10 October 2016
EMA/CHMP/611664/2016 Rev.2
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 10-13 October 2016

Chair: Tomas Salmonson – Vice-Chair: Pierre Demolis

10 October 2016, 13:00 – 19:30, room 2A

11 October 2016, 08:30 – 19:30, room 2A

12 October 2016, 08:30 – 19:30, room 2A

13 October 2016, 08:30 – 15:00, 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 10-13 October 2016. See October 2016 CHMP minutes (to be published post November 2016 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 10-13 October 2016

1.3. Adoption of the minutes

CHMP minutes for 12-15 September 2016.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. dinutuximab beta - Orphan - EMEA/H/C/003918

APEIRON Biologics AG; treatment of neuroblastoma

Scope: Oral explanation

Action: Oral explanation to be held on Thursday 13 October 2016 at 09:00

List of Outstanding Issues adopted on 26.05.2016. List of Questions adopted on 24.09.2015.

BWP report

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: Report from the SAG Neurology meeting held 29 September 2016. Oral explanation to be held on Tuesday 11 October 2016 at 14.00.

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."
Request for Supplementary Information adopted on 21.07.2016, 01.04.2016.

Renewal of Marketing Authorisation
Request for Supplementary Information adopted on 21.07.2016, 28.04.2016.

Action: For adoption

See 9.1.1

2.3.1. Helicobacter Test INFAI - 13C-urea - EMEA/H/C/000140/II/0019

MAH: INFAI GmbH

Rapporteur: Andrea Laslop

Scope: "Update of the SmPC section 4.2, 4.3, 5.1 and 6.5 in order to add information on use of Refex test meal prior to the Helicobacter Test INFAI 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."

Oral explanation to be held on Wednesday 12 October 2016 at 14.00.

Action: For adoption

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

See 9.1.3

2.4. Referral procedure oral explanations

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. - mercaptamine - Orphan - EMEA/H/C/003769

Orphan Europe S.A.R.L.; treatment of cystinosis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 19.11.2015, 22.10.2015, 25.06.2015. List of Questions adopted on 22.01.2015.

3.1.2. - emtricitabine / tenofovir disoproxil - EMEA/H/C/004050

treatment of HIV

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 21.07.2016, 26.05.2016. List of Questions adopted on 19.11.2015.

3.1.3. - emtricitabine / tenofovir disoproxil - EMEA/H/C/004215

treatment of HIV-1 infection

Scope: Opinion

Action: For adoption

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

3.1.4. - obeticholic acid - Orphan - EMEA/H/C/004093

Intercept Pharma Ltd; treatment of primary biliary cirrhosis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 21.07.2016. List of Questions adopted on 22.10.2015.

3.1.5. - follitropin delta - EMEA/H/C/003994

indicated for controlled ovarian stimulation

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 21.07.2016. List of Questions adopted on 25.02.2016.

BWP report

3.1.6. - edotreotide - Orphan - EMEA/H/C/004140

Advanced Accelerater Applications; Diagnosis of gastro-entero-pancreatic neuroendocrine tumours

Scope: Opinion

Action: For adoption

2nd List of Outstanding Issues was adopted via written procedure on 23.09.2016. List of Outstanding Issues adopted on 21.07.2016. List of Questions adopted on 25.02.2016.

3.1.7. - tenofovir disoproxil - EMEA/H/C/004049

treatment of HIV-1 infection and hepatitis B infection

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 21.07.2016, 26.05.2016. List of Questions adopted on 17.12.2015.

3.1.8. - venetoclax - Orphan - EMEA/H/C/004106

AbbVie Ltd.; treatment of adult patients with chronic lymphocytic leukaemia (CLL)

Scope: Opinion

Action: For adoption

Oral explanation held on 15.09.2016. List of Outstanding Issues adopted on 21.07.2016. List of Questions adopted on 01.04.2016.

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

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

GMP-Orphan SA; Wilson's disease

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 28.04.2016.

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

treatment of vulvovaginal atrophy

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 26.05.2016.

3.2.3. - baricitinib - EMEA/H/C/004085

treatment of moderate to severe active rheumatoid arthritis (RA)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.06.2016.

3.2.4. . - pregabalin - EMEA/H/C/004277

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

Scope: List of Outstanding Issues

Action: For adoption

List of questions adopted on 21.07.2016

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

for the treatment of adults with type 2 diabetes mellitus

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.07.2016.

BWP report

3.2.6. - rituximab - EMEA/H/C/004112

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

Scope: Day 180 list of outstanding issues

Action: For adoption

List of Questions adopted on 25.02.2016.

BWP report

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

treatment of neutropenia

Scope: Day 180 list of outstanding issue

Action: For adoption

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

BWP report

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

treatment of neutropenia

Scope: Day 180 list of outstanding issue

Action: For adoption

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

BWP report

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

3.3.1. - carmustine - EMEA/H/C/004326

treatment of brain tumors, multiple myeloma, Hodgkin's disease and non-Hodgkin's lymphomas

Scope: Day 120 list of questions

Action: For adoption

3.3.2. - pegfilgrastim - EMEA/H/C/004262

treatment of neutropenia

Scope: Day 120 list of questions

Action: For adoption

BWP report

3.3.3. - tigecycline - EMEA/H/C/004419

Treatment of: - complicated skin and soft tissue infections, excluding diabetic foot infections
- complicated intra-abdominal infections
should be used only in situations where other alternative antibiotics are not suitable.

Scope: Day 120 list of questions

Action: For adoption

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

3.4.1. - adalimumab - EMEA/H/C/004373

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

Scope: Clockstop extension requested to respond to LoOI.

Action: For adoption

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

3.4.2. - miglustat - EMEA/H/C/004366

treatment of Gaucher disease

Scope: Assessment Report on similarity

Action: For adoption

3.4.3. - nitisinone - EMEA/H/C/004281

treatment of hepatorenal tyrosinemia type 1

Scope: Clockstop extension requested to respond to LoQ.

Action: For adoption

List of Questions adopted on 21.07.2016.

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

Novo Nordisk A/S; treatment of haemophilia B

Scope: Clockstop extension requested. List of Questions to ad-hoc expert group meeting .

Action: For adoption

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

3.4.5. - rurioctocog alfa pegol - EMEA/H/C/004195

treatment of haemophilia A

Scope: List of Questions to ad-hoc expert group meeting

Action: For adoption

List of Questions adopted on 21.07.2016.

3.4.6. - cariprazine - EMEA/H/C/002770

treatment of schizophrenia

Scope: Clockstop extension requested to respond to LoQ.

Action: For adoption

List of Questions adopted on 21.07.2016.

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

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

Scope: Amended timetable and draft list of experts for the SAG meeting

Action: For adoption

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

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

indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4

Scope: Clockstop extension requested to respond to LoQ.

Action: For adoption

List of Questions adopted on 21.07.2016.

3.4.9. - iloperidone - EMEA/H/C/004149

treatment of schizophrenia

Scope: Letter from the applicant dated 5 October 2016 requesting an extension of clock stop to respond to the List of Questions adopted on 28.04.2016

Action: For information

List of Questions adopted on 28.04.2016.

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

3.7.1. - ertapenem - EMEA/H/C/004080

treatment of bacterial infections and prophylaxis of surgical site infection following elective colorectal surgery

Scope: Withdrawal of initial marketing authorisation application

Action: For information

3.7.2. - pemetrexed - EMEA/H/C/004306

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

Scope: Withdrawal of initial marketing authorisation application

Action: For information

List of Questions adopted on 21.07.2016.

3.7.3. cediranib - Orphan - EMEA/H/C/004003

AstraZeneca AB; treatment of platinum sensitive relapsed (PSR) ovarian cancer relapsed (PSR) ovarian cancer

Scope: Withdrawal of initial marketing authorisation application

Action: For information

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. Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/X/0050/G

Bial - Portela & Cª, S.A.

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

Scope: “Grouping of a line extension application to add a new pharmaceutical form (50 mg/ml oral suspension) and a type II variation (C.I.6.a New indication (paediatric indication)) to add treatment of children aged 2 years and older. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC have been updated and 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.
The application included a revised RMP version 14.0.”

Action: For adoption

List of Outstanding Issues adopted on 21.07.2016. List of Questions adopted on 19.11.2015.

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. Celsentri - maraviroc - EMEA/H/C/000811/X/0046/G

ViiV Healthcare UK Limited

Rapporteur: Filip Josephson, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Qun-Ying Yue

Scope: “Extension application to introduce new pharmaceutical form (20mg/ml oral solution) and 2 new strenghts of film-coated tablets (25mg and 75mg) to the currently approved presentations for Celsentri, grouped with extension of indication to include paediatric use (2 to 18 years).

As a consequence, sections 4.2 and 4.4 of the SmPC are updated to detail posology in paediatric patients and to update the safety information, respectively.

The Package Leaflet and Labelling are updated in accordance.

Furthermore, the PI is brought in line with the latest QRD template version 10.”

Action: For adoption

4.3.2. Humira - adalimumab - EMEA/H/C/000481/X/0157

AbbVie Ltd.

Rapporteur: Kristina Dunder

Scope: “Extension application to add a new strength of 80 mg (80 mg/0.8 ml) for adalimumab solution for injection in single-use pre-filled syringe, for subcutaneous injection.”

Action: For adoption

4.3.3. Isentress - raltegravir - EMEA/H/C/000860/X/0059

Merck Sharp & Dohme Limited

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

Scope: "Extension application to add a new strength of 600mg film coated tablets."

