26 February 2016
EMA/CHMP/162442/2016
Procedure Management and Committees Support Division

Committee for medicinal products for human use (CHMP)

Minutes for the meeting on 25-28 January 2016

Chair: Tomas Salmonson – Vice-Chair: Pierre Demolis

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

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified as included in the pre-meeting list of participants and restrictions. See (current) January 2016 CHMP minutes for the 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 25-28 January 2016.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 22 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The Committee welcomed new Croatian member Ines Baotić and alternate member Katarina Vučić, replacing Viola Macolić Šarinić and Ana Dugonjić. The Committee welcomed the Co-opted member Koenraad Norga.

1.2. Adoption of agenda

CHMP agenda for 25-28 January 2016.

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 14-17 December 2015.

The CHMP adopted the minutes.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

No items

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. 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: Oral explanation to be held on Tuesday 26 January 2016 at 11.00

II/0003 “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.”

Request for Supplementary Information adopted on 22.10.2015.

Action: For adoption

An oral explanation was held on Tuesday 26 January 2016 at 11.00.

See also 5.1.4 and 5.1.5. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008; Opinions or Requests for supplementary information

2.4. Referral procedure oral explanations

2.4.1. Novantrone and associated names - mitoxantrone - EMEA/H/A-30/1399

MEDA group of companies and associated companies

Rapporteur: Pieter de Graeff, Co-Rapporteur: Robert Hemmings,

Scope: Oral explanation to be held on Tuesday 26 January 2016 at 15.00 and Opinion

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

Action: For adoption

Scientific Advisory Group meeting held on 06.11.2015.

An oral explanation was held on Tuesday 26 January 2016 at 15.30.

See also 10.5.2. Harmonisation - Referral procedure under Article 30 of Directive 2001/83/EC

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Amlodipine-Valsartan Mylan - amlodipine / valsartan - EMEA/H/C/004037

MYLAN S.A.S.; treatment of essential hypertension

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Exforge

List of Outstanding Issues adopted on 19.11.2015. List of Questions adopted on 25.06.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

3.1.2. Coagadex - human coagulation factor x - Orphan - EMEA/H/C/003855

Accelerated assessment

BIO PRODUCTS LABORATORY; treatment of factor X deficiency

Scope: Opinion

Action: For adoption

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

List of Questions adopted on 19.11.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendations dated 28 January 2016.

The summary of opinion was circulated for information.

The Committee adopted the BWP report.

3.1.3. Empliciti - elotuzumab - Orphan - EMEA/H/C/003967

Accelerated assessment

Bristol-Myers Squibb; treatment of multiple myeloma

Scope: Opinion

Action: For adoption

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

List of Questions adopted on 19.11.2015.

The Committee discussed the wording of the indication, specifically whether the number of prior therapies should be part of the indication for myeloma therapies and wording for SmPC sections 4.1 and 5.1.

The Committee considered not to restrict the treatment to patients with 3 prior lines of therapy but only to mention at least one line of treatment in the indication.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that elotuzumab is a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendation dated 25 January 2016.

The summary of opinion was circulated for information.

The Committee adopted the BWP report.

3.1.4. Rasagiline Mylan - rasagiline - EMEA/H/C/004064

MYLAN S.A.S.; treatment of idiopathic Parkinson's disease

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of AZILECT

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

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

3.1.5. Uptravi - selexipag - Orphan - EMEA/H/C/003774

Actelion Registration Ltd.; treatment of pulmonary arterial hypertension (PAH; WHO Group I)

Scope: Opinion

Action: For adoption

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

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

The Committee discussed the wording of the indication and divergent views were expressed. However it was considered that proposed wording including references to "long-term treatment" and "insufficiently controlled" are appropriate and agreeable.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (25 positive out of 32 votes) together with the CHMP assessment report and translation timetable.

The divergent position (Sol Ruiz, Concepcion Prieto Yerro, Daniela Melchiorri, Nela Vilceanu, Bruno Sepodes, Milena Stain, Pieter de Graeff, Karsten Bruins Slot) was appended to the opinion.

Furthermore, the CHMP considered that selexipag is a new active substance, as claimed by the applicant.

The Icelandic Member was in agreement with the CHMP recommendation, the Norwegian Member was not.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

3.1.6. Zonisamide Mylan - zonisamide - EMEA/H/C/004127

MYLAN S.A.S.; treatment of epilepsy

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Zonegran

List of Questions adopted on 22.10.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

3.2. Initial applications; Day 180 list of outstanding issues

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

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

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 22.10.2015.

BWP report

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.2. - atazanavir - EMEA/H/C/004048

treatment of HIV-1

Scope: 2nd List of outstanding Issues

Action: For adoption

List of Outstanding Issues adopted on 22.10.2015. List of Questions adopted on 21.05.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

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

treatment of multiple myeloma

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.07.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

Post-meeting note: After the Plenary a revised List of Outstanding Issues including an additional question as well as an updated timetable was adopted by written procedure on 4 February 2016.

