22 February 2016
EMA/CHMP/139839/2016
Procedure Management and Committees Support Division

Committee for medicinal products for human use (CHMP)

Agenda for the meeting on 22-25 February 2016

Chair: Tomas Salmonson – Vice-Chair: Pierre Demolis

22 February 2016, 13:00 – 19:30, room 2A

23 February 2016, 08:30 – 19:30, room 2A

24 February 2016, 08:30 – 19:30, room 2A

25 February 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 22-25 February 2016. See February 2016 CHMP minutes (to be published post April 2016 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 22-25 February 2016.

1.3. Adoption of the minutes

CHMP minutes for 25-28 January 2016.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. - emtricitabine / tenofovir alafenamide - EMEA/H/C/004094

treatment of HIV

Scope: Oral explanation

Report from SAG HIV/viral diseases held on 15 February 2016.

Action: Oral explanation to be held on Tuesday 23 February 11:00

List of Outstanding Issues adopted on 17.12.2015. List of Questions adopted on 24.09.2015.

2.1.2. - infliximab - EMEA/H/C/004020

treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, psoriasis and ulcerative colitis

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday 24 February 2016 at 9.00.

List of Outstanding Issues adopted on 17.12.2015. List of Questions adopted on 23.07.2015.

BWP Report

2.1.3. - migalastat - Orphan - EMEA/H/C/004059

Amicus Therapeutics UK Ltd; treatment of patients with Fabry disease

Scope: Possible Oral Explanation and Opinion

Action: Possible Oral explanation to be held on Tuesday 23 February 2016 at 14.00.

List of Outstanding Issues adopted on 17.12.2015. List of Questions adopted on 22.10.2015.

2.1.4. - opicapone - EMEA/H/C/002790

Parkinson's disease and motor fluctuations

Scope: Oral explanation / Opinion

Action: Possible Oral explanation to be held on Tuesday 23 February 2016 at 9.00.

List of Outstanding Issues adopted on 19.11.2015, 24.09.2015. List of Questions adopted on 23.04.2015.

2.2. Re-examination procedure oral explanations

2.3. Post-authorisation procedure oral explanations

2.4. Referral procedure oral explanations

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. - eftrenonacog alfa - Orphan - EMEA/H/C/004142

Biogen Idec Ltd; treatment and prophylaxis of bleeding in patients with haemophilia B

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.01.2016. List of Questions adopted on 22.10.2015.

BWP Report

3.1.2. - migalastat - Orphan - EMEA/H/C/004059

Amicus Therapeutics UK Ltd; treatment of patients with Fabry disease

Scope: Oral explanation and Opinion

Action: For adoption

List of Outstanding Issues adopted on 17.12.2015. List of Questions adopted on 22.10.2015.

3.1.3. - albutrepenonacog alfa - Orphan - EMEA/H/C/003955

CSL Behring GmbH; treatment and prophylaxis of bleeding in patients with haemophilia B

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 19.11.2015. List of Questions adopted on 23.07.2015.

BWP Report

3.1.4. - trifluridine / tipiracil - EMEA/H/C/003897

treatment of colorectal cancer

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 17.12.2015. List of Questions adopted on 23.07.2015.

3.1.5. - palonosetron - EMEA/H/C/004069

prevention of nausea and vomiting associated with cancer chemotherapy

Scope: Opinion

Action: For adoption

List of Questions adopted on 24.09.2015.

3.1.6. - ixekizumab - EMEA/H/C/003943

treatment of moderate to severe plaque psoriasis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 17.12.2015. List of Questions adopted on 24.09.2015.

BWP Report

3.2. Initial applications; Day 180 list of outstanding issues

3.2.1. - amikacin - Orphan - EMEA/H/C/003936

Insmed Limited; treatment of Mycobacterium avium Complex (MAC) lung disease in adult patients who have persistent positive sputum cultures despite the use of medically appropriate first-line therapy

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 25.06.2015.

3.2.2. - bortezomib - EMEA/H/C/004076

treatment of multiple myeloma

Scope: Revised day 180 list of outstanding issue as adopted by written procedure on 4 February 2016

Action: For information

List of Outstanding Issues adopted on 28.01.2016. List of Questions adopted on 23.07.2015.

3.2.3. - lutetium (177 lu) chloride - EMEA/H/C/003999

radiolabelling of carrier molecules, which have been specifically developed for radiolabelling with this radionuclide

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 24.09.2015.

3.2.4. - pancreas powder - EMEA/H/C/002070

treatment in exocrine pancreatic insufficiency

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 25.06.2015.

BWP Report

3.2.5. - irinotecan - Orphan - EMEA/H/C/004125

Baxter Innovations GmbH; treatment of pancreatic cancer

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 24.09.2015.

3.2.6. - ixazomib - Orphan - EMEA/H/C/003844

Accelerated review

Takeda Pharma A/S; multiple myeloma

Scope: Day 150 list of outstanding issues

Action: For adoption

List of Questions adopted on 17.12.2015.

3.2.7. - palonosetron - EMEA/H/C/004129

prevention of nausea and vomiting associated with cancer chemotherapy

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 24.09.2015.

3.2.8. - saxagliptin / dapagliflozin - EMEA/H/C/004057

treatment of type 2 diabetes

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 24.09.2015.

3.2.9. - autologous cd34+ enriched cell fraction that contains cd34+ cells transduced with retroviral vector that encodes for the human ada cdna sequence - Orphan - ATMP - EMEA/H/C/003854

GlaxoSmithKline Trading Services; severe combined immunodeficiency

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 24.09.2015.

BWP Report

3.2.10. - ceftazidime / avibactam - EMEA/H/C/004027

Complicated intra-abdominal infections (cIAI), Complicated urinary tract infections (cUTI), including pyelonephritis, Nosocomial pneumonia, including ventilator-associated pneumonia, Infections due to aerobic Gram-negative organisms in patients with limited treatment options

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 24.09.2015.

3.2.11. - grazoprevir / elbasvir - EMEA/H/C/004126

treatment of chronic hepatitis C (CHC) in adults

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 19.11.2015.

3.3. Initial applications; Day 120 list of questions

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

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

Scope: Day 120 list of questions

Action: For adoption

3.3.2. - alendronic acid / colecalciferol - EMEA/H/C/004172

treatment of postmenopausal osteoporosis

Scope: Day 120 list of questions

Action: For adoption

3.3.3. - begelomab - Orphan - EMEA/H/C/004144

ADIENNE S.r.l. S.U.; Treatment of graft-versus-host disease

Scope: Day 120 list of questions

Action: For adoption

BWP Report

3.3.4. - bortezomib - EMEA/H/C/004207

treatment of multiple myeloma

Scope: Revised day 120 list of questions as adopted by written procedure on 4 February 2016.

Action: For information

3.3.5. - chenodeoxycholic acid - Orphan - EMEA/H/C/004061

Accelerated review

Sigma-tau Arzneimittel GmbH; treatment of inborn errors of primary bile acid synthesis

Scope: Day 120 list of questions

Action: For adoption

3.3.6. - emtricitabine / tenofovir disoproxil - EMEA/H/C/004137

treatment of HIV-1 infection

Scope: Day 120 list of questions

Action: For adoption

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

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

Scope: Day 120 list of questions

Action: For adoption

3.3.8. - empagliflozin / linagliptin - EMEA/H/C/003833

treatment of type 2 diabetes mellitus

Scope: Day 120 list of questions

Action: For adoption

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

indicated for controlled ovarian stimulation

Scope: Day 120 list of questions

Action: For adoption

BWP Report

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

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

Scope: Day 120 list of questions

Action: For adoption

3.3.11. - 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 120 list of questions

Action: For adoption

BWP Report

3.3.12. - chlorhexidine - Article 58 - EMEA/H/W/003799

Accelerated review; prophylaxis of omphalitis

Scope: Day 120 list of questions

Action: For adoption

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

3.4.1. - palbociclib - EMEA/H/C/003853

treatment of breast cancer

Scope: Letter from the applicant dated 9 February 2016 requesting a extension of clock stop

Action: For information

List of Questions adopted on 17.12.2015.

3.4.2. - rociletinib - EMEA/H/C/004053

treatment of patients with mutant epidermal growth factor receptor (EGFR) non-small cell lung cancer (NSCLC).

Scope: Letter from the applicant dated 11 February 2016 requesting a extension of clock stop

Action: For information

List of Questions adopted on 17.12.2015.

3.4.3. - daclizumab - EMEA/H/C/003862

treatment of multiple sclerosis (RMS)

Scope: Letter from the applicant dated 15 February 2016 requesting a delay of the planned oral explanation until March CHMP meeting.

Action: For information

List of Outstanding Issues adopted on 17.12.2015. List of Questions adopted on 23.07.2015.

BWP Report

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

3.5.1. Dropcys - mercaptamine - Orphan - EMEA/H/C/004038

Lucane Pharma; treatment of corneal cystine deposits

Scope: Grounds for re-examination and procedural timetable

Action: For information

3.6. Initial applications in the decision-making phase

3.7. Withdrawals of initial marketing authorisation application

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

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

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

Amgen Europe B.V.

Rapporteur: Pieter de Graeff, PRAC Rapporteur: Kimmo Jaakkola

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

Action: For adoption

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

4.4.1. 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: Letter from the MAH dated 6 January 2016 requesting 3- month extension of clock stop to respond to Day 120 List of Questions.

"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 information

List of Questions adopted on 19.11.2015.

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. Abilify - aripiprazole - EMEA/H/C/000471/II/0110

Otsuka Pharmaceutical Europe Ltd

Rapporteur: Bruno Sepodes,

Scope: "Extension of Indication to include treatment of schizophrenia in adolescents between 13 – 15 years of age based on paediatric studies 31-09-266 and 31-09-267 submitted according to Article 46 of the paediatric regulation. As a consequence sections 4.1, 4.2 and 4.8 of the SmPC have been updated and the Package Leaflet has been updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 24.09.2015.

5.1.2. Afinitor - everolimus - EMEA/H/C/001038/II/0048

Novartis Europharm Ltd

Rapporteur: Harald Enzmann, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber

Scope: "Extension of Indication to include a new indication for the treatment of unresectable or metastatic, well-differentiated non-functional neuroendocrine tumours of gastrointestinal or lung origin in adults with progressive disease for Afinitor.
As a consequence, sections 4.1, 4.4, 4.8 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

Request for Supplementary Information adopted on 19.11.2015.

5.1.3. Arzerra - ofatumumab - Orphan - EMEA/H/C/001131/II/0041

Novartis Europharm Ltd

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

Scope: "Extension of Indication to include maintenance therapy in Chronic Lymphocytic Leukemia (CLL).
As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
In accordance with the new QRD template version 9.1, the MAH is also taking the opportunity of this procedure to update the Annex II and combine the 2 SmPCs for the 100mg an 1,000mg vials."

Action: For adoption

Request for Supplementary Information adopted on 22.10.2015.

5.1.4. Ferriprox - deferiprone - EMEA/H/C/000236/II/0103

Apotex Europe BV

Rapporteur: Pierre Demolis, Co-Rapporteur: Concepcion Prieto Yerro

Scope: "Extension of Indication to include a new indication for Ferriprox in combination with another chelator.
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the MAH took the opportunity of this procedure to update the Product Information in compliance with the QRD template version 9.1 and combine the SmPC for the 500mg and 1000mg tablets. The contact details of France and Portugal have been updated in the PL."

Action: For adoption

Request for Supplementary Information adopted on 17.12.2015.

5.1.5. Giotrif - afatinib - EMEA/H/C/002280/II/0012

Boehringer Ingelheim International GmbH

Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of Indication to include patients with locally advanced or metastatic NSCLC of squamous histology progressing on or after platinum-based chemotherapy for Giotrif. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and RMP are updated in accordance. Furthermore, minor editorial changes have been introduced throughout the PI.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 22.10.2015.

5.1.6. Humira - adalimumab - EMEA/H/C/000481/II/0149

AbbVie Ltd.

Rapporteur: Kristina Dunder

Scope: "Extension of Indication to include 1st line treatment of moderate to severe chronic plaque psoriasis in adult patients. As a consequence SmPC section 4.1 has been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement minor changes in sections 4.2 and 5.1 of the SmPC."

Action: For adoption

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

Boehringer Ingelheim International GmbH

Rapporteur: Pieter de Graeff, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Miguel-Angel Macia

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

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

Action: For adoption

5.1.8. Opdivo - nivolumab - EMEA/H/C/003985/II/0002

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Pieter de Graeff, PRAC Rapporteur:

Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include treatment as monotherapy of locally advanced or metastatic non-squamous NSCLC after prior chemotherapy in adults based on study CA209057. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly. Further, SmPC section 4.8 has been revised with updated combined clinical trial exposure numbers to reflect inclusion of studies in non-squamous NSCLC and in nivolumab in combination with ipilimumab in advanced melanoma. In addition, the MAH took the opportunity to align the annexes with the latest QRD template version 9.1 and to implement minor editorial changes. A revised RMP version 3.0 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 28.01.2016, 22.10.2015.

5.1.9. Opdivo - nivolumab - EMEA/H/C/003985/II/0008

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Pieter de Graeff, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to add treatment as monotherapy of patients with advanced renal cell carcinoma (RCC) after prior therapy in adults, based on Study CA209025; a phase 3 study of nivolumab vs. everolimus in subjects with advanced or metastatic clear-cell RCC who have received prior anti-angiogenic therapy, and the CA209010 addendum study report; phase 2 dose-ranging study of nivolumab in subjects with progressive advanced/metastatic clear-cell RCC who have received prior anti-angiogenic therapy. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are proposed to be updated and the Package Leaflet is proposed to be updated accordingly. In addition, the MAH took the opportunity to make editorial changes in the SmPC and Package Leaflet.
An updated RMP version 4.0 was provided as part of the application. Further, the MAH requested one additional year of market protection for a new indication."

Action: For adoption

Request for Supplementary Information adopted on 28.01.2016.

5.1.10. Orencia - abatacept - EMEA/H/C/000701/II/0097

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kirsti Villikka

Scope: "Extension of Indication to extend the use of Orencia in combination with methotrexate (MTX) in the treatment of adults with rheumatoid arthritis (RA) who have highly active disease with poor prognostic factors (such as ACPA+ and/or RF+, joint erosion) not previously treated with MTX. As a consequence, sections 4.1 and 5.1 of the SmPC are updated based on results from AVERT study (IM101226). The Package Leaflet is updated accordingly. Moreover, the updated RMP version 20 has been submitted."

Action: For adoption

5.1.11. Ruconest - conestat alfa - EMEA/H/C/001223/II/0031

Pharming Group N.V

Rapporteur: Greg Markey

Scope: "Extension of Indication to include adolescents in the treatment of acute angioedema attacks in adults with hereditary angioedema (HAE) due to C1 esterase inhibitor deficiency. As a consequence sections 4.1, 4.2, and 5.1 of the SmPC have been updated. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 17.12.2015.

5.1.12. TachoSil - human thrombin / human fibrinogen - EMEA/H/C/000505/II/0057

Takeda Austria GmbH

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication for the use of Tachosil as suture line sealing in dura mater closure. As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC and the Package leaflet are updated. The MAH also took the opportunity to make minor editorial corrections to the product information."

Action: For adoption

Request for Supplementary Information adopted on 24.09.2015, 21.05.2015, 22.01.2015.

5.1.13. Zydelig - idelalisib - EMEA/H/C/003843/II/0011

Gilead Sciences International Ltd

Rapporteur: Kristina Dunder, PRAC Rapporteur: Rafe Suvarna

Scope: "Extension of Indication to include new indication for Zydelig to include the combination of idelalisib with ofatumumab. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for United Kingdom and Ireland in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 17.12.2015, 22.10.2015.

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. Opdivo - nivolumab - EMEA/H/C/003985/II/0003

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Pieter de Graeff, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Revised timetable

"Extension of Indication to include treatment in combination with ipilimumab of advanced (unresectable or metastatic) melanoma in adults based on interim data from study CA209067 and the final CSR of study CA209069. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been revised accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC, Annex II and Package Leaflet. An updated RMP version 3.0 was provided as part of the application as well as a paediatric non-clinical biomarker study provided to fulfil paediatric requirements."

Action: For information

Request for Supplementary Information adopted on 28.01.2016, 22.10.2015.

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

6. Ancillary medicinal substances in medical devices

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

6.2. Update of Ancillary medicinal substances in medical devices

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

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

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. - H0004308

Ancillary human blood derivative incorporated in a medical device: human fibrinogen and human thrombin

Scope: Letter from the company dated 14 January 2016 requesting an accelerated assessment

Rapporteur's briefing note

Action: For adoption

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Humalog - Insulin Lispro - EMEA/H/C/000088

Eli Lilly Nederland B.V., treatment of diabetes mellitus

Rapporteur: Robert James Hemmings, Co-Rapporteur: Kristina Dunder

Scope: Humalog Basal (EU/1/96/007/010 and 037) - Cessation for commercial reasons in Lithuania, Italy and Spain

Action: For discussion

9.1.2. Rapamune - sirolimus - EMEA/H/C/000273/II/0160

Pfizer Limited,

Rapporteur: Kristina Dunder

Scope: Request for Supplementary information / Opinion

Submission of the final Clinical Study Report of study B1741007 ("Planned Transition to Sirolimus-based Therapy Versus Continued Tacrolimus (TAC)-based Therapy in Renal Allograft Recipients"). No changes to the PI are proposed.

Action: For adoption

Request for Supplementary Information adopted on 10.12.2015.

10. Referral procedures

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

10.1.1. Tysabri - Natalizumab - EMEA/H/A-20/1416/C/000603/0083

Biogen Idec Ltd, treatment of multiple sclerosis

Rapporteur: Jan Mueller-Berghaus, Co-rapporteur: Daniela Melchiorri, PRAC Rapporteur: Brigitte Keller-Stanislawski;

Scope: Opinion

Review of the benefit-risk balance following notification by the European Commission of a referral under Article 20(8) of Regulation (EC) No 726/2004, based on pharmacovigilance data

Action: For adoption

Scientific Advisory Group meeting held on 06.11.2015. PRAC recommendation.

10.1.2. Sodium-glucose co-transporter-2 (SGLT2) inhibitors: canagliflozin – INVOKANA; canagliflozin, metformin – VOKANAMET; dapagliflozin – FORXIGA; dapagliflozin, metformin – XIGDUO; empagliflozin - JARDIANCE; empagliflozin, metformin – SYNJARDY - EMEA/H/A-20/1419

Applicant: AstraZeneca AB (Forxiga, Xigduo), Boehringer Ingelheim International GmbH (Jardiance, Synjardy), Janssen-Cilag International N.V. (Invokana, Vokanamet)

PRAC Rapporteur: Menno van der Elst;

Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise (Forxiga), Rapporteur: Kristina Dunder, Co-Rapporteur: Agnes Gyurasics (Xigduo), Rapporteur: Pieter de Graeff, Co-Rapporteur: Bart Van der Schueren (Jardiance), Rapporteur: Pieter de Graeff, Co-Rapporteur: Daniela Melchiorri (Synjardy), Rapporteur: Martina Weise, Co-Rapporteur: Kristina Dunder (Invokana), Rapporteur: Martina Weise, Co-Rapporteur: Karsten Bruins Slot (Vokanamet),

Scope: Opinion

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

Action: For adoption

PRAC recommendation

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

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

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

10.4.1. Otipax 1% (11 mg/ml) ear drops, solution – lidocaine hydrochloride - EMEA/H/A-29/1426

Biocodex Benelux SA/NV

Rapporteur: Daniel Brasseur, Co-Rapporteur: Martina Weise,

RMS: BE, CMS: AT, CY, DE, DK, EL, ES, FI, IT, NO, PL, PT, SE, Mutual recognition procedure number: BE/H/0213/001/MR

Scope: List of Outstanding Issues / Opinion

Disagreement regarding efficacy and the evidence of well-established use.

Action: For adoption

List of Questions adopted on 22 October 2015.

10.4.2. Diclofenac 50 mg Tablets - Diclofenac epolamine - EMEA/H/A-29/1434

Altergon Italia srl

Rapporteur: TBA, Co-Rapporteur: TBA,

RMS: UK, CMS: CZ, FR, SK

Decentralised Procedure number: UK/H/5906/001/DC

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

Disagreements regarding the demonstration of bioequivalence in the fed state

Action: For adoption

Letter from HMRA in the UK dated 5 February 2016 notifying of official referral under Article 29 (4) and its grounds.

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

10.5.1. Cymevene IV and associated names - ganciclovir - EMEA/H/A-30/1406

F. Hoffmann-La Roche
Rapporteur: Rugile Pilviniene, Co-Rapporteur: Alar Irs,

Scope: Opinion

Harmonisation exercise for Cymevene IV and associated names. The review was triggered by the European Commission in September 2014, due to the need of harmonisation of the Summary of Product Characteristics across Member State.

Action: For adoption

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

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

Rapporteur: Greg Markey, Co-Rapporteur: Pieter de Graeff,

Scope: List of Outstanding Issues

Harmonisation exercise for Etopophos and associated names

Action: For adoption

List of Questions adopted on 22 October 2015.

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

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

Rapporteur: Greg Markey, Co-Rapporteur: Pieter de Graeff

Scope: List of Outstanding Issues

Harmonisation exercise for Vepesid and associated names

Letter from the European Commission dated 14 October 2015 notifying of an official referral under Article 30.

Action: For adoption

List of Questions adopted on 22 October 2015.

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

Dienogest/Ethinylestradiol containing products indicated in acne - Dienogest / Rapporteur: TBC, Co-Rapporteur: TBC,

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

Action: For adoption

Letter from the MHRA in the UK dated 18 February 2016 notifying of official referral under Article 31 and its grounds

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)

10.11.1. Levonelle 1500mcg tablets and associated names – Levonorgestrel - EMEA/H/A-13/1427

MAH: Gedeon Richter Plc Group of companies

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Daniela Melchiorri RMS: UK, CMS:

AT, BE, CZ, DE, EL, ES, FR, IE, ES, IS, IT, LT, LU, NL, NO, PL, PT, SE, Mutual recognition procedure: UK/H/0803/001/II/022

Scope: Opinion

Action: For adoption

List of Questions adopted on 22 October 2015.

11. Pharmacovigilance issue

11.1. Early Notification System

February 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

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

Meeting date: 23 February 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

13.4.1. 3rd Teleconference of the IPRF Nano Working Group on 11 February 2016

Action: For information

Agenda

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Benefit-risk assessment of the CHMP assessment report template

Scope: Revision of section 5, benefit-risk assessment template and guidance revision: second draft

Action: For adoption

14.1.2. Draft Pilot report Parallel advice Regulators and HTA

Scope: EMA report and annexes on the Pilot of parallel regulatory-HTA scientific advice

Action: For discussion

14.1.3. Proposal for a pre-marketing risk-based model for medicinal product testing – Pilot procedure for human CAPs

Scope: Interim report halfway through the pilot

Action: For discussion

14.1.4. Initial marketing authorisation - revised accelerated assessment procedural timetables

Action: For adoption

14.1.5. Risk Management Plan (RMP) revised assessment process in initial marketing authorisation(s) - performance indicators

Action: For discussion

14.1.6. Enhanced early dialogue to foster development and facilitate accelerated assessment (PRIME)

Scope: Reflection paper

Action: For adoption

14.1.7. Guideline on the scientific application and the practical arrangements necessary to implement Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004

Scope: CHMP guideline on conditional marketing authorisation, Overview of public consultation comments received

Action: For adoption

14.1.8. Strategic Review & Learning Meeting

Reflection on OTC switch in the centralised procedure (follow-up item from Luxembourg presidency meeting)

Action: For discussion and appointment of sponsors

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 **08-11 February 2016**

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 18-19 February 2016
Action: For information

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 1-4 February 2016

Action: For information

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at February 2016 PDCO

Action: For information

Report from the PDCO meeting held on 24-26 February 2016

Action: For information

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 16-18 February 2016
Action: For information

14.2.6. CMDh

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 25-27 February 2016

Action: For information

Scope: Response to CMDh request to CHMP/ PKWP regarding exenatide

Action: For adoption

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 8-11 February 2016. Table of conclusions

Action: For information

Scientific advice letters: Disclosure of information related to scientific advice letters

cannot be released at present time as these contain commercially confidential information.

14.3.2. Invented Names Group (NRG)

Scope: Request for PRAC advice

Potential for name-related confusion identified post-authorisation with 2 CAPs and 1 NAP

Action: For adoption

List of Questions to PRAC

14.3.3. Respiratory Drafting Group (RDG)

Chair: Karolina Törneke

Scope: Nomination of core members to the Respiratory drafting group

Action: For adoption

Scope: Work Plan for 2016

Action: For adoption

14.3.4. Cardiovascular Working Party (CVSWP)

Scope: Reflection paper on assessment of cardiovascular safety profile of medicinal products for the treatment of cardiovascular and metabolic diseases (EMA/CHMP/50549/2015)

Action: For discussion

14.3.5. Blood Products Working Party (BPWP)

Scope: Work Plan for 2016

Action: For adoption

14.3.6. Central Nervous System Working Party (CNSWP)

Scope: Overview of comments received on Guideline on the clinical investigation of medicinal products for the treatment of Duchenne and Becker muscular dystrophy (EMA/30262/2016)

Action: For information

14.3.7. Biologics Working Party (BWP)

Chair: Sol Ruiz

Scope: Revision Guideline on Epidemiological Data on Blood Transmissible Infections and Overview stakeholder comments - (EMA/CHMP/548524/2008 Rev. 1)

Overview of comments (EMA/651460/2015)

Appendices (EMA/735037/2015)

Action: For adoption

14.4. Cooperation within the EU regulatory network

14.5. Cooperation with International Regulators

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

14.7. CHMP work plan

14.8. Planning and reporting

14.9. Others

15. Any other business

15.1. AOB topic

15.1.1. Zika virus update

Action: For information

15.1.2. Update on French clinical trial

Action: For information

15.1.3. EMA notification system

Scope: Test of the EMA notification system

16. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

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)*

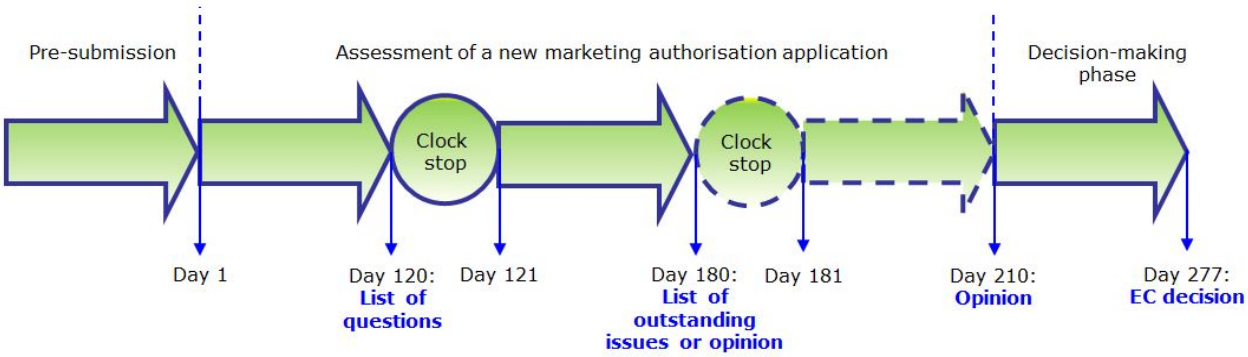
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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