Action: For adoption

4.3.4. Mimpara - cinacalcet - EMEA/H/C/000570/X/0055/G

Amgen Europe B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to introduce a new pharmaceutical form associated with new strengths (1 mg, 2.5 mg and 5 mg hard capsules) grouped with a type II variation (C.1.6.a) to include paediatric use in the approved indication. As a consequence, sections 4.2 and 4.4 of the SmPC are updated to detail posology in paediatric patients and to update the safety information, respectively.

The Package Leaflet and Labelling are updated in accordance.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.

Furthermore, the PI is brought in line with the latest QRD template version 10."

Action: For adoption

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

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

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

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

5.1.1. 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.”

Action: For adoption

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

5.1.2. Humira - adalimumab - EMEA/H/C/000481/II/0158

AbbVie Ltd.

Rapporteur: Kristina Dunder

Scope: “Extension of Indication to include new indication for moderate to severe nail psoriasis in adult patients who are candidates for systemic therapy for Humira.
As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 9.1.”

Action: For adoption

5.1.3. Lucentis - ranibizumab - EMEA/H/C/000715/II/0061

Novartis Europharm Ltd

Rapporteur: Kristina Dunder, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Extension of Indication to include treatment of visual impairment due to choroidal neovascularization (CNV) based on 6-month data from the pivotal study CRFB002G2301 (MINERVA). Consequential changes are proposed to SmPC sections 4.1, 4.2, 4.8 and 5.1 and the Package Leaflet is proposed to be updated accordingly.
The application included an updated RMP version 16.0.”

Action: For adoption

Request for Supplementary Information adopted on 26.05.2016.

5.1.4. Opdivo - nivolumab - EMEA/H/C/003985/II/0012

Bristol-Myers Squibb Pharma EEIG

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

Scope: “Extension of Indication to include the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL):
-after autologous stem cell transplant (ASCT) and treatment with brentuximab vedotin, or
-after at least two prior therapies in patients who are not candidates for ASCT,
for OPDIVO as monotherapy.
As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the proposed new indication, add a warning that patients with active autoimmune disease and symptomatic interstitial lung disease were excluded from clinical trials of cHL, and update the safety and pharmacodynamic information. The Package Leaflet is updated

in accordance.
Furthermore, the PI is brought in line with the latest QRD template version 10.0.
Moreover, the updated RMP version 5.0 has been submitted"

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016, 23.06.2016.

5.1.5. Opdivo - nivolumab - EMEA/H/C/003985/II/0017

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of Indication to include treatment of recurrent or metastatic squamous cell cancer of the head and neck (SCCHN) after platinum-based therapy in adults for Opdivo. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, of the SmPC are updated in order to add the proposed new indication, add a warning that patients with a baseline performance score ≥ 2, untreated brain metastasis, active autoimmune disease, or medical conditions requiring systemic immunosuppression were excluded from the SCCHN clinical trial and update the undesirable effect and safety information. Labelling is updated in accordance. Moreover, the updated RMP version 6.0 has been submitted"

Action: For adoption

5.1.6. Tasigna - nilotinib - Orphan - EMEA/H/C/000798/II/0084/G

Novartis Europharm Ltd

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Doris Stenver

Scope: "This grouped variation application consists of three Type II variation applications as follows:
- Update of the 150 mg SmPC sections 4.1, 4.2, 4.4, 4.8 and 5.1, and Package Leaflet based on the results from study CAMN107I2201 (ENESTfreedom): A Phase II, single-arm study evaluating nilotinib treatment discontinuation (treatment-free remission (TFR)) in newly-diagnosed patients with Philadelphia chromosome-positive chronic myelogenous leukemia in chronic phase (Ph+ CML-CP) who achieved a sustained deep molecular response.
- Update of the 150 mg and 200 mg Tasigna SmPC sections 4.1, 4.2, 4.4, 4.8 and 5.1, and Package Leaflet based on the results from study CAMN107A2408 (ENESTop): A Phase II, single-arm study evaluating nilotinib treatment discontinuation (treatment-free remission (TFR)) in patients with Ph+ CML-CP who achieved a sustained deep molecular response on nilotinib treatment after switching from imatinib treatment.
- Update of the 200 mg Tasigna SmPC sections 4.8 and 5.1, based on the results from study CAMN107A2405 (ENESTcmr): A Phase III open-label, randomised study to evaluate nilotinib or imatinib treatment in patients with Ph+ CML-CP who have not achieved a deep molecular response after previous imatinib therapy.
Additional changes to the labelling are proposed to comply with the latest QRD template

version 10.
An updated RMP, version 16, is also provided in this application."

Action: For adoption

5.1.7. Trisenox - arsenic trioxide - EMEA/H/C/000388/II/0058

Teva B.V.

Rapporteur: Pierre Demolis, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Claire Ferard

Scope: "Extension of Indication to include induction of remission, and consolidation in adult patients with newly diagnosed low-to-intermediate risk acute promyelocytic leukaemia (APL) (white blood cell count, ≤ 10 x 103/µl) characterised by the presence of the t(15;17) translocation and/or the presence of the Pro-Myelocytic Leukaemia/Retinoic-Acid-Receptor-alpha (PML/RAR-alpha) gene for Trisenox.
As a consequence, sections 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated regarding the posology, efficacy and safety information and warnings. In addition, a Risk Management Plan is introduced. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 23.06.2016.

5.1.8. Xgeva - denosumab - EMEA/H/C/002173/II/0045

Amgen Europe B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of Indication to include treatment of hypercalcemia of malignancy refractory to intravenous bisphosphonate for Xgeva.
As a consequence, sections 4.2, 4.3, 4.8, 5.1 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

5.1.9. Trajenta Jentadueto - linagliptin linagliptin / metformin - EMEA/H/C/WS0915

Boehringer Ingelheim International GmbH

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

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

Trajenta) and version 12 (for Jentadueto) have been submitted."

Action: For adoption

Request for Supplementary Information adopted on 26.05.2016.

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

5.2.1. Jardiance - empagliflozin - EMEA/H/C/002677/II/0014

Boehringer Ingelheim International GmbH

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

Scope: Clockstop extension requested.

"Extension of indication to include a new indication on prevention of cardiovascular events, based on the final data of the cardiovascular safety phase III clinical trial EMPA-REG OUTCOME. As a consequence, section 4.1 of the SmPC is updated. The Package Leaflet is also updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make some editorial changes."

Action: For adoption

Oral explanation was held on 14.09.2016, Request for Supplementary Information adopted on 15.09.2016, 23.06.2016, 25.02.2016.

5.2.2. Synjardy - empagliflozin / metformin - EMEA/H/C/003770/II/0015

Boehringer Ingelheim GmbH

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Dolores Montero Corominas

Scope: Clockstop extension requested.

"Extension of Indication to include treatment with Synjardy as adjunct to standard care therapy in adult patients with type 2 diabetes mellitus and high cardiovascular risk when treatment with empagliflozin and metformin is appropriate and empagliflozin is needed to reduce the risk of all-cause mortality by reducing cardiovascular death and cardiovascular death or hospitalization for heart failure. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated based on the final CSR of study EMPA-REG OUTCOME. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes/corrections in the SmPC. Moreover, the updated RMP version 5.0 has been submitted."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016, 26.05.2016.

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

6.1.1. - human serum albumin - EMEA/H/D/004287

Human serum albumin ancillary action prevents adsorption to the container of various amino acids, vitamins which may be present in trace quantities and acts as a carrier of these substances to support growth and maintenance of gametes and/or embryos. Scavenges embryotoxic components generated prevents adsorption to the container of various amino acids and vitamins, acts as a carrier of these substances to support growth and maintenance of gametes and/or embryos, Scavenges embryotoxic components generated during embryo's metabolism in vitro

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.01.2016.

BWP report

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. metreleptin - Orphan - H0004218

Aegerion Pharmaceuticals Limited;

Treatment of patients with generalised lipodystrophy and of a subset of patients with partial lipodystrophy with low leptin levels and metabolic abnormalities.

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

Action: For adoption

8.1.2. rucaparib - Orphan - H0004272

Clovis Oncology; Rucaparib is indicated as monotherapy treatment of advanced ovarian cancer in adult patients with deleterious BRCA-mutated tumours (inclusive of both germline and somatic BRCA mutations), and who have been treated with two or more prior lines of chemotherapy.

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. 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: Report from the SAG Neurology meeting held 29 September 2016. Oral explanation to be held on Tuesday 11 October 2016 at 14.00.

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."
Request for Supplementary Information adopted on 21.07.2016, 01.04.2016.

Renewal of Marketing Authorisation
Request for Supplementary Information adopted on 21.07.2016, 28.04.2016.

Action: For adoption

See 2.3.1

9.1.2. Emtriva - emtricitabine - EMEA/H/C/000533/II/0113

MAH: Gilead Sciences International Ltd,

Rapporteur: Greg Markey,

Scope: Readoption of opinion due to change in administration time from 24-48 hours to 24 hours.

"Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to allow administration of Emtriva 200 mg hard capsule every 24 hours in patients with renal impairment (eGFRCG ≥ 30 mL/min) and corresponding update the SmPC for Emtriva 10mg/ml oral solution. The Package Leaflet is updated accordingly."

Action: For adoption

Opinion adopted on 15.09.2016. Request for Supplementary Information adopted on 23.06.2016.

9.1.3. Helicobacter Test INFAI - 13C-urea - EMEA/H/C/000140/II/0019

MAH: INFAI GmbH

Rapporteur: Andrea Laslop

Scope: "Update of the SmPC section 4.2, 4.3, 5.1 and 6.5 in order to add information on use of Refex test meal prior to the Helicobacter Test INFAI 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."

Oral explanation to be held on Wednesday 12 October 2016 at 14.00.

Action: For adoption

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

See 2.3.1.

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 - EMEA/H/A-20/1438

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

Scope: Final List of experts to the SAG HIV/viral meeting

Action: For information, the final list was adopted via written procedure on 7th October 2016.

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: Amendment of timetable

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

10.5. 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: List of outstanding issues/Opinion

Action: For adoption

List of outstanding issues adopted 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: List of outstanding issues/Opinion

Action: For adoption

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

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

Sanofi Aventis group of companies and associated companies

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

Scope: List of outstanding issues

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

Action: For adoption

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

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

Lundbeck group of companies and associated companies

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

Scope: List of Outstanding Issues

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

Action: For adoption

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

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

10.6.1. Metformin and metformin containing fixed-dose combinations – metformin containing products – EMEA/H/A-31/1432

Rapporteur: Kristina Dunder, Co-Rapporteur: Johann Lodewijk Hillege, Scope: Opinion

Review of use in patients with renal impairment and precautions regarding lactic acidosis

Action: For adoption

List outstanding issues adopted 23.06.2016. List of Questions adopted 28.01.2016.

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 question to Ad-hoc expert meeting

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

10.6.3. Pharmaceutics International – EMEA/H/A-31/1444

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: David Lyons,

Scope: Request from the European Commission for clarification in relation to the Opinion adopted by the CHMP for Pharmaceutical International Article 31 referral at its September meeting.

Article 31 triggered by the European Commission

Action: For discussion

Opinion adopted on 15.09.2016. List of Questions adopted on 23.06.2016. List of Outstanding Issues adopted on 21 July 2016.

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

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

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Action: For information

13.2. Innovation Task Force briefing meetings

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

13.2.1. ITF Briefing Meeting

ITF Briefing Meeting Meeting date: 22 November 2016

Action: For adoption

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. Election of CHMP Vice-Chair

Action: For adoption

14.1.2. Review of CHMP assessment reports templates for initial MAA, Generics, Ancillary (Autumn 2016 Roll out) (EMA/629410/2016)

Action: For discussion

14.1.3. Pilot Project on a model for a pre-marketing risk-based model for product testing

Scope: Outcome report of pilot project

Action: For information

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on **26-29 September 2016**

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 05-07 October 2016
Action: For information

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 19-20 September 2016

Action: For information

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at October 2016 PDCO

Action: For information

Report from the PDCO meeting held on 14-15 September 2016

Action: For information

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 04-06 October 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 10-12 October 2016

Action: For information

Letter from the CMDh dated 5th July 2016 to the PGWP on applicability of Art. 31 referral outcome on codeine-containing medicinal products to medicinal products containing morphine derivatives

Action: For information

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

14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 26-29 September 2016. Table of conclusions

Action: For information

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

Scope: SA new initiative: Biosimilar Pilot

Action: For adoption

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 21 September 2016.

Action: For adoption

14.3.3. Biosimilar Medicinal Product Working Party (BMWP)

Scope: Election of BMWP Chair

Action: For adoption

Scope: Appointment of new core member to BMWP

Action: For adoption

Scope: Nomination of new observer Sandra Bright (IE) to BMWP

Action: For adoption

14.3.4. Vaccines Working Party (VWP)

Scope: Election of VWP Chair

Action: For adoption

14.3.5. Pharmacogenomics Working Party (PGWP)

Scope: Election of PGWP Chair

Action: For adoption

14.3.6. Quality Working Party (QWP)

Scope: Q&As on quality requirements for orally inhaled products

Action: For adoption

14.3.7. Central Nervous System Working Party (CNSWP)

Chair: Karl Broich

Scope: Concept paper on the need for revision of the guideline on clinical investigation of medicinal product for the treatment of migraine (EMA/179671/2016)

Action: For adoption

Scope: Concept paper on the need for revision of the guideline on clinical investigation of medicinal products in the treatment of epileptic disorders (EMA/CHMP/179692/2016).

Action: For adoption for 3 months public consultation

Scope: Nomination of new observer Ewa Balkowiec Iskra (PL) to CNSWP

Action: For adoption

14.3.8. Radiopharmaceutical Drafting Group (RadDG)

Chair: Anabel Cortes

Scope: Guideline on core SmPC and Package Leaflet for nanocolloidal technetium (99mTc) albumin

Action: For adoption

Scope: Guideline on core SmPC and Package Leaflet for sodium iodide (131I) therapy capsule

Action: For adoption and release for 4 months public consultation

14.3.9. Pharmacokinetics Working Party (PKWP)

Scope: Election of PKWP Chair

Action: For adoption

14.3.10. Rheumatology/Immunology Working Party (RIWP)

Scope: Election of RIWP Chair

Action: For adoption

14.3.11. Oncology Working Party (ONCWP)

Chair: Pierre Demolis

Scope: Election of Vice-Chair

Action: For adoption

14.3.12. Extrapolation Working Group

Report on Public Workshop on extrapolation of efficacy and safety in medicine development across age groups

Action: For information

14.3.13. Biostatistics Working Party (BSWP)

Chair: Thomas Lang (acting)

Call for nomination of a new core member following resignation of David Jonathan Wright (UK)

Action: For information

Expertise sought: professionally qualified senior assessor within the European regulatory network, with relevant expertise in the field of biostatistics.

Nominations should be sent by **15 October 2016**.

Election is going to take place at the November 2016 CHMP Plenary meeting.

14.3.14. Cardiovascular Working Party (CVSWP)

Chair: Pieter de Graeff

Scope: Appointment of new expert Bart Van der Schueren (BE) to CVSWP

Action: For adoption

14.3.15. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan / Sonja Beken,

Scope: Election of Vice-Chair

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

14.9.1. Adaptive pathways

Scope: Workshop and report

Action: For information

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: The concept paper was adopted at the July 2016 CHMP Plenary. The public consultation ended on 30 September. The guideline is being revised.

Action: For information

16. Explanatory notes

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

Oral explanations *(section 2)*

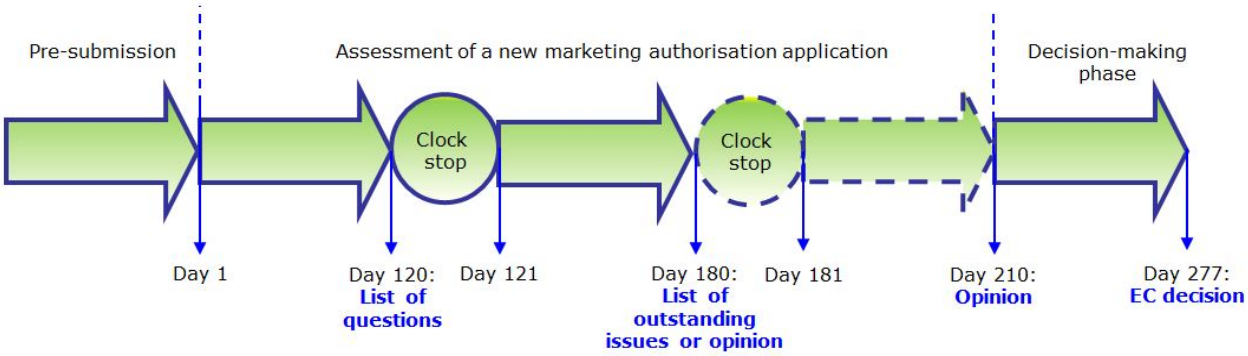
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the EU. Further information on such procedures can be found here.

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

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

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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

10 October 2016
EMA/CHMP/657076/2016 Rev. 2

Annex[1] to October 2016 CHMP Agenda

Pre submission and post authorisations issues

[1] From October 2016 onwards Annexes to CHMP Agendas and Minutes will be published

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A. Pre Submission Issues

A.1. Eligibility Requests

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

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

Final Outcome of Rapporteurship allocation for October 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 expected outcomes

B.1. Annual reassessment expected outcomes

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

Evoltra - clofarabine -
EMEA/H/C/000613/S/0050
MAH: Genzyme Europe BV, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard

B.2. Renewals of Marketing Authorisations expected outcomes

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

Sebivo - telbivudine -
EMEA/H/C/000713/R/0045
MAH: Novartis Europharm Ltd, Rapporteur: Joseph Emmerich, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Claire Ferard

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Ecansya - capecitabine -
EMEA/H/C/002605/R/0018
MAH: KRKA, d.d., Novo mesto, Generic, Generic of Xeloda, Rapporteur: Kristina Dunder, PRAC Rapporteur: Martin Huber

Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - EMEA/H/C/002450/R/0008, Orphan, ATMP
MAH: Chiesi Farmaceutici S.p.A., Rapporteur: Egbert Flory, Co-Rapporteur: Paolo Gasparini, CHMP Coordinators: Jan Mueller-Berghaus, , PRAC Rapporteur: Julie Williams

Pioglitazone Accord - pioglitazone hydrochloride - EMEA/H/C/002277/R/0011
MAH: Accord Healthcare Ltd, Generic, Generic of Actos, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner

Pioglitazone Teva - pioglitazone - EMEA/H/C/002297/R/0016
MAH: Teva B.V., Generic, Generic of Actos, Glustin, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner

Pioglitazone Teva Pharma - pioglitazone - EMEA/H/C/002410/R/0013
MAH: Teva B.V., Generic, Generic of Actos, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner

Zoledronic acid Actavis - zoledronic acid - EMEA/H/C/002488/R/0017
MAH: Actavis Group PTC ehf, Generic, Generic of Zometa, Rapporteur: Milena Stain, PRAC Rapporteur: Doris Stenver

B.2.3. Renewals of Conditional Marketing Authorisations

TAGRISSO - osimertinib - EMEA/H/C/004124/R/0007
MAH: AstraZeneca AB, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Sabine Straus

Translarna - ataluren - EMEA/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 September 2016 meeting:

EMEA/H/C/PSUSA/00000390/201602
(betaine anhydrous (centrally authorised product only))
CAPS:
Cystadane (EMEA/H/C/000678) (betaine anhydrous), MAH: Orphan Europe S.A.R.L., Rapporteur: Harald Enzmann, PRAC Rapporteur: Valerie Strassmann, "01/03/2015 - 28/02/2016"

EMEA/H/C/PSUSA/00000756/201602
(cinacalcet)
CAPS:
Mimpara (EMEA/H/C/000570) (cinacalcet), MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "(01 March 2013 to 28 February 2016)"

EMEA/H/C/PSUSA/00001393/201602
(fingolimod)
CAPS:
Gilenya (EMEA/H/C/002202) (fingolimod), MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, "01-Mar-2015 to 28-Feb-2016"

EMEA/H/C/PSUSA/00010073/201603
(bosutinib)
CAPS:
Bosulif (EMEA/H/C/002373) (bosutinib), MAH: Pfizer Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, "04/03/2015-03/03/2016"

EMEA/H/C/PSUSA/00010180/201603
(cabozantinib)
CAPS:
Cometriq (EMEA/H/C/002640) (cabozantinib), MAH: Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "22 September 2015 to 21 March 2016"

EMEA/H/C/PSUSA/00010311/201603
(dulaglutide)
CAPS:
Trulicity (EMEA/H/C/002825) (dulaglutide), MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Carmela Macchiarulo, "19th September 2015 to 18th March 2016"

EMEA/H/C/PSUSA/00010338/201603
(apremilast)
CAPS:

Otezla (EMEA/H/C/003746) (apremilast), MAH: Celgene Europe Limited, Rapporteur: Patrick Salmon, PRAC Rapporteur: Dolores Montero Corominas, “September 21- March 20 2016”

B.4. EPARs / WPARs for adoption

Chenodeoxycholic acid sigma-tau - chenodeoxycholic acid - EMEA/H/C/004061, Orphan
Applicant: Sigma-tau Arzneimittel GmbH, treatment of inborn errors of primary bile acid synthesis, Hybrid application (Article 10(3) of Directive No 2001/83/EC)

Emtricitabine - Tenofovir disoproxil Zentiva - emtricitabine / tenofovir disoproxil - EMEA/H/C/004137
Applicant: Zentiva k.s., treatment of HIV-1 infection, Generic, Generic of Truvada, Generic application (Article 10(1) of Directive No 2001/83/EC)

Glyxambi - empagliflozin / linagliptin - EMEA/H/C/003833
Applicant: Boehringer Ingelheim International GmbH, treatment of type 2 diabetes mellitus, Fixed combination application (Article 10b of Directive No 2001/83/EC)

Granpidam - sildenafil - EMEA/H/C/004289
Applicant: Accord Healthcare Ltd, treatment of patients with pulmonary arterial hypertension, Generic, Generic of Revatio, Generic application (Article 10(1) of Directive No 2001/83/EC)

Ibrance - palbociclib - EMEA/H/C/003853
Applicant: Pfizer Limited, treatment of breast cancer, New active substance (Article 8(3) of Directive No 2001/83/EC)

Ivabradine JensonR - ivabradine - EMEA/H/C/004217
Applicant: JensonR+ Limited, treatment of angina pectoris, Generic, Generic of Procoralan, Generic application (Article 10(1) of Directive No 2001/83/EC)

Ivabradine Zentiva - ivabradine - EMEA/H/C/004117
Applicant: Zentiva, k.s., treatment of angina pectoris, Generic, Generic of Procoralan, Generic application (Article 10(1) of Directive No

2001/83/EC)	
Lartruvo - olaratumab - EMEA/H/C/004216, Orphan Applicant: Eli Lilly Nederland B.V., treatment of soft tissue sarcoma, New active substance (Article 8(3) of Directive No 2001/83/EC)	
Ninlaro - ixazomib - EMEA/H/C/003844, Orphan Applicant: Takeda Pharma A/S, multiple myeloma,	
Parsabiv - etelcalcetide - EMEA/H/C/003995 Applicant: Amgen Europe B.V., treatment of secondary hyperparathyroidism (SHPT) in adult patients with chronic kidney disease (CKD) on haemodialysis therapy, treatment of secondary hyperparathyroidism (SHPT) in adult patients with chronic kidney disease (CKD) on haemodialysis therapy., New active substance (Article 8(3) of Directive No 2001/83/EC)	
Zemfirza - cediranib - EMEA/H/C/004003, Orphan Applicant: AstraZeneca AB, treatment of platinum sensitive relapsed (PSR) ovarian cancer relapsed (PSR) ovarian cancerNew active substance (Article 8(3) of Directive No 2001/83/EC) **WPAR**	

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

BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0138 MAH: Pfizer Limited, Rapporteur: Jan Mueller-Berghaus,	Weekly start timetable.
ELOCTA - efmoroctocog alfa - EMEA/H/C/003964/II/0008/G MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus	
Empliciti - elotuzumab - EMEA/H/C/003967/II/0003 MAH: Bristol-Myers Squibb, Rapporteur: Paula	Weekly start timetable.

Boudewina van Hennik,	
Flixabi - infliximab - EMEA/H/C/004020/II/0003 MAH: Samsung Bioepis UK Limited (SBUK), Rapporteur: Jan Mueller-Berghaus	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0013/G, Orphan MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac	Weekly start timetable.
NexoBrid - bromelain enriched proteolytic enzyme preparation from Ananas comosus - EMEA/H/C/002246/II/0027/G, Orphan MAH: MediWound Germany GmbH, Rapporteur: Harald Enzmann Request for Supplementary Information adopted on 29.09.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
NutropinAq - somatropin - EMEA/H/C/000315/II/0065 MAH: Ipsen Pharma, Rapporteur: Hanne Lomholt Larsen	
Nuwiq - simoctocog alfa - EMEA/H/C/002813/II/0012/G MAH: Octapharma AB, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 14.07.2016.	Weekly start timetable.
Obizur - susoctocog alfa - EMEA/H/C/002792/II/0005 MAH: Baxalta Innovations GmbH, Rapporteur: Nithyanandan Nagercoil, Opinion adopted on 29.09.2016.	Positive Opinion adopted by consensus on 29.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Orencia - abatacept - EMEA/H/C/000701/II/0103/G MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola	Weekly start timetable.
Orencia - abatacept - EMEA/H/C/000701/II/0104/G MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola	
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0106/G MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 22.09.2016.	Positive Opinion adopted by consensus on 22.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Scintimun - besilesomab -	Positive Opinion adopted by consensus on

EMEA/H/C/001045/II/0010/G MAH: CIS BIO International, Rapporteur: Greg Markey Opinion adopted on 22.09.2016.	22.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Unituxin - dinutuximab - EMEA/H/C/002800/II/0008, Orphan MAH: United Therapeutics Europe Ltd, Rapporteur: Robert James Hemmings, Request for Supplementary Information adopted on 04.08.2016.	Weekly start timetable.
Vimpat - lacosamide - EMEA/H/C/000863/II/0064/G MAH: UCB Pharma S.A., Rapporteur: Filip Josephson Request for Supplementary Information adopted on 29.09.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS0898/G **Vfend-EMEA/H/C/000387/WS0898/0120/G** MAH: Pfizer Limited, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 22.09.2016. Request for Supplementary Information adopted on 28.07.2016.	Positive Opinion adopted by consensus on 22.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0922/G **Hexacima-EMEA/H/C/002702/WS0922/0052/G** **Hexaxim-EMEA/H/W/002495/WS0922/0059/G** **Hexyon-EMEA/H/C/002796/WS0922/0055/G** MAH: Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus	
WS0967 **Hexacima-EMEA/H/C/002702/WS0967/0048** **Hexaxim-EMEA/H/W/002495/WS0967/0055** **Hexyon-EMEA/H/C/002796/WS0967/0051** MAH: Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 21.07.2016.	
WS0969 **Infanrix hexa-EMEA/H/C/000296/WS0969/0204**	Weekly start timetable.

MAH: GlaxoSmithKline Biologicals, Lead Rapporteur: Bart Van der Schueren	
WS0976/G **Infanrix hexa-EMEA/H/C/000296/WS0976/0205/G** MAH: GlaxoSmithKline Biologicals, Lead Rapporteur: Bart Van der Schueren	
WS0977 **Tivicay-EMEA/H/C/002753/WS0977/0021** **Triumeq-EMEA/H/C/002754/WS0977/0029** MAH: ViiV Healthcare UK Limited, Lead Rapporteur: Filip Josephson	Weekly start timetable.
WS0983 **ProQuad-EMEA/H/C/000622/WS0983/0110** **Zostavax-EMEA/H/C/000674/WS0983/0106** MAH: Sanofi Pasteur MSD SNC, Lead Rapporteur: Jan Mueller-Berghaus	Weekly start timetable.

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

Cerdelga - eliglustat - EMEA/H/C/003724/II/0008, Orphan MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, "Update of SmPC section 5.1 to include 2, 3 and 4 years composite stability endpoint data based on the final results of the ENCORE study."	
Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0075 MAH: GlaxoSmithKline Biologicals, Rapporteur: Bart Van der Schueren, "Variations that do not affect the PI (C.I.13) Submission of study HPV-015 (MEA 083): A phase III, double-blind, randomized, controlled study to evaluate the safety, immunogenicity and efficacy of GlaxoSmithKline Biologicals' HPV_16/18 L1/AS04 vaccine administered intramuscularly according to a three-dose schedule (0, 1, 6 month) in healthy adult female subjects aged 26 years and above. At final analysis (M84) of study HPV-015, a new medical review of new onset of adverse events	

(NOADs) collected up to M48 was performed at M84. An additional analysis on potential immune mediated diseases (pIMDs) and pregnancy outcomes collected at M48 was also done at M84. No changes in the PI are proposed" Request for Supplementary Information adopted on 23.06.2016, 25.02.2016.	
Deltyba - delamanid - EMEA/H/C/002552/II/0014, Orphan MAH: Otsuka Novel Products GmbH, Rapporteur: Greg Markey, "Update of section 5.1 of the SmPC further to the submission of final clinical study report for trial 242-12-244 "Determination of Delamanid MIC Values and Sub-species Analysis of Mycobacterium tuberculosis Complex Isolates". Moreover the MAH has taken the occasion to implement version 10.0 of the QRD template. The date of the latest renewal has been included as well." Request for Supplementary Information adopted on 04.08.2016.	Weekly start timetable.
Evotaz - atazanavir / cobicistat - EMEA/H/C/003904/II/0010 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, "Proposed changes to the EVOTAZ SmPC to aling with the current Company Core Data Sheet (CCDS). During the EVOTAZ MAA procedure, an interim Week 144 CSR for Gilead study GS-US-216-0114 was submitted and the SmPC efficacy and safety data were updated and approved accordingly. However, the resistance data were not updated at that time. As a result, the MAH proposes to update the resistance sub-section in SmPC section 5.1 with study GS-US-216-0114 Week 144 resistance data that were submitted in the context of the MAA. In addition, for clarification purposes, the MAH proposes to use the specific designation of tenofovir disoproxil fumarate throughout the EVOTAZ Product Information (PI) to differentiate this pharmaceutical entity from the tenofovir alafenamide (for which no studies with EVOTAZ have been conducted). Finally, the MAH would like to take this opportunity to implement QRD version 10." Request for Supplementary Information adopted on 29.09.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

Exjade - deferasirox - EMEA/H/C/000670/II/0048, Orphan MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, “Update of section 4.8 of the SmPC in order to add information on paediatric population from the final results of the study A2411. This submission serves to comply with Article 46 of the Regulation (EC) No 1901/2206 on medicinal products for paediatric use. (EMEA-001103-PIP01-10-M02).” Request for Supplementary Information adopted on 01.04.2016.	
Firdapse - amifampridine - EMEA/H/C/001032/II/0042, Orphan MAH: BioMarin Europe Ltd, Rapporteur: Greg Markey, “Update of section 5.1 of the SmPC in order to reflect the efficacy results of the clinical study report LMS-002. In addition, the MAH took the opportunity of this procedure to update the Product Information in compliance with the QRD template version 9.1.” Request for Supplementary Information adopted on 23.06.2016.	Weekly start timetable.
Galafold - migalastat - EMEA/H/C/004059/II/0001, Orphan MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege, “Submission of 30 month data for Study AT1001-012, with updates to sections 4.8 and 5.1 of SmPC. Study AT1001-012 is a randomized, open-label study to compare the efficacy and safety of migalastat HCl and ERT in patients with Fabry disease and migalastat HCl-responsive GLA mutations, who were previously treated with ERT Please note that this variation meets a post approval commitment, Cat 3 : 01 as defined in the risk management plan. The variation also includes some editorial changes to product information (contact details of country representtives).” Request for Supplementary Information adopted on 15.09.2016.	Weekly start timetable.
Galafold - migalastat - EMEA/H/C/004059/II/0002, Orphan MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege, “Submission of updates to the Galafold SmPC section 5.1 Pharmacodynamic properties; specifically, addition of guidance related to searching the	

mutation tables, moving text from below the tables to above the tables and new and updated mutations in Table 2: Galafold amenability table and Table 3: Mutations not amenable to Galafold. Changes introduced into the tables are based on a) a direct physician request for Amicus to confirm a mutation, b) a new nucleotide change or protein sequence change identified in the literature or 3) a mutations that does not qualify for testing being added to the non-amenable table 3. Individual Mutant Form Summary of Results (IMFSR) are included in the application for the new mutations. Editorial changes are also highlighted in the tables, which result from a thorough check of the tables/mutations against the source documents. Updates to the contact details in the PIL have been included." Request for Supplementary Information adopted on 15.09.2016.	
Gilenya - fingolimod - EMEA/H/C/002202/II/0039 MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, "Update of sections 4.4 and 4.8 of the SmPC to add an approximate time of onset of multifocal leukoencephalopathy (PML) and for cryptococcal meningitis (CM), and to remove the term isolated from "isolated cases of CM"."	
Giotrif - afatinib - EMEA/H/C/002280/II/0017 MAH: Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, "Update of sections 4.2 and 5.2 of the SmPC in order to update the information regarding renal impairment, which has been introduced following completing of the Phase I study 1200.2016. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement editorial changes in the SmPC and to update the labelling (Annex IIIA) in line with QRD template, version 9.1." Request for Supplementary Information adopted on 14.07.2016.	Weekly start timetable.
Helicobacter Test INFAI - 13C-urea - EMEA/H/C/000140/II/0019 MAH: INFAI GmbH, Rapporteur: Andrea Laslop, "Update of the SmPC section 4.2, 4.3, 5.1 and 6.5 in order to add information on use of Refex test	See also 9.1.3

meal prior to the Helicobacter Test INFAI 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." Request for Supplementary Information adopted on 15.09.2016, 21.07.2016, 23.06.2016, 01.04.2016, 28.01.2016.	
Instanyl - fentanyl - **EMEA/H/C/000959/II/0040** MAH: Takeda Pharma A/S, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, "Submission of PASS Study (Instanyl-5001: An Evaluation of the Effectiveness of Risk Minimisation Measures: A Survey among Health Care Professionals to Assess their Knowledge and Attitudes on Prescribing Conditions of Instanyl in France and the Netherlands) included in the RMP." Request for Supplementary Information adopted on 21.07.2016.	
Intuniv - guanfacine - **EMEA/H/C/003759/II/0003/G** MAH: Shire Pharmaceuticals Ireland Ltd., Rapporteur: Johann Lodewijk Hillege"In compliance with requests in the RMP adopted at the time of MA, the MAH submitted final results of 4 completed non-clinical studies as follows: - Study V7613M-SPD503 (Secondary Pharmacodynamics) - Study V7089M-SPD503 (Drug Interaction) - Study V7400M-SPD503 and Study V7401M-SPD503 (Metabolism)" Request for Supplementary Information adopted on 15.09.2016, 23.06.2016.	
Intuniv - guanfacine - **EMEA/H/C/003759/II/0004** MAH: Shire Pharmaceuticals Ireland Ltd., Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 (Posology and Method of Administration), 4.4 (Special Warnings and Precautions for Use), and 4.8 (Undesirable Effects) of the SmPC in order to include a warning and update the safety information as a result of a post-marketing case of hypertensive encephalopathy upon abrupt discontinuation of Intuniv (guanfacine hydrochloride). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted	

on 23.06.2016.	
Iressa - gefitinib - EMEA/H/C/001016/II/0026 MAH: AstraZeneca AB, Rapporteur: Filip Josephson, “Submission of final study report for IMPRESS study (D791LC00001) and discussion to address one of the ‘PRAC Recommendations as per procedure regarding the gefitinib Periodic Safety Update Report (PSUR: EMA/PRAC/4284/2016). No Changes in the PI and in the RMP are proposed”	
Isentress - raltegravir - EMEA/H/C/000860/II/0061 MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, “Update of section 4.2 of the SmPC of Isentress 100 mg granules for oral suspension, upon request by PRAC following the assessment of the latest PSUR for raltegravir (EMEA/H/C/PSUSA/00010373/201509), to add information relating to the maximum dose of Isentress being 100 mg twice a day, and that each single-use packet for oral suspension is suspended in 5mL of water giving a final concentration of 20mg/ml. In addition, the MAH took the opportunity to implement minor editorial changes in the annexes, to update the contact details of the local representative in Luxembourg in the Package Leaflet and to align the annexes with the latest QRD templates (versions 9.1 and 10).”	Weekly start timetable.
Kalydeco - ivacaftor - EMEA/H/C/002494/II/0050, Orphan MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Concepcion Prieto Yerro, “Update of sections 4.6 and 5.3 of the SmPC following a revision of the animal:human exposure ratio. 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 10.0 and to align the PIL text with the current SmPC.”	Weekly start timetable.
NovoRapid - insulin aspart - EMEA/H/C/000258/II/0114 MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, “Update of sections 4.4 and 4.8 of the SmPC with additional information regarding avoidance of accidental mix-ups and medication errors.”	

NovoSeven - eptacog alfa / eptacog alfa (activated) - EMEA/H/C/000074/II/0092 MAH: Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.4 of the SmPC in order to delete sucrose warning. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes/corrections in the SmPC and Package Leaflet and to bring the PI in line with the latest QRD template version 10 (combined SmPC has been introduced)." Request for Supplementary Information adopted on 04.08.2016.	Weekly start timetable.
Plenadren - hydrocortisone - EMEA/H/C/002185/II/0022, Orphan MAH: Shire Services BVBA, Rapporteur: Kristina Dunder, "To update the SmPC section 4.8 (Undesirable Effects) and PIL section 4 (Possible side effects) of the Plenadren 5mg and 20 mg (hydrocortisone) modified release tablets."	
Praluent - alirocumab - EMEA/H/C/003882/II/0009/G MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege"Update of section 4.2 of the SmPC to include a 300 mg Q4W dosing regimen as a starting dose, based on the results of study CHOICE I (MEA 005). Section 4.8, 5.1 and 5.2 of the SmPC and the PL have also been updated to reflect the study results. In addition, the MAH submitted the final study report of study CHOICE II (MEA 009) and additional analysis of the two studies." Request for Supplementary Information adopted on 21.07.2016.	
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0145 MAH: Pfizer Limited, Rapporteur: Kristina Dunder, "Update of the SmPC section 5.1 with information on Prevenar 13 effects on invasive pneumococcal disease, antimicrobial resistance and otitis media caused by nontypeable H. influenzae. Editorial changes have also been proposed throughout the SmPC."	
Saxenda - liraglutide - EMEA/H/C/003780/II/0010 MAH: Novo Nordisk A/S, Rapporteur: Johann	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

Lodewijk Hillege, “Update of sections 4.2 and 5.1 of the SmPC in order to update the documented treatment effect currently limited to 1 year. The proposed update of the current labelling for long-term efficacy, safety and tolerable use in the management of obesity is based on 3-year data from trial 1839. In addition, the Marketing authorisation holder took the opportunity to bring the PI in line with the latest QRD template version 10 and implement minor linguistic updates.” Request for Supplementary Information adopted on 29.09.2016.	
Stivarga - regorafenib - EMEA/H/C/002573/II/0018 MAH: Bayer Pharma AG, Rapporteur: Paula Boudewina van Hennik, “Update the SmPC section 4.2 and 5.2 based on results from phase 1 study which evaluated the pharmacokinetics and safety of regorafenib in cancer subjets with severe renal impairment compared to cancer subjects without or mild renal impairment. The package leaflet is updated accordingly.”	
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0008, Orphan MAH: Alexion Europe SAS, Rapporteur: Greg Markey, “Update of sections 4.4 and 4.8 of the SmPC in order to reinforce the wording on the risk of anaphylaxis. The Package Leaflet is updated accordingly. The MAH took the opportunity to include the Pharmacotherapeutic group in section 5.1.” Request for Supplementary Information adopted on 21.07.2016.	
Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0031 MAH: ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, “Update of section 4.4 of the SmPC with revised wording related to mitochondrial dysfunction, and section 4.2 of the SmPC with an amended recommendation related to dose reduction in patients with hepatic impairment, in line with the SmPCs of other abacavir containing products. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement minor changes in Annex II and the labelling in line with the latest QRD template.”	Weekly start timetable.

WS0990 **Actos-EMEA/H/C/000285/WS0990/0074** **Competact-EMEA/H/C/000655/WS0990/0061** **Glubrava-EMEA/H/C/000893/WS0990/0046** **Glustin-EMEA/H/C/000286/WS0990/0072** **Tandemact-EMEA/H/C/000680/WS0990/0050** MAH: Takeda Pharma A/S, Lead Rapporteur: Patrick Salmon, Lead PRAC Rapporteur: Almath Spooner, "Submission of the final drug utilization study report (Pioglitazone_5019) conducted in Denmark designed to assess utilization of pioglitazone in Denmark after July 2011 when labeling changes were introduced following conclusion of an Article 20 procedure."

B.5.3. CHMP-PRAC assessed procedures

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0054 MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Final clinical study report for study AS001 is submitted. Sections 4.8 and 5.1 of the Summary of Product Characteristics (SmPC) are revised in order to update the efficacy and safety information (Week 204) for study AS001. The package leaflet remains unchanged. A revised RMP (version 11.0) is also submitted."
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0055 MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Final clinical study report for study PsA001 is submitted to provide data on long-term use of Cimzia in psoriatic arthritis subjects up to 216 weeks of treatment. Sections 4.8 and 5.1 of the Summary of Product Characteristics (SmPC) are revised in order to update the efficacy and safety information (Week 216) for study PsA001. The package leaflet remains unchanged. A revised RMP (veriosn 11) is also submitted. This corresponds to MEA 027"
Gilenya - fingolimod - EMEA/H/C/002202/II/0040

MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, "Update of section 4.6 of the SmPC to add information on the use of the product in pregnancy. In addition, update of section 5.3 of the SmPC to include information about the dose correspondence between human and the species used for the preclinical tests of teratogenicity. An updated RMP is submitted (version 12.0). The MAH took the opportunity to make minor editorial changes in sections 4.4, 4.5, 4.6 and 5.2 and also in Annex II.D."

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

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

Jetrea - ocriplasmin - EMEA/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 26.05.2016.

Odomzo - sonidegib - EMEA/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."

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

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

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

MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.6 of the SmPC in order to delete references to the Pregnancy and Lactation Surveillance programs. The Package Leaflet is updated accordingly.
The RMP has been revised to remove all references to the Pregnancy and Lactation Program.
In addition, the Marketing authorisation holder took the opportunity to make minor editorial updates to the SmPC and Package Leaflet."

Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0032

MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Dolores Montero Corominas, "Update of the SmPC section 4.4 and 4.8 with new information on the drug-induced liver injury. Consequently, the section of the Annex II 'Key elements to be included in the educational material' has been updated. The RMP (v. 39) has been revised accordingly."
Request for Supplementary Information adopted on 21.07.2016.

Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0035/G

MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Dolores Montero Corominas“Submission of final report of study TRC112765 assessing safety of eltrombopag in subjects with solid tumours receiving gemcitabine monotherapy or gemcitabine plus cisplatin or carboplatin. The RMP version 40 has been updated accordingly. In addition, the MAH took the opportunity to revise due dates for submission of final reports for two studies in the Pharmacovigilance Plan.”
Request for Supplementary Information adopted on 21.07.2016.

Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0036/G
MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Eva A. Segovia“This is a grouped variation consisting of:
Update to the Annex II of the Product Information based on the study assessing Effectiveness of eltrombopag Educational Materials for Hepatitis C associated thrombocytopenia.
The RMP (v. 41) is also being revised by removing the PASS Study PLATELET.
Submission of the ENABLE-TEE study (WWE116951/CET115A2404).”

Simponi - golimumab - EMEA/H/C/000992/II/0067
MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information with the data from the final CSRs of studies C0524T18 and P07642 in fulfilment of PAM (MEA 31 and MEA 32).
In addition, the Marketing authorisation holder (MAH) took the opportunity to combine SmPC for the pre-filled pen and pre-filled syringe for 50 mg strength and for the pre-filled pen and pre-filled syringe for 100 mg strength respectively, in line with the latest QRD template version 9.1.
Moreover, the updated RMP version 15 has been submitted.”
Request for Supplementary Information adopted on 26.05.2016.

Torisel - temsirolimus - EMEA/H/C/000799/II/0063, Orphan
MAH: Pfizer Limited, Rapporteur: Harald

Enzmann, PRAC Rapporteur: Martin Huber, "Submission of final results from Study 3066K1-4438-WW (B1771007) titled "A Randomized Phase 4 Study Comparing 2 Intravenous Temsirolimus (TEMSR) Regimens in Subjects with Relapsed, Refractory Mantle Cell Lymphoma" and fulfilment of obligation to conduct post authorisation measure ANX 027.2. The MAH also evaluate the toxic effects of interest [e.g., bleeding, infection- and mucositis-related events] for study 3066K1-4438-WW (Post-Marketing Commitment MEA 028) together with a review discussing potential new safety concerns arising from the results.
The RMP (v.3.0) is updated accordingly to add myocardial infarction and cardiovascular events in patient with coexisting cardiovascular conditions as important potential risks, and anaemia, thrombocytopenia, hypercholesterolemia, and hypertriglyceridemia as important identified risks.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."

Translarna - ataluren - EMEA/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 21.07.2016, 23.06.2016, 01.04.2016.
SAG meeting held on 16.06.2016.

Trulicity - dulaglutide - EMEA/H/C/002825/II/0012

MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Carmela Macchiarulo, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information to reflect findings from a recently completed phase 3b study (Study H9X-MC-GBDG (GBDG)) concerning the use of dulaglutide in combination with

sulphonylurea alone.
In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10."
Request for Supplementary Information adopted on 21.07.2016.

Trulicity - dulaglutide - EMEA/H/C/002825/II/0013
MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Carmela Macchiarulo,
"Update of sections 4.2, 4.7, 4.8 and 5.1 of the Summary of Product Characteristics (SmPC) for Trulicity following completion of a phase 3b Study (Study H9X-MCGBDI
(GBDI)) to reflect the study's findings concerning the use of dulaglutide in combination with basal insulin.
The Package Leaflet is updated in accordance."
Request for Supplementary Information adopted on 21.07.2016.

Ventavis - iloprost - EMEA/H/C/000474/II/0051/G
MAH: Bayer Pharma AG, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard
Request for Supplementary Information adopted on 21.07.2016, 25.02.2016.

Votrient - pazopanib - EMEA/H/C/001141/II/0038
MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver,
"Update of section 4.6 to add male contraception wording following a review of pazopanib according to the MAH's guideline on prevention of pregnancies. The PL is proposed to be updated accordingly. An updated RMP version 16 is proposed.
In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10 and combine the SmPC of the 2 tablets strengths."

Xgeva - denosumab - EMEA/H/C/002173/II/0046
MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga,
"Update of section 4.6 of the SmPC in order to delete references to the Pregnancy and Lactation Surveillance programs. The Package Leaflet is updated accordingly.
The RMP has been revised to remove all

references to the Pregnancy and Lactation Program. In addition, the Marketing authorisation holder took the opportunity to make minor editorial updates to the SmPC and Package Leaflet.”	
WS0991 **Actos-EMEA/H/C/000285/WS0991/0075** **Competact-EMEA/H/C/000655/WS0991/0062** **Glubrava-EMEA/H/C/000893/WS0991/0047** **Glustin-EMEA/H/C/000286/WS0991/0073** **Tandemact-EMEA/H/C/000680/WS0991/0051** MAH: Takeda Pharma A/S, Lead Rapporteur: Patrick Salmon, Lead PRAC Rapporteur: Almath Spooner, “Submission of the final study report for the Clinical Practice Research Datalink (CPRD) GOLD linkage study (Pioglitazone_5018) conducted to investigate a possible association of the use of pioglitazone with prostate cancer and data on the incidence of adjudicated prostate cancer in patients receiving pioglitazone in the long-term Insulin Resistance Intervention after Stroke (IRIS) trial.”	
WS0992/G **Relvar Ellipta-EMEA/H/C/002673/WS0992/0022/G** **Revinty Ellipta-EMEA/H/C/002745/WS0992/0017/G** MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, “Type II C.I.4:-Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update the safety information and include data from the HZC113782 (SUMMIT) study (designed to investigate whether FF/VI-Furoate/Vilanterol could improve survival in patients with moderate COPD- chronic obstructive pulmonary disease who had, or were at increased risk for CV-cardiovascular disease). The Package Leaflet and Labelling are updated accordingly. The RMP v.8.1 is updated accordingly. Type II C.I.4:- Update of section 4.8 of the SmPC in order to add "paradoxical bronchospasm" to the list of adverse reactions. The Package Leaflet and Labelling are updated accordingly.	

Type IB C.I.z:- Update of section 5.1 the SmPC in order to correct an error identified in the pharmacodynamic section."

B.5.4. PRAC assessed procedures

PRAC Led
Angiox - bivalirudin -
EMEA/H/C/000562/II/0068
MAH: The Medicines Company UK Ltd., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, , "Submission of the drug utilization study Eurovision 2. The RMP has been amended to refine the additional risk minimisation measures in line with the findings of the study."
Request for Supplementary Information adopted on 23.06.2016.

PRAC Led
Defitelio - defibrotide -
EMEA/H/C/002393/II/0019, Orphan
MAH: Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, , "Submission of a revised RMP in order to include information regarding the additional risk minimisation measures (i.e. Healthcare professional material that highlights the existence of the Registry as well as the means to patients into the registry) as outlined in Annex II. In addition, the MAH took the opportunity to add administrative changes to the protocol of the registry study, to add information about the renal pharmacokinetics study, to add updated information about off-label use during postmarketing experience and to include further administrative changes to the RMP."

PRAC Led
Eliquis - apixaban -
EMEA/H/C/002148/II/0040
MAH: Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Submission of the final study report of the AEGEAN study (CV185-220) which assess the education and guidance programme for Eliquis (apixaban) adherence in non-valvular atrial fibrillation patients. The updated risk management plan is also submitted to reflect the results of the study."

PRAC Led

Enbrel - etanercept -

EMEA/H/C/000262/II/0199

MAH: Pfizer Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Rafe Suvarna, , "Submission of a revised RMP (version 6.0) in order to remove 'injection site reactions' as an important potential risk and 'use in pregnant women' , 'use in hepatic and renal impaired subjects' and 'use in different ethnic origins' as missing information. In addition the MAH has taken the opportunity to amend the due dates of several category 3 studies, to align the RMP with GVP module V on Risk Management Systems (revision 1), to review the list of studies included in the Pharmacovigilance plan and to update the clinical trials and post-marketing experience."

PRAC Led

Glivec - imatinib -

EMEA/H/C/000406/II/0103

MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Dolores Montero Corominas, , "Submission of an updated RMP version 9.0 in order to add Hepatitis B reactivation as a new important identified risk."
Request for Supplementary Information adopted on 21.07.2016.

PRAC Led

Noxafil - posaconazole -

EMEA/H/C/000610/II/0040

MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna, , "Submission of a Type II variation C.I.11.b Type II to provide the updated Risk Management Plan (RMP), version 12.0 for the medicinal product Noxafil (40 mg / mL Oral Suspension, 100 mg Tablet and 300 mg concentrate for solution for infusion). The RMP is updated with the study results showing a lack of interaction effect of OATP1B1 and OATP1B3 substrates and inhibitors."
Request for Supplementary Information adopted on 26.05.2016, 25.02.2016.

PRAC Led

Tasigna - nilotinib -

EMEA/H/C/000798/II/0083, Orphan

MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, , "Submission of a revised RMP version 15 in order

to add the new important identified risk “Hepatitis B reactivation”.”
Request for Supplementary Information adopted on 21.07.2016.

PRAC Led
WS0973
Levitra-EMEA/H/C/000475/WS0973/0053
Vivanza-EMEA/H/C/000488/WS0973/0049
MAH: Bayer Pharma AG, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, , “To include in the RMP a safety concern (identified risk) already assessed and implemented in the Levitra/Vivanza product information , positive CHMP Opinion dated 17 December 2015 and EC Decisions dated 22 Jan 2016, respectively; that concomitant use of riociguat with PDE5 inhibitors, including vardenafil, is contraindicated”
Request for Supplementary Information adopted on 15.09.2016.

PRAC Led
WS1011
Abseamed-EMEA/H/C/000727/WS1011/0057
Binocrit-EMEA/H/C/000725/WS1011/0058
Epoetin alfa
Hexal-EMEA/H/C/000726/WS1011/0056
MAH: SANDOZ GmbH, Lead PRAC Rapporteur: Claire Ferard, , “To update the RMP following the PRAC PSUR Assessment Report (EMEA/H/C/PSUSA/00001237/201508) dated 14 April 2016.
PRAC requested the change in the risk classification for “hyperkalemia” and “hypersensitivity reactions (including anaphylactic reactions)” from important potential risks to important identified risks and the review of the table of safety concerns accordingly.
Furthermore the MAH took the opportunity to update RMP to include changes related to the approval of the variation to add the subcutaneous route of administration in nephrology indications (EMEA/H/C/725-727/WS/0877) dated 31 Mar 2016. Appropriate minor updates of RMP have also been made as needed in order to reflect period covered since the last update of RMP (01 Sep 2015 until 29 Feb 2016).”

PRAC Led

WS1015

Ariclaim-EMEA/H/C/000552/WS1015/0065

Cymbalta-EMEA/H/C/000572/WS1015/0069

Duloxetine Lilly-EMEA/H/C/004000/WS1015/0005

Xeristar-EMEA/H/C/000573/WS1015/0072

Yentreve-EMEA/H/C/000545/WS1015/0055

MAH: Eli Lilly Nederland B.V., Duplicate, Duplicate of Yentreve, Lead Rapporteur: Aranzazu Sancho-Lopez, Lead PRAC Rapporteur: Dolores Montero Corominas, , “To update the RMP to add a new Observational Study to Assess Maternal and Fetal Outcomes Following Exposure to Duloxetine (F1J-MC-B057), and to update the plans for the existing pregnancy registry (F1JMC-B034) in section III.4.3 of the RMP.”

PRAC Led

WS1037

Daliresp-EMEA/H/C/002398/WS1037/0029

Daxas-EMEA/H/C/001179/WS1037/0033

Libertek-EMEA/H/C/002399/WS1037/0030

MAH: Takeda GmbH, Lead PRAC Rapporteur: Dolores Montero Corominas, , “To update the due date for FUM 004 in the RMP for a phase 3 clinical study (study number: RO-2455-302-RD) from 'Q3 2016' to 'Q2 2017'.”

B.5.5. CHMP-CAT assessed procedures

Glybera - alipogene tiparvovec - EMEA/H/C/002145/II/0056, Orphan, ATMP

MAH: uniQure biopharma B.V., Rapporteur: Christiane Niederlaender, CHMP Coordinators: Greg Markey,
Request for Supplementary Information adopted on 09.09.2016.

Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - EMEA/H/C/003854/II/0001/G, Orphan,

ATMP MAH: GlaxoSmithKline Trading Services, Rapporteur: Christiane Niederlaender, CHMP Coordinators: Robert James Hemmings,	

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

Cosentyx - secukinumab - EMEA/H/C/003729/II/0011 MAH: Novartis Europharm Ltd, Rapporteur: Tuomo Lapveteläinen Request for Supplementary Information adopted on 21.07.2016.	Weekly start timetable
WS0945/G **Herceptin-EMEA/H/C/000278/WS0945/0115/G** **Kadcyla-EMEA/H/C/002389/WS0945/0026/G** MAH: Roche Registration Limited, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 22.09.2016.	Positive Opinion adopted by consensus on 22.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0970 **Infanrix hexa-EMEA/H/C/000296/WS0970/0203** MAH: GlaxoSmithKline Biologicals, Lead Rapporteur: Bart Van der Schueren This WS also includes NAP products." Opinion adopted on 22.09.2016.	Positive Opinion adopted by consensus on 22.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0979 **Anoro-EMEA/H/C/002751/WS0979/0012** **Incruse-EMEA/H/C/002809/WS0979/0012** **Laventair-EMEA/H/C/003754/WS0979/0013** MAH: Glaxo Group Ltd, Lead Rapporteur: Nithyanandan Nagercoil	Weekly start timetable.
WS0986 **Anoro-EMEA/H/C/002751/WS0986/0010** **Laventair-EMEA/H/C/003754/WS0986/0011** **Relvar Ellipta-EMEA/H/C/002673/WS0986/0024** **Revinty Ellipta-EMEA/H/C/002745/WS0986/0019** MAH: Glaxo Group Ltd, Lead Rapporteur:	Positive Opinion adopted by consensus on 29.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Nithyanandan NagercoilOpinion adopted on 29.09.2016.	
WS0994 **Clopidogrel** **Zentiva-EMEA/H/C/000975/WS0994/0054** **Iscover-EMEA/H/C/000175/WS0994/0127** **Plavix-EMEA/H/C/000174/WS0994/0123** MAH: Sanofi Clir SNC, Lead Rapporteur: Bruno SepodesOpinion adopted on 22.09.2016.	Positive Opinion adopted by consensus on 22.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0997/G **Silodyx-EMEA/H/C/001209/WS0997/0026/G** **Urorec-EMEA/H/C/001092/WS0997/0028/G** MAH: Recordati Ireland Ltd, Lead Rapporteur: Nithyanandan Nagercoil Opinion adopted on 29.09.2016.	Positive Opinion adopted by consensus on 29.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0999/G **Silodyx-EMEA/H/C/001209/WS0999/0025/G** **Urorec-EMEA/H/C/001092/WS0999/0027/G** MAH: Recordati Ireland Ltd, Lead Rapporteur: Nithyanandan Nagercoil Opinion adopted on 29.09.2016.	Positive Opinion adopted by consensus on 29.09.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1008 **Harvoni-EMEA/H/C/003850/WS1008/0034** **Sovaldi-EMEA/H/C/002798/WS1008/0032** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Filip Josephson	Weekly start timetable.
WS1018 **Helixate** **NexGen-EMEA/H/C/000276/WS1018/0179** **KOGENATE** **Bayer-EMEA/H/C/000275/WS1018/0186** MAH: Bayer Pharma AG, Duplicate, Duplicate of KOGENATE Bayer, Lead Rapporteur: Jan Mueller-Berghaus	Weekly start timetable.
WS1025 **Relvar** **Ellipta-EMEA/H/C/002673/WS1025/0026** **Revinty** **Ellipta-EMEA/H/C/002745/WS1025/0022** MAH: Glaxo Group Ltd, Lead Rapporteur:	

Concepcion Prieto Yerro, “To update section 4.4 of the SmPC for FF/VI (Relvar/Revinty) 184/22 mcg strength following the conclusion of the Article 31 Referral (Procedure number: EMEA/H/A-31/1415) regarding pneumonia risk for `Inhaled corticosteroids containing medicinal products indicated in the treatment of chronic obstructive pulmonary disease' (PRAC recommendation March 2016; Commission Decision 29th June 2016) during which section 4.4 of the SmPC for FF/VI 92/22 mcg (Relvar/Revinty) was updated.”	
WS1032 **Abseamed-EMEA/H/C/000727/WS1032/0058** **Binocrit-EMEA/H/C/000725/WS1032/0059** **Epoetin alfa** **Hexal-EMEA/H/C/000726/WS1032/0057** MAH: Hexal AG, Duplicate, Duplicate of Binocrit, Lead Rapporteur: Pierre Demolis, “Alignment with the originator Eprex: sections 2, 4.2, 4.4, 5.1 and 5.2 of the SmPC have been updated as a consequence. The PI has been also updated accordingly. Update of the Instruction For Use (IFU) to include the additional statement (in blue) as minor change: “Instructions on how to inject yourself (for patients with symptomatic anaemia caused by kidney disease, for patients receiving chemotherapy or adult patients scheduled for orthopaedic surgery only).” Alignment to the latest QRD template version 10. Minor typo and format corrections and an update of the Greek, French and Romanian local representatives for Binocrit only were included.”	

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

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

Zinforo (EMEA/H/C/002252/II/0029), (ceftaroline fosamil), MAH: AstraZeneca AB, Rapporteur: Greg Markey, “Update of sections 4.2, 4.4 and 5.1 to amend the S.aureus breakpoints (Susceptible and Resistant). Consequently the package leaflet is amended.” Request for Supplementary Information adopted on 21.07.2016.	Revised timetable for adoption.

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

Information in this section will only be published after start of procedure.

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 during October

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

Opdivo - nivolumab -
EMEA/H/C/003985/II/0022/G
MAH: Bristol-Myers Squibb Pharma EEIG,
Rapporteur: Aranzazu Sancho-Lopez

ReFacto AF - moroctocog alfa -
EMEA/H/C/000232/II/0135
MAH: Pfizer Limited, Rapporteur: Hanne Lomholt Larsen

Savene - dexrazoxane -
EMEA/H/C/000682/II/0031, Orphan
MAH: Clinigen Healthcare Ltd, Rapporteur: Pierre Demolis

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

Levemir - insulin detemir -
EMEA/H/C/000528/II/0082
MAH: Novo Nordisk A/S, Rapporteur: Hanne Lomholt Larsen, “Update of sections 4.4 of the SmPC with additional information regarding avoidance of accidental mix-ups and medication errors.
In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 9.1 and

10.0 and to correct a mistake in the recommendation for use of the first of the two titration algorithms in section 4.2 of the SmPC."

Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0014

MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil, "Update of section 5.3 of the SmPC in order to revise the ivacaftor animal:human exposure ratio. The Package Leaflet is updated accordingly."

Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0097

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen, "Submission of final study report of study 1160.173 "A prospective, open label study to evaluate the pharmacokinetics of dabigatran in non-valvular atrial fibrillation (NVAF) patients with severely impaired renal function on dabigatran etexilate 75 mg BID therapy"."

Rapamune - sirolimus - EMEA/H/C/000273/II/0163/G

MAH: Pfizer Limited, Rapporteur: Kristina Dunder"Update of section 4.4 of the SmPC to update the current warning on angioedema to include a possible dose-dependent effect between sirolimus and angioedema based on post-marketing data. Update of section 4.8 of the SmPC to include neuroendocrine carcinoma of the skin and malignant carcinoma as new ADRs and to include squamous cell carcinoma of the skin and basal cell carcinoma as part of the ADR 'skin cancer' based on post-marketing data. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to combine the 0.5 mg, 1 mg and 2 mg tablets SmPC, to fully detail all components of the Rapamune printing ink in section 6.1 of the SmPC and in the Package Leaflet, to align the wording in section 4 of the Package Leaflet with section 4.8 of the SmPC regarding Clostridium difficile, to update the list of local representatives for the Czech republic, Norway and Sweden in the Package Leaflet and to bring the PI in line with the latest QRD template version 10."

Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0025

MAH: AbbVie Ltd., Rapporteur: Filip Josephson,

"Update of sections 4.3 and 4.5 of the SmPC to add three additional contraindication medications with dronedarone, lurasidone and ranolazine. The Package Leaflet is updated accordingly."	
WS1045 **Entresto-EMEA/H/C/004062/WS1045/0008** **Neparvis-EMEA/H/C/004343/WS1045/0006** MAH: Novartis Europharm Ltd, Lead Rapporteur: Johann Lodewijk Hillege, "Submission of study no. 1570187: Effect of LBQ657 on cloned hERG potassium channels expressed in human embryonic kidney cells. No changes to PI has been proposed."	

B.6.10. CHMP-PRAC assessed procedures

Epclusa - sofosbuvir / velpatasvir - EMEA/H/C/004210/II/0003 MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Margarida Guimarães, "Update of sections 4.4, 4.5 and 5.1 of the SmPC in order to reflect on emerging clinical data from study GS-US-342-1202 investigating efficacy and safety in subjects with chronic hepatitis C virus (HCV) and human immunodeficiency virus (HIV)-1 coinfection. In addition, minor administrative changes are implemented throughout the Product Information."	
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0027/G MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver"C.I.4 (Type II): Submission of the final study report for the study TDM4997g/BO25734 (TH3RESA tudy) to address the safety concerns in Left Ventricular Dysfunction and Safety in Elderly patients. The RMP and Annex II.D are updated. C.I.11.z (Type IB): To update the RMP following the submission of the third annual report of study H4621g. The MAH takes the opportunity to implement the following administrative changes to the RMP: - Inclusion of standard post-authorization data based on PSUR number 4 (reporting period from	

22 February 2015 to 21 February 2016).
- Change of Herceptin picture in the Kadcyla Educational Material to align the picture with the recently approved version of the Herceptin vial label and carton."

Lyxumia - lixisenatide -
EMEA/H/C/002445/II/0020
MAH: Sanofi-Aventis Groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Submission of the final clinical study report for study EFC12382, a randomized double-blind, placebo-controlled, 2 arm parallel group, multicentre study with a 24-week treatment period to assess the efficacy and safety of lixisenatide in patients with T2DM insufficiently controlled with basal insulin or without metformin, in order to fulfil MEA 004. In addition the MAH took the opportunity to update the RMP (version 4.0) accordingly."

Tasigna - nilotinib -
EMEA/H/C/000798/II/0087, Orphan
MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Submission of the final CSR from the clinical drug-drug interaction study CAMN107A2132. An updated RMP version 17 was included as part of the application."

Torisel - temsirolimus -
EMEA/H/C/000799/II/0064, Orphan
MAH: Pfizer Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, "Update of section 4.5 of the SmPC in order to add drug-drug interaction information based upon the PK analysis of Study 3066K1-148-US and supportive literature. The Package Leaflet is updated accordingly."

B.6.11. PRAC assessed procedures

PRAC Led
Zypadhera - olanzapine -
EMEA/H/C/000890/II/0032
MAH: Eli Lilly Nederland B.V., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola "Submission of the final study report of the PASS: Post-Injection Syndrome in Patients with Schizophrenia Receiving Olanzapine Long-Acting Injection.

The Risk Management Plan (version 12) has been revised to reflect the results of the study."

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

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 - EMA Certification Of Plasma Master Files

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

E.1. PMF Certification Dossiers

E.1.1. Annual Update

E.1.2. Variations

E.1.3. Initial PMF Certification

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

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

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

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

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

G. ANNEX G

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

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

Qualification of Biomarkers:

HTA:

G.2. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 10-13 October 2016 CHMP plenary:

G.3.2. List of procedures starting in September 2016 for November 2016 CHMP adoption of outcomes

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