3.2.4. - pandemic influenza vaccine h5n1 (live attenuated, nasal) - EMEA/H/C/003963

prophylaxis of influenza

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.07.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.5. - allogeneic t cells genetically modified to express suicide gene - Orphan - ATMP - EMEA/H/C/002801

MolMed SpA; treatment in haploidentical haematopoietic stem cell transplantation

Scope: 2nd List of Outstanding Issues

Action: For adoption

List of Outstanding Issues adopted on 26.03.2015. List of Questions adopted on 24.07.2014.

The CHMP was updated on discussions at the CAT and was reminded of the status of this application and its remaining outstanding issues.

The Committee agreed to the 2nd list of outstanding issues as adopted by CAT with a specific timetable.

The CHMP adopted the BWP report.

3.3. Initial applications; Day 120 list of questions

3.3.1. - aceneuramic acid - Orphan - EMEA/H/C/004176

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

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.2. - alectinib - EMEA/H/C/004164

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

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

treatment of multiple myeloma

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

Post-meeting note: After the Plenary a revised List of Outstanding Issues, including an additional question as well as an updated timetable, was adopted by written procedure on 4 February 2016.

3.3.4. - daratumumab - Orphan - EMEA/H/C/004077

Janssen-Cilag International N.V.; treatment of patients with relapsed and refractory multiple myeloma

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application,

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

The CHMP adopted the BWP report.

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

ERYTECH Pharma S.A.; treatment of leukaemia

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

The CHMP adopted the BWP report.

3.3.6. - etelcalcetide - EMEA/H/C/003995

treatment of secondary hyperparathyroidism (SHPT) in adult patients with chronic kidney disease (CKD) on haemodialysis therapy

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.7. - tenofovir disoproxil - EMEA/H/C/004120

treatment of HIV-1 infection and hepatitis B infection

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

3.4.1. - sirolimus - Orphan - EMEA/H/C/003978

Santen Oy; treatment of chronic non-infectious uveitis

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

Action: For adoption

List of Outstanding Issues adopted on 17.12.2015. List of Questions adopted on 25.06.2015.

The CHMP adopted a list of questions to an ad-hoc expert group meeting.

3.4.2. - emtricitabine / rilpivirine / tenofovir alafenamide - EMEA/H/C/004156

treatment of HIV-1

Scope: List of Questions and List of experts to SAG

Action: For adoption

List of Questions adopted on 17.12.2015.

The CHMP adopted a list of questions to the SAG HIV/Viral diseases. The meeting will be held 15 February 2016.

The CHMP adopted the draft list of experts and noted the call for nomination for additional experts to this SAG.

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

treatment of HIV

Scope: List of Questions and List of experts to SAG

Action: For adoption

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

The CHMP adopted the list of experts for the SAG together with a list of questions to this group. The SAG HIV/viral diseases meeting will be held 15 February 2016.

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

treatment of HIV

Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Rafe Suvarna

Scope: Letter from the applicant dated 19 January 2016 requesting an extension of clock stop to submit responses to Day 120 List of Questions adopted on 19.11.2015.

Action: For information

List of Questions adopted on 19.11.2015.

The CHMP agreed to the request by the applicant for an extension of clock stop to submit responses to Day 120 List of Questions adopted on 19.11.2015.

3.4.5. - parathyroid hormone - Orphan - EMEA/H/C/003861

NPS Pharma Holdings Limited; treatment of hypoparathyroidism

Scope: Letter from the applicant dated 21 January 2016 requesting an extension of clock stop to respond to Day 180 list of outstanding issues adopted on 24 September 2015.

Action: For adoption

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to Day 180 list of outstanding issues adopted on 24 September 2015.

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

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

Scope: List of questions to BMWP

Action: For adoption

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

The CHMP agreed to consult the BMWP.

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

APEIRON Biologics AG; treatment of neuroblastoma

Scope: Letter from the applicant dated 11 January 2016 requesting an extension of clock stop to respond to Day 120 list of questions adopted on 24 September 2015 .

Action: For adoption

List of Questions adopted on 24.09.2015.

The Committee agreed to the request from the applicant dated 11 January 2016 requesting an extension of clock stop to respond to Day 120 list of questions adopted on 24 September 2015.

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: Letter from the applicant dated 23 December 2015 requesting the re-examination of the CHMP Opinion adopted 17 December 2015, appointment of Re-examination (Co)Rapporteur

Action: For information

The CHMP noted the letter from the applicant requesting a re-examination and appointed re-examination Rapporteur and re-examination Co-Rapporteur.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. - aripiprazole - EMEA/H/C/004236

treatment of schizophrenia, treatment and prevention of bipolar disorder (manic episodes)

Scope: Letter from the applicant dated 8 January 2016 informing of the decision to withdraw the MAA

Action: For information

List of Questions adopted on 22.10.2015.

Withdrawal assessment Report

Question and answer document

The CHMP noted the letter from the applicant dated 8 January 2016 informing of the decision to withdraw the MAA and agreed to the wording of the withdrawal question-and-answer document.

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. Exjade - deferasirox - Orphan - EMEA/H/C/000670/X/0043

Novartis Europharm Ltd

Rapporteur: Pierre Demolis, PRAC Rapporteur: Corinne Fechant

Scope: "Extension application for a new pharmaceutical form and new strengths (Exjade 90, 180 and 360 mg film-coated tablets)."

Action: For adoption

List of Questions adopted on 23.07.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

4.1.2. Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/X/0022/G

Novartis Europharm Ltd

Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension of indication for paediatric (age 1 year and above) chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients who had an insufficient response to other treatments (e.g. corticosteroids, immunoglobulins).
Grouping with the line extension for one new tablet strength (12.5mg) and a new Powder for Oral Suspension formulation (25mg).

The Type II variation and the Extension are grouped within this Application. This grouping is justified, as one of the variations in the group is an extension of the marketing authorisation (Annex III of Commission Regulation (EC) No 1234/2008 of November 2008). Agreed justification. 120 day TT follows Line extension."

Action: For adoption

List of Outstanding Issues adopted on 19.11.2015. List of Questions adopted on 25.06.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

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

4.2.1. Reyataz - atazanavir / atazanavir sulfate - EMEA/H/C/000494/X/0094/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Joseph Emmerich, Co-Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Arnaud Batz

Scope: “An extension application covering a new pharmaceutical form (oral powder), a new strength for the oral powder presentation (50mg), and a new paediatric indication (patients from 3 months of age and weighing at least 5kg); a type II variation (C.1.6) to updated Reyataz capsules in light of new paediatric data; a type IB (C.I.11) variation to make minor revisions to the RMP with regards to nephrolithiasis, following PRAC's assessment of RMP version 7.3.”

Action: For adoption

List of Questions adopted on 23.07.2015.

The Committee discussed the issues identified in this application, which were related to the PPK model, paediatric dose and quality aspects.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of outstanding issues and a specific timetable.

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

No items

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

4.4.1. Instanyl - fentanyl / fentanyl citrate - EMEA/H/C/000959/X/0030/G

Takeda Pharma A/S

Rapporteur: Pierre Demolis, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Arnaud Batz

Scope: Revised timetable

"Annex I_2.(c) To add the new strength of 400 micrograms/dose in a multi-dose nasal spray in pack size of 10's, 20's, 30's & 40 doses.
Type II cat. B.II.e.4.b) To replace the current multi-dose nasal spray by a new improved child resistant multi-dose nasal spray.
3 X Type IB cat. B.II.e.5.d) To add a new packsize of 30 doses for each current strength (50 micrograms/dose, 100 micrograms/dose & 200 micrograms/dose).
Type IA cat. B.II.d.1.a) – To tighten the assay release limit of the multi-dose finished product to 98.0%-102.0%.
Type IA cat. B.II.f.1.a) 1. – To reduce the shelf life of all strengths of the multi-dose finished product to 24 months.
Additionally, the Applicant took the opportunity to include an editorial change, as to change the wording of the specification footnote regarding the droplet size distribution test from "The test is performed by the vendor on every pumping system batch" to "The test is performed at release of the pumping system"."

Action: For adoption

List of Outstanding Issues adopted on 17.12.2015, 23.07.2015. List of Questions adopted on 26.02.2015.

The CHMP adopted a revised timetable.

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. Humira - adalimumab - EMEA/H/C/000481/II/0147

AbbVie Ltd.

Rapporteur: Kristina Dunder, Co-Rapporteur: Daniela Melchiorri

Scope: “Extension of Indication to include the treatment of patients with moderately paediatric active Crohn’s disease.
As a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated.
In addition, the Marketing authorisation holder (MAH) took the opportunity to implement editorial corrections to the Labelling.”

Action: For adoption

The Committee discussed the issues identified in this application, which were related to the new indication and its rationale.

The Committee adopted Request for Supplementary Information with a specific timetable.

5.1.2. HyQvia - human normal immunoglobulin - EMEA/H/C/002491/II/0021

Baxalta Innovations GmbH

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop,

Scope: “Extension of Indication to include paediatric population for HyQvia.
As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.”

Action: For adoption

The Committee discussed the issues identified in this application and agreed that further clarification on the SmPC wording with regard to presentation of paediatric data was required. In addition some explanation on two conducted clinical trials as well as one planned study was sought.

The Committee adopted Request for Supplementary Information with a specific timetable.

5.1.3. Imbruvica - ibrutinib - Orphan - EMEA/H/C/003791/II/0016

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams

Scope: “Extension of Indication to broaden the existing indication for chronic lymphocytic leukaemia (CLL) to include all previously untreated patients including those with 17p deletion or TP53 mutation based on the results from the final CSR of study PCYC-1115-CA (MEA 021) for Imbruvica. As a consequence, sections 4.1, 4.6, 4.8, 5.1 and 5.3 of the SmPC are being updated. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the SmPC and to bring Annex II in line with the latest QRD template version 9.1. Moreover, the updated RMP version 5.0 has been submitted.”

Action: For adoption

The Committee discussed the issues identified in this application, which were related to the wording of indication, which should reflect present treatment as well as the studied population.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.4. 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: Opinion / Request for Supplementary information, Report by SAG vice-chair, Jonas Bergh from SAG Oncology meeting held on 14 January 2016

"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 22.10.2015.

The Committee discussed the indication and agreed that broad indication (not restricting the indication to patients showing PD-L1 expression) is acceptable, therefore it was considered not relevant to discuss it during oral explanation and oral explanation on this variation was cancelled. The Committee discussed the PD-L1 expression cut-off values and safety data. The Committee concluded that additional analysis on the cut-off points are needed.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

See also 2.3.1. Post-authorisation procedure oral explanations and 5.1.5. for SAG report.

5.1.5. 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: Opinion / Request for Supplementary information, Report by SAG vice-chair, Jonas Bergh from SAG Oncology meeting held on 14 January 2016

Scope: “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 adoption

Request for Supplementary Information adopted on 22.10.2015.

An oral explanation was held on Tuesday 26 January 2016 at 11.00.

The CHMP noted the report from the SAG Oncology meeting held on 14 January 2016. The SAG report concluded that positive association between PD-L1 expression and activity of nivolumab appears to be consistent across trials in the non-SQ NSCLC and melanoma indications. Concerns were expressed about the reliability and clinical utility of the method in view of the dynamic nature of this marker and tumour environment, and the difficulties with PD-L1 determination in clinical practice. The overall effect in terms of progression-free survival (PFS) was considered convincing and of clinical relevance but only at levels of PD-L1 expression <1%. At higher level of expression, the addition of ipilimumab was associated with significant toxicity and there were no added benefit in terms of PFS.

The Committee discussed the wording of indication (indicated only for a subgroup of patients with no or very low PD-L1 expression) and discussed the need to have more mature data. The Committee had different views on it.

The Company’s presentation focussed on describing efficacy results through different endpoints and addressing safety issues. Furthermore PFS data by PD-L1 expressions levels were presented.

The CHMP further discussed the wording of the indication, possible sub-group of patients, efficacy endpoints and agreed that more deliberation was required. Furthermore SmPC changes should be proposed and safety issues addressed.

The Committee adopted 2nd Request for Supplementary Information with a specific timetable.

See also 2.3.1. Post-authorisation procedure oral explanations.

5.1.6. 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

The Committee discussed the issues identified in this application, which were related to the wording of indication.

The Committee adopted Request for Supplementary Information with a specific timetable.

The CHMP agreed by consensus on the one additional year of market protection for a new indication.

5.1.7. Revlimid - lenalidomide - Orphan - EMEA/H/C/000717/II/0079

Celgene Europe Limited

Rapporteur: Pierre Demolis, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Corinne Fechant

Scope: "Extension of Indication to add treatment of adult patients with relapsed and/ or refractory mantle cell lymphoma (MCL). As a consequence, SmPC sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 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. A revised version of the RMP (version 25.0) was provided as part of this application."

Action: For adoption

Request for Supplementary Information adopted on 22.10.2015, 23.07.2015, 26.03.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.8. Ryzodeg - insulin degludec / insulin aspart - EMEA/H/C/002499/II/0017

Novo Nordisk A/S

Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue

Scope: "Extension of Indication to include paediatric population from 1 to 18 year of age for Ryzodeg. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 9.1."

Action: For adoption

The Committee discussed the issues identified in this application. The Committee agreed that further data for children below the age of 6 years should be requested.

The Committee adopted Request for Supplementary Information with a specific timetable.

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. Caprelsa - vandetanib - EMEA/H/C/002315/II/0016

AstraZeneca AB

Rapporteur: Pierre Demolis

Scope: Letter from the MAH dated 22 December 2015 requesting an extension of timeframe to respond to Request for Supplementary Information adopted on 19.11.2015,

"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 19.11.2015.

The CHMP agreed to the request by the applicant for an extension of timeframe to respond to Request for Supplementary Information adopted on 19.11.2015.

5.2.2. Humira - adalimumab - EMEA/H/C/000481/II/0146

AbbVie Ltd.

Rapporteur: Kristina Dunder, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga

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

"Extension of Indication to include treatment of non-infectious intermediate, posterior and panuveitis in adult patients for Humira.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 17.12.2015.

The CHMP adopted a list of questions to an ad-hoc expert group.

5.2.3. Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0022

AstraZeneca AB

Rapporteur: Greg Markey

Scope: Letter from the MAH dated 11 January 2016 requesting an extension of timeframe to respond to Request for Supplementary Information adopted on 24.09.2015.

“Extension of Indication to include new population, children over the age of 2 months and adolescents, for Zinforo. As a consequence, sections 4.1, 4.2, 5.2, 5.3 and 6.6 of the SmPC are updated with new information on dosing, PK and pre-clinical safety. The Package Leaflet is updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.”

Action: For adoption

Request for Supplementary Information adopted on 17.12.2015, 24.09.2015.

The CHMP agreed to the request by the applicant for an extension of timeframe to respond to Request for Supplementary Information adopted on 24.09.2015

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

No items

6. Ancillary medicinal substances in medical devices

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

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: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application, which were related to the quality and clinical data.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

The CHMP adopted the BWP report.

6.2. Update of Ancillary medicinal substances in medical devices

6.2.1. Floseal Hemostatic Matrix (Floseal VH S/D) - Human Thrombin - EMEA/H/D/000956

TÜV SÜD Product Service GmbH, increase in the haemostatic effect

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Greg Markey,

Scope: CHMP recommendation to the Notified Bodies on the risk of intestinal obstruction in Floseal VH SD, Hemoblast and SurgiFlo

Action: For adoption

Ancillary medicinal substance/blood derivative substance (Article 1(4)/1(4a) of both Directives No 93/42/EEC and 90/385/EEC)

Background: In December 2015 CHMP requested PRAC to investigate on the potential risk of intestinal obstruction in Floseal VH SD.

On 12 January 2016 a PRAC Advice to CHMP has been adopted on the risk of intestinal obstruction in Floseal VH SD, Hemoblast and SurgiFlo.

The CHMP adopted the CHMP recommendation by consensus, based on the PRAC advice.

The Icelandic and the Norwegian CHMP members agreed with the above-mentioned recommendation of the CHMP.

6.2.2. Hemoblast – Thrombin - EMEA/H/D/002769

BSI Group, is indicated in surgical procedures

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Robert James Hemmings,

Scope: CHMP recommendation to the Notified Bodies on the risk of intestinal obstruction in Floseal VH SD, Hemoblast and SurgiFlo

Action: For adoption

Ancillary medicinal substance/blood derivative substance (Article 1(4)/1(4a) of both Directives No 93/42/EEC and 90/385/EEC)

The CHMP adopted the CHMP recommendation by consensus, based on the PRAC advice.

The Icelandic and the Norwegian CHMP members agreed with the above-mentioned recommendation of the CHMP.

6.2.3. Surgiflo Haemostatic Matrix Kit Ferrosan - human thrombin - EMEA/H/D/002301

Presafe Denmark A/S, to provide more rapid and consistent haemostasis and support the endogenous clotting process and provide a more stable clot

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Greg Markey,

Scope: CHMP recommendation to the Notified Bodies on the risk of intestinal obstruction in Floseal VH SD, Hemoblast and SurgiFlo

Action: For adoption

Ancillary medicinal substance/blood derivative substance (Article 1(4)/1(4a) of both Directives No 93/42/EEC and 90/385/EEC)

The CHMP adopted the CHMP recommendation by consensus, based on the PRAC advice.

The Icelandic and the Norwegian CHMP members agreed with the above-mentioned recommendation of the CHMP.

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. - masitinib mesylate - Orphan - H0004159

AB Science; Treatment of smouldering or indolent systemic mastocytosis with severe handicaps
Claim 1: Treatment of adult patients with smouldering or indolent systemic mastocytosis with severe handicaps unresponsive to optimal symptomatic treatments.
Claim 2: Treatment of adult patients with aggressive forms of mastocytosis not bearing c-Kit mutation Asp-816-Val (D816V) in at least one organ.

Scope: Request for an accelerated assessment

Action: For adoption

Letter from the company dated 7 January 2016 requesting an accelerated assessment

Rapporteur's briefing note

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.1.2. tenofovir alafenamide - H0004169

treatment of chronic hepatitis B in adults

Scope: Request for an accelerated assessment

Action: For adoption

Letter from the company dated 22 December 2015 requesting an accelerated assessment

Rapporteur's briefing note.

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.1.3. - olaratumab - Orphan - H0004216

Eli Lilly Netherlands; indicated in combination with doxorubicin for the treatment of adult patients with advanced or metastatic soft tissue sarcoma (STS) who are not amenable to curative treatment with surgery or radiotherapy.

Scope: Request for an accelerated assessment

Action: For adoption

Letter from the company dated 8 December 2015 requesting an accelerated assessment

Rapporteur's briefing note.

The CHMP agreed to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Xarelto - Rivaroxaban - EMEA/H/C/000944 - LEG 37

Bayer Pharma AG, prevention of venous thromboembolism (VTE), prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation

Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise,

Scope: Update on ROCKET Trial. Issue with International Normalized Ratio (INR) device used in ROCKET trial and potential impact on the study results for AF indication

Action: For discussion

Request for Supplementary Information adopted on 17.12.2015 and 19.11. 2015.

The CHMP concluded that the defect with the INR device used in the ROCKET study does not change the conclusions on the overall safety or benefit-risk balance of Xarelto. The benefit risk is maintained in the AF population with no need to update the SmPC.

The CHMP concluded that any incorrect measurements obtained with the defective device would have had only a marginal effect on the study results, and the safety of Xarelto remains unchanged.

The CHMP adopted the CHMP assessment report. The CHMP assessment report will be published on the EMA website.

Post-meeting note: the final CHMP assessment report was adopted (for publication on the EMA website) via written procedure on 5 February 2016.

9.1.2. DOAC - Direct oral anticoagulants

Scope: Review of existing scientific information on PK and PD in DOACs

Action: For information

The CHMP agreed with the principle of finalising the legally binding post-authorisation measures (LEGs) as per timelines agreed for individual products. The possibility to evaluate further PK/PD data as part of a research project will be explored. Further discussion expected at future CHMP.

9.1.3. Deltyba - delamanid - Orphan - EMEA/H/C/002552/R/0010

Otsuka Novel Products GmbH,

Rapporteur: Greg Markey, Co-Rapporteur: Daniel Brasseur, PRAC Rapporteur: Rafe Suvarna,

Scope: Renewal

The CHMP adopted an opinion by consensus concluding that the risk-benefit balance of Deltyba remains favourable and therefore recommended by consensus, the renewal of the conditional Marketing Authorisation in accordance with Article 6(3) of Regulation (EC) No 507/2006.

The Icelandic and the Norwegian CHMP members agree with the recommendation of the CHMP.

The CHMP noted the letter of recommendation.

The assessment report will be published on the EMA website.

9.1.4. Review of seed sequencing data - annual influenza vaccines 2015-2016

EMA: Ragini Shivji

Action: For information and adoption

CHMP noted the information gained from this data-gathering exercise and adopted the BWP report.

9.1.5. EYLEA - Aflibercept - EMEA/H/C/002392/MEA/015

Bayer Pharma AG

Rapporteur: Pierre Demolis, PRAC Rapporteur: Isabelle Robine,

Scope: PRAC advice to CHMP

PASS protocol for study 18218: assessment of the safety and drug utilisation of intravitral Eylea in real world clinical practice

Action: For discussion

The PRAC concluded by a majority decision during its January 2016 meeting, that the current PASS proposals were unlikely to provide meaningful results with a substantial impact on the understanding of the risk of Arterial Thromboembolic Events (ATEs) for Eylea and on which a regulatory action can be envisaged. In light of this and the accumulating data, the PRAC concluded that the previously agreed category 3 PASS was no longer justified.

The PRAC also concluded that the MAH should continue to monitor the safety of Eylea in PSURs. In particular, the MAH is requested in the context of the next PSUR (due on 8th February 2016) to review the cumulative evidence with regards to systemic safety and especially ATEs including data from the scientific literature such as the meta-analysis performed by Schmid et al. (Br J Ophthalmol. 2015) and discuss the potential impact on the SmPC wording as applicable.

The Committee discussed the PRAC advice and divergent views were expressed by members.

The CHMP adopted a positive opinion based on the advice by PRAC by majority (27 positive out of 32 votes) together with the assessment report.

The Committee concluded that the previously agreed category 3 PASS was not justified anymore and can be removed from the pharmacovigilance plan in the RMP.

The divergent position (John Joseph Borg, Daniela Melchiori, Pierre Demolis, Bruno Sepodes, Concepcion Prieto Yerro) was appended to the opinion.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

9.1.6. Raxone - idebenone - Orphan - EMEA/H/C/003834/II/0002

Santhera Pharmaceuticals (Deutschland) GmbH,

Rapporteur: John Joseph Borg,

Scope: Opinion or Request for supplementary information

Re-definition of the starting materials

The Committee discussed the new API manufacturer and noted that there are issues, which should be addressed.

The CHMP adopted a request for supplementary information with a specific timetable.

10. Referral procedures

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

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

10.2.1. Medicinal products under development for the treatment of Ebola (EMEA/H/A-5(3)/1410)

Lead Rapporteur: Filip Josephson, Co-Rapporteurs: Pierre Demolis, Jan Mueller-Berghaus, Daniel Brasseur, Johann Lodewijk Hillege, Robert James Hemmings, Sol Ruiz

Scope: CHMP assessment report

Action: For adoption

The CHMP was updated on the latest situation and agreed to close the article 5(3) procedure. The Committee adopted an opinion by consensus. The final CHMP assessment report will be published on the EMA website after deletion of confidential information.

Post-meeting note: A revised opinion was adopted via written procedure after the Plenary on 3 February 2016.

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

No items

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

10.4.1. Linxyd 2 mg/ml, solution for infusion and associated names – linezolid – EMEA/H/A-29/1423

Helm AG

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Greg Markey,

Scope: Procedure withdrawn from the RMS NL and from all CMS

Disagreements regarding the suitability of the manufacturing process.

Action: For discussion

RMS: NL, CMS: IE, UK, Mutual Recognition procedure number: NL/H/3416/001/MR

The CHMP noted the letter from Medicines Evaluation Board in the Netherlands dated 30 July 2015 notifying of an official referral under article 29 and its grounds.

The CHMP noted the letter from Polpharma dated 29 December 2015.

The CHMP noted that the MAH has withdrawn the marketing authorisation from the RMS and all the marketing authorisation applications of the concerned products in Europe. The CHMP agreed to close the procedure.

10.4.2. Linezolid Accord 2 mg/ml, solution for infusion and associated names – linezolid – EMEA/H/A-29/1424

Accord Healthcare Ltd

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Greg Markey,

Scope: Procedure withdrawn from the RMS NL and from 13/14 CMS

Disagreements regarding the suitability of the manufacturing process.

Action: For adoption

RMS: NL, CMS: AT, BE, CY, DE, EE, ES, FI, FR, IE, IT, MT, PL, PT, UK, Mutual Recognition procedure number: NL/H/3365/001/MR

The CHMP noted the letter from Polpharma dated 29 December 2015.

The CHMP noted that the MAH has withdrawn the marketing authorisation from the RMS and all the marketing authorisation applications of the concerned products in Europe. The CHMP agreed to close the procedure.

10.4.3. Tobramycin VVB 300 mg/5 ml nebuliser solution – Tobramycin - EMEA/H/A-29/1428

UAB VVB

Rapporteur: Romaldas Maciulaitis, Co-Rapporteur: Piotr Fiedor

RMS: LT, CMS: BG, EE, HU, LV, PL, RO, Decentralised Procedure Number: LT/H/0112/001/DC

Scope: Opinion

Action: For adoption

The CHMP noted the letter from the State Medicines Control Agency in Lithuania dated 09 October 2015 and updated letter dated 14 October 2015 notifying of an official referral under Article 29(4) and its grounds.

The Committee discussed the clinical relevance of differences between Tobramycin VVB and Tobi Podhaler and noted that the clinical superiority of Tobramycin VVB over Tobi Podhaler is demonstrated based on greater safety in a substantial portion of the target population.

The CHMP adopted a final opinion by consensus concluding that the clinical superiority of Tobramycin VVB has been established over Tobi Podhaler. The Assessment Report was adopted.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

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

10.5.1. Durogesic transdermal patches – fentanyl - EMEA/H/A-30/1413

Janssen-Cilag group of companies and associated companies

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise,

Scope: List of outstanding Issues

Action: For adoption

The CHMP adopted a list of outstanding Issues with a specific timetable.

Submission of responses: 17.03.016

Re-start of the procedure: 31.03.2016

Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 13.04.2016

Comments: 18.04.2016

Updated Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 21.04.2016

LoOI or CHMP opinion: April 2016 CHMP

10.5.2. Novantrone and associated names - mitoxantrone - EMEA/H/A-30/1399

MEDA group of companies and associated companies

Rapporteur: Pieter de Graeff, Co-Rapporteur: Robert Hemmings,

Scope: Oral explanation to be held on Tuesday 26 January 2016 at 15.30 and Opinion

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

Action: For adoption

Scientific Advisory Group meeting held on 06.11.2015

See also 2.4.1. Referral procedure oral explanations

The CHMP noted the PRAC advice on the need for additional risk minimisation measures regarding the risks of leukaemia and cardiotoxicity in the multiple sclerosis (MS) indication.

An oral explanation was held on Tuesday 26 January 2016 at 15.30. The Company presented the safety profile of the product, the risk minimisation measures and its view on the need for additional risk minimisation measures, or the need to monitor adherence to the monitoring requirements. The Company considered the risk minimisation measures already in place sufficient to secure the safety of MS patients, particularly with regard to the risks of cardiomyopathy and leukaemia. The company further considered that the monitoring requirements were known and adequately applied by doctors.

The Committee discussed the educational materials as well as the need to conduct a study to monitor the adherence to the risk minimisation measures. The Committee concluded that proposals should be made in this regard and included in RMP synopsis.

The CHMP adopted a 4th list of outstanding issues with a specific timetable.

Submission of responses: 17.03.2016

Re-start of the procedure: 31.03.2016

Rapporteur joint assessment report circulated to CHMP: 13.04.2016

Comments from CHMP members: 18.04.2016

Updated rapporteur joint assessment report: 21.04.2016

CHMP opinion: April 2016 CHMP

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

10.6.1. Salbutamol 100 microgram/dose, pressurised inhalation suspension – salbutamol/ R03AC02 - EMEA/H/A-31/1433

Sandoz B.V.

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

Article 31 triggered by the MEB in the Netherlands due to a signal of lack of efficacy associated with the use of Salbutamol pressurised inhalation suspension

Action: For adoption

Letter from the MEB in the Netherlands dated 14 January 2016 notifying of official referral under Article 31 and its grounds.

The members were informed that the notification has been withdrawn.

10.6.2. Fusafungine (NAP), nasal and oral solution - EMEA/H/A-31/1420

Les Laboratoires Servier, various

PRAC Rapporteur: Julia Pallos; PRAC Co-rapporteur: Jana Mladá

Scope: Final List of questions and final List of experts for SAG anti-infectives meeting held on 21 January 2016

Action: Adopted by written procedure on 20 January 2016

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

Rapporteur: Kristina Dunder, Co-Rapporteur: Pieter de GraeffScope: Appointment of (Co)Rapporteur, List of Questions and timetable

Article 31 triggered by the MEB in the Netherlands

The CHMP noted the letter from the MEB in the Netherlands dated 25 January 2016 notifying of official referral under Article 31 and its grounds.

The CHMP appointed Kristina Dunder (interest level 1) as Rapporteur and Pieter de Graeff (interest level 1) as Co-Rapporteur.

The Committee adopted a list of questions with a specific timetable.

Notification: 25 January 2016

Start of the procedure (CHMP): January 2016 CHMP

List of questions: 28.01.2016

Submission of responses: 17.03.2016

Re-start of the procedure: 31.03.2016

(Co-)Rapporteur assessment report(s) circulated to CHMP: 13.04.2016

Comments: 18.04.2016

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 21.04.2016

CHMP LoOI/ opinion: April 2016 CHMP

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Action: For information

13.2. Innovation Task Force briefing meetings

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

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Initial marketing authorisation - revised accelerated assessment procedural timetables

Action: For discussion

The CHMP discussed the revised accelerated assessment procedural timetables. Further discussions will be held in February CHMP.

14.1.2. Guideline on safety and efficacy follow-up – RMP of ATMPs Appointment of CHMP Rapporteurs for the revision of the guideline

Scope: Appointment of CHMP Rapporteurs for the revision of the guideline

Action: For discussion

The CHMP appointed CHMP sponsors for the revision of the guideline.

14.1.3. GCP Inspections programme for 2016-2017

Action: For adoption

The CHMP adopted the programme.

14.1.4. 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

Postponed to February 2016 CHMP.

14.1.5. Procedural Advice on the evaluation of advanced medicinal product in accordance with Article 8 of Regulation (EC) No 1394/2007

Action: For discussion

Some of the points that have been identified for the update are as follows:

- Reflect PRAC involvement (as this procedural guideline was issued before the creation of the PRAC) and reflect committee coordination, strengthen CAT/CHMP coordination to avoid as possible divergent views between CAT and CHMP (e.g. Glybera case)

- Discuss the double OE and propose to reduce OE at CHMP only if requested by CHMP

- Give guidance regarding clock-stops

- Update the accelerated assessment section

- Update the re-examination section

The CHMP was informed about the update of the procedural advice. Members from CAT and CHMP were invited to be involved in the update.

14.1.6. Review of experience with the revised RMP review process

Action: For discussion

The members were informed about the experience with the revised RMP review process. As way forward a questionnaire should be developed.

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

Action: For adoption for circulation to the European Commission as per Article 11 of Regulation (EC) No 507/2006

The CHMP adopted the guideline for circulation to the European Commission.

14.1.8. Revision of the benefit-risk assessment section of the CHMP assessment reports

Action: For adoption for circulation to the European Commission as per Article 11 of Regulation (EC) No 507/2006

Postponed to February 2016 CHMP. Members were invited to provide input.

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

Scope: Update on the public consultation of the reflection paper

Action: For discussion

The CHMP was updated on the public consultation of the reflection paper. Further comments can be provided.

14.1.10. Article 83 experience on compassionate use

Action: For discussion

The CHMP discussed the results of analysis. Since the introduction of Article 83 of Regulation EC No 726/2004 in 2005, the CHMP adopted 5 scientific opinions for Compassionate Use for two conditions (hepatitis C and influenza). CHMP was invited to share its views on this topic and identify questions for consideration by the Commission Expert Group on Safe and Timely Access to Medicines for Patients (STAMP). Further comments on the use of the programme should be sent.

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 11-14 January 2016

Action: For information

The CHMP noted the Summary of recommendations and PRAC advice.

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

Action: For adoption

The CHMP adopted the list.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 21-22 January 2016
Action: For information

The CHMP noted the draft minutes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Not applicable this month

14.2.4. Paediatric Committee (PDCO)

Not applicable this month

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 19-21 January 2016
Action: For information

The CHMP noted the report.

14.2.6. CMDh

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

Action: For information

The CHMP noted the report.

Response from PKWP and RIWP to CMDh request for classification of everolimus in the transplant setting as a narrow therapeutic index drug

Action: For adoption

The CHMP adopted the response to CMDh.

Request from CMDh dated 14 January 2016 to CHMP to develop a specific scientific guidance for allergies with lower prevalence to address critical issues in relation to the data generation for corresponding allergen products

Action: For discussion

The CHMP discussed the request. The CHMP agreed for a drafting group to propose a possible scope of this request with further discussions expected.

Response to CMDh request to CHMP/BWP regarding on Biosimilars of Low Molecular Weight Heparins (EMA/CHMP/BWP/764782/2015)

Action: For adoption

The CHMP adopted the response to CMDh.

Response to CMDh request to CHMP/ PKWP regarding exenatide

Action: For adoption

The CHMP adopted the response to CMDh.

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 11-14 January 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. Radiopharmaceuticals Drafting Group

Scope: **Work Plan for the Radiopharmaceuticals Drafting Group 2016**

Action: For adoption

The CHMP adopted the Work Plan.

Scope: **Guideline on core SmPC and Package Leaflet for nanocolloidal technetium (99mTc) albumin** (EMA/CHMP/831653/2015)

Action: For adoption

The CHMP adopted the guideline for 3-months public consultation. The guideline describes the information to be included in the SmPC and package leaflet for nanocolloidal technetium (99mTc) albumin.

Scope: **Guideline on core SmPC and Package Leaflet for gadopentetate dimeglumine** (EMA/CHMP/831877/2015)

Action: For adoption

The CHMP adopted the guideline for 3-months public consultation. The guideline describes the information to be included in the SmPC and package leaflet for gadopentetate dimeglumine.

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz,

Scope: **Draft agