QTc prolongation and update safety information following the submission of study report EGF114271 (A Phase IV placebo controlled single sequence crossover study to evaluate the effect of repeat oral doses of lapatinib on cardiac repolarization in patients with advanced cancer). The Package Leaflet is updated accordingly.
2) C.I.4 (type II): Update of section 4.8 of the SmPC in order to further elaborate on the undesirable effect 'serious cutaneous reactions' based on the review of the Novartis safety database. The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10. Moreover, the MAH took the opportunity to update Annex II to delete an Annex II condition which has been fulfilled with procedure ANX. 28.2.

The RMP (version 32) is updated accordingly to the scopes presented above and also to introduce template-related changes, study milestones updates, and to upgrade 'food effect' to an important identified risk (from procedure EMA/H/C/000795/II/0024)."

**Vectibix - panitumumab -
EMA/H/C/000741/II/0079**

MAH: Amgen Europe B.V., Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams, "Update of section 4.6 of the SmPC in order to remove the references to the Pregnancy Surveillance Program (PSP) and Lactation

Surveillance Programs (LSP). The Package Leaflet is updated accordingly.
The RMP was also submitted in order to remove references to PSP and LSP.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make further administrative updates to the RMP.”

**Vectibix - panitumumab -
EMA/H/C/000741/II/0080**

MAH: Amgen Europe B.V., Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams, “Update of Annex II in order to provide the results of biomarker analyses from the Vectibix clinical programme including Study 20080763 (according to Supplementary Statistical Analysis Plan dated 20 September 2013), Study 20070820 and Study 20060447. The data submitted are in fulfilment of Annex II obligation ANX017.
The Risk Management Plan (version 21.0) has been updated accordingly.
The requested variation proposed amendments to Annex II and the Risk Management Plan.”

**Voncento - human coagulation factor VIII /
human von willebrand factor -
EMA/H/C/002493/II/0017/G**

MAH: CSL Behring GmbH, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus
C.I.4 (type II): Update of section 4.8 of the SmPC in order to update the frequencies of undesirable effects to reflect the final clinical study data from study CSLCT-BIO-08-53 in haemophilia A paediatric patients. The Package Leaflet is updated accordingly. The submission of the final CSR CSLCT-BIO-08-53 also leads to changes to the RMP (ver. 6.1) in order update the Company Core Safety Information (CCSI).
C.I.11.z (type IB): Submission of a revised RMP in order to remove the commitment to conduct a post-marketing study for haemophilia A patients (CSLCT-BIO-12-78) for Voncento as consequence of new data from study CSLCT-BIO-08-53.
In addition, the Marketing authorisation holder (MAH) took the opportunity to combine different strengths in the SmPC and Package Leaflet.”
Request for Supplementary Information adopted on 01.04.2016, 19.11.2015.

Zykadia - ceritinib -**EMA/H/C/003819/II/0006/G**

MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Ulla Wandel Liminga“Update of section 4.5 of the SmPC based on the final results of the clinical pharmacology study LDK378A2113 and results of a sub-group evaluating the impact of gastric PH-elevating agents on the steady-state PK, efficacy, and safety of ceritinib in ALK-positive NSCLC patients. The provision of the final CSR for study CLDK378A2113 addresses the post-authorisation measure (PAM) MEA 003. In addition, the MAH is proposing a change to the due date for the provision of the final study report for study CLDK378A2110 (PAM, MEA 001). An updated RMP version 3.0 was included as part of the application.”

Request for Supplementary Information adopted on 21.07.2016, 26.05.2016.

WS0926**Jardiance-EMA/H/C/002677/WS0926/0017****Synjardy-EMA/H/C/003770/WS0926/0016**

MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Dolores Montero Corominas, “Update of sections 4.8 and 5.1 of the SmPC in order to include data from the study 1275.9. In addition, the Worksharing applicant (WSA) took the opportunity to remove optional sentence ‘Medicinal product subject to medical prescription.’ from Annex IIIA. Moreover, the updated RMP version 8.0 (for Jardiance) and version 6.0 (for Synjardy) have been submitted as part of this application.”

Request for Supplementary Information adopted on 21.07.2016.

WS0993**Adcirca-EMA/H/C/001021/WS0993/0025****Cialis-EMA/H/C/000436/WS0993/0085**

MAH: Eli Lilly Nederland B.V., Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, “Update of section 4.4 of the SmPC in order to add a new warning on the risk of non-arteritic anterior ischemic optic neuropathy (NAION) based on the final results of study H6D-MC- LVHQ (category 3 study). In addition the Worksharing applicant (WSA) took

the opportunity to update the RMP (version 8.0) accordingly.”

Request for Supplementary Information adopted on 15.09.2016.

WS1031

Anoro-EMEA/H/C/002751/WS1031/0013
Laventair-EMEA/H/C/003754/WS1031/0014

MAH: Glaxo Group Ltd, Lead Rapporteur:
Nithyanandan Nagercoil, Lead PRAC Rapporteur:
Carmela Macchiarulo, “Update of section 4.8 of the SmPC in order to add the adverse reactions “vision blurred”, “intraocular pressure increased” and “paradoxical bronchospasm” and to change the frequency of the adverse reaction “glaucoma” from “not known” to “rare”. The Package Leaflet is updated accordingly.

In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.

The risk management plan is submitted to reflect the changes proposed for the SmPC and also includes revision requested as part of the outcome of previous PSURs.”

B.5.4. PRAC assessed procedures

PRAC Led

Abilify - aripiprazole -
EMEA/H/C/000471/II/0122

MAH: Otsuka Pharmaceutical Europe Ltd,
Rapporteur: Bruno Sepodes, PRAC Rapporteur:
Leonor Chambel, , “Submission of the final Clinical Study Report of non-interventional, non-imposed PASS study 31-13-300 (“ABILIFY® for the Adolescent Bipolar I Mania Indication Tool Effectiveness Evaluation Survey”) to fulfil a post-authorisation measure (MEA 068.2). Annex II has been updated to delete additional risk minimisation measures based on the study results and to delete PASS study 31-13-300 included by mistake during variation IB/112/G. Moreover, the updated RMP version 10 has been submitted as part of this application.”

PRAC Led

Adempas - riociguat -
EMEA/H/C/002737/II/0014, Orphan

MAH: Bayer Pharma AG, PRAC Rapporteur: Julie Williams, , "Submission of a revised RMP in order to add Off-label use in patients with idiopathic pulmonary pneumonia, with or without pulmonary hypertension as an important identified risk."

PRAC Led

EXJADE - deferasirox -

EMA/H/C/000670/II/0050, Orphan

MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, , "Submission of the final study report from the additional pharmacovigilance activity in the RMP (category 3, MEA): study C1CL670A2301 "International sentinel site surveillance of patients with transfusional hemosiderosis treated with Exjade in actual practice setting". This submission also serves to comply with Article 46 submission of the Regulation (EC) No 1901/2203 on medicinal products for paediatric use." Request for Supplementary Information adopted on 21.07.2016.

PRAC Led

Humira - adalimumab -

EMA/H/C/000481/II/0159

MAH: AbbVie Ltd., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, , "Submission of study P06-134: "A Long-Term Non-Interventional Registry to Assess Safety and Effectiveness of Humira in Subjects with Moderately to Severely Active Crohn's Disease" in fulfilment fo MEA 056.9. The study includes also some paediatric patients and fulfils article 46 paediatric obligations."

PRAC Led

MULTAQ - dronedarone -

EMA/H/C/001043/II/0035

MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, , "To update the Risk Management Plan and Annex II.D (Conditions or restrictions with regard to the safe and effective use of the medicinal product) of the Marketing Authorization." Request for Supplementary Information adopted on 15.09.2016.

PRAC Led

Nevanac - nepafenac -

EMA/H/C/000818/II/0033

MAH: Alcon Laboratories (UK) Ltd, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, , "Submission of the final study Report for the Drug Utilisation Study, "Evaluation of the Use of Nepafenac in Selected European Populations" (category 3)-EU PAS register number ENCEPP/SDPP/5278 to quantify and describe off-label use of nepafenac in order to fulfil MEA12. This PAM was requested during EMEA/H/C/818/RMP/011." Request for Supplementary Information adopted on 21.07.2016.

PRAC Led

Trobalt - retigabine -

EMEA/H/C/001245/II/0045

MAH: Glaxo Group Ltd, PRAC Rapporteur: Doris Stenver, "Submission of a revised RMP (version 18) in order to remove a postauthorisation study (PASS) RTG116158, an open label study evaluating the effects of ezogabine/retigabine added to existing anti-epileptic drug(s) on urinary voiding function in subjects with partial onset seizures. In addition, routines change have also been introduced."

PRAC Led

Victrelis - boceprevir -

EMEA/H/C/002332/II/0039

MAH: Merck Sharp & Dohme Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard, , "Submission of the final report for the cat 3 Observational Post-Authorization Safety Study of Victrelis among Chronic Hepatitis C patients (P08518). An updated RMP version 10.0 is proposed accordingly." Request for Supplementary Information adopted on 15.09.2016.

PRAC Led

Zytiga - abiraterone -

EMEA/H/C/002321/II/0045

MAH: Janssen-Cilag International N.V., Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Eva A. Segovia, , "To update the RMP to modify the Planned dates for assessment in the Risk Minimisation Measures for all the Important Identified and Potential Risks as well as the Missing information."

PRAC Led

WS0968

Ebymect-EMEA/H/C/004162/WS0968/001

2

Edistride-EMEA/H/C/004161/WS0968/00

09

Forxiga-EMEA/H/C/002322/WS0968/002

8

Xigduo-EMEA/H/C/002672/WS0968/0023

MAH: AstraZeneca AB, Lead PRAC Rapporteur:
Qun-Ying Yue, "To provide a revised RMP in order to implement the recommendations given in the Article 20 assessment report dated 18th February (EMA/PRAC/50218/2016). The changes introduced are the following:

- The inclusion of atypical DKA as an identified Risk.
- Upgrade of a DUS from category 4 to 3 'required additional pharmacovigilance activities to address specific safety concerns or to measure effectiveness of risk minimisation measures'.
- Addition of a description of an ongoing mechanistic study. This is a short description as it is an ongoing post-doctorate research project and no protocol will be reviewed.
- Addition of a description of a DKA epidemiological study assessing the incidence of DKA to the RMP."

Request for Supplementary Information adopted on 15.09.2016.

PRAC Led

WS1005

Ultibro

Breezhaler-EMEA/H/C/002679/WS1005/0

013

Ulunar

Breezhaler-EMEA/H/C/003875/WS1005/0

013

Xoterna

Breezhaler-EMEA/H/C/003755/WS1005/0

015

MAH: Novartis Europharm Ltd, Lead Rapporteur:
Hanne Lomholt Larsen, Lead PRAC Rapporteur:
Torbjorn Callreus, "Update of the SmPC section 4.8 to add Dysphonia and revise the ADRs selection and frequencies based on the MAH's review of all safety data. As a consequence, section 4.4 was updated.

The Package Leaflet is updated accordingly.

The MAH took the opportunity of this procedure to update the Product Information as per the latest QRD template.

An RMP version 2.0 has been submitted.”
Request for Supplementary Information adopted
on 15.09.2016.

PRAC Led

WS1012

IDflu-EMEA/H/C/000966/WS1012/0047

Intanza-EMEA/H/C/000957/WS1012/005

0

MAH: Sanofi Pasteur SA, Duplicate, Duplicate of
Intanza, Lead Rapporteur: Aranzazu

Sancho-Lopez, Lead PRAC Rapporteur: Dolores

Montero Corominas, , “Update of the RMP (v
11.0) to include information on the enhanced
safety surveillance for NH 2016-2017 flu”

Request for Supplementary Information adopted
on 15.09.2016.

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

WS0984

AZILECT-EMEA/H/C/000574/WS0984/007

3

Rasagiline

ratiopharm-EMEA/H/C/003957/WS0984/0

007

MAH: Teva B.V., Lead Rapporteur: Bruno

Sepodes

Request for Supplementary Information adopted
on 27.10.2016.

Weekly start timetable. The Committee adopted
a Request for Supplementary information
together with a specific timetable.

WS1009

Cervarix-EMEA/H/C/000721/WS1009/008

4

Fendrix-EMEA/H/C/000550/WS1009/005

4

MAH: GSK Biologicals SA, Lead Rapporteur: Bart
Van der Schueren

Weekly start timetable.

WS1024

Humalog-EMEA/H/C/000088/WS1024/01

47

Liprolog-EMEA/H/C/000393/WS1024/011

1

MAH: Eli Lilly Nederland B.V., Informed Consent
of Humalog, Lead Rapporteur: Robert James

Hemmings

Weekly start timetable. The Committee adopted
a Request for Supplementary information
together with a specific timetable.

Request for Supplementary Information adopted on 20.10.2016.

WS1035/G Weekly start timetable.
Epclusa-EMEA/H/C/004210/WS1035/0002/G
Harvoni-EMEA/H/C/003850/WS1035/0036/G
Sovaldi-EMEA/H/C/002798/WS1035/0034/G
MAH: Gilead Sciences International Ltd, Lead Rapporteur: Filip Josephson

WS1036 Weekly start timetable.
Helixate
NexGen-EMEA/H/C/000276/WS1036/0181
KOGENATE
Bayer-EMEA/H/C/000275/WS1036/0188
MAH: Bayer Pharma AG, Lead Rapporteur: Jan Mueller-Berghaus

WS1054
Humalog-EMEA/H/C/000088/WS1054/0149
Liprolog-EMEA/H/C/000393/WS1054/0113
MAH: Eli Lilly Nederland B.V., Lead Rapporteur: Robert James Hemmings, "To update sections 1, 2.2, 4.2, 4.4, 5.1, 6.6 of the SmPC with minor amendments, e.g. to change "u/ml" to "units/ml". The package leaflet and labelling were updated accordingly and minor editorial changes were also included in annex II.
In addition a newly formatted user manual for insulin lispro KwikPen 100 units/ml was introduced. The new format aims to present the information related to the operating the pen in a simpler manner and to reduce the repetition of information as compared to the previous version."

B.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

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

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

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

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Bexsero - meningococcal group B vaccine

(rDNA, component, adsorbed) -

EMA/H/C/002333/II/0048

MAH: GSK Vaccines S.r.l, Rapporteur: Kristina Dunder

Pixuvri - pixantrone -

EMA/H/C/002055/II/0032/G

MAH: CTI Life Sciences Limited, Rapporteur: Greg Markey

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

Cinryze - c1-esterase inhibitor, human -

EMA/H/C/001207/II/0048

MAH: Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus, , "To replace Unit (U) by International Unit (IU) in labelling for harmonization with the registration dossier Module 3 information"

HyQvia - human normal immunoglobulin -

EMA/H/C/002491/II/0032

MAH: Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.2 and 4.8 of the SmPC in order to add information on infusion site leakage. The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD

template version 10.”

OPDIVO - nivolumab -

EMA/H/C/003985/II/0023

MAH: Bristol-Myers Squibb Pharma EEIG,
Rapporteur: Aranzazu Sancho-Lopez, “Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and pharmacological information with the 24 months data from the completed NSCLC studies CA209017 and CA209057.”

Travatan - travoprost -

EMA/H/C/000390/II/0053

MAH: Alcon Laboratories (UK) Ltd, Rapporteur: Concepcion Prieto Yerro, “Following the submission of final CSR for study C-01-79 and a review of supporting clinical studies and post-marketing data, update to SmPC section 4.8 is proposed. The package leaflet is updated accordingly.

In addition, MAH took the opportunity to update number of the Spanish representative in the PL.”

Triumeq - dolutegravir / abacavir /

lamivudine - EMA/H/C/002754/II/0035

MAH: ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, “Update of section 5.1 of the SmPC to include Week 48 data from the Phase IIIb clinical study ING117172 (ARIA) to support the use of Triumeq in HIV-infected antiretroviral (ART)-naïve women.”

Triumeq - dolutegravir / abacavir /

lamivudine - EMA/H/C/002754/II/0036

MAH: ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, “Update of section 5.1 of the SmPC to include Week 24 (primary analysis) and Week 48 data from the Phase IIIb clinical study 201147 (STRIIVING), to support the use of Triumeq in HIV-infected antiretroviral (ART)-experienced adults.”

Xagrid - anagrelide -

EMA/H/C/000480/II/0074, Orphan

MAH: Shire Pharmaceutical Contracts Ltd.,
Rapporteur: Pierre Demolis, , “Submission of the final Clinical Study Report of the study SPD422-403, a phase IIIb, randomised, open-label study conducted as a specific obligation to compare the safety, efficacy, and tolerability of anagrelide hydrochloride versus hydroxyurea in high-risk essential

thrombocythaemia patients. No changes to the approved product information have been requested as a consequence of this study report.”

WS1055

Ebymect-EMEA/H/C/004162/WS1055/001

6

Edistride-EMEA/H/C/004161/WS1055/00

12

Forxiga-EMEA/H/C/002322/WS1055/003

1

Qtern-EMEA/H/C/004057/WS1055/0004

Xigduo-EMEA/H/C/002672/WS1055/0027

MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC in order to update the safety information related to rash. The Package Leaflet is updated accordingly. Additional editorial changes were made in sections 5.1, 5.2 of the SmPC to Qtern.”

WS1056

Ebymect-EMEA/H/C/004162/WS1056/001

5

Edistride-EMEA/H/C/004161/WS1056/00

11

Forxiga-EMEA/H/C/002322/WS1056/003

0

Qtern-EMEA/H/C/004057/WS1056/0003

Xigduo-EMEA/H/C/002672/WS1056/0026

MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, “Update of sections 4.5 to add information on the interaction between 1,5-anhydroglucitol assay (monitoring glycaemic control method) and the SGLT2 inhibitors. In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10. Combined SmPCs are introduced in line with the EMA Policy on combined Summaries of Product Characteristics (SmPCs) (EMA/333423/2015).”

- B.6.10. CHMP-PRAC assessed procedures**
 - B.6.11. PRAC assessed procedures**
 - 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**
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WS1029

M-M-RVAXPRO-EMEA/H/C/000604/WS102

9/0078

ProQuad-EMEA/H/C/000622/WS1029/011

2

MAH: Sanofi Pasteur MSD SNC, Lead Rapporteur:

Jan Mueller-Berghaus

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

G.3.1. List of procedures concluding at 07-10 November 2016 CHMP plenary:

G.3.2. List of procedures starting in October 2016 for December 2016 CHMP adoption of outcomes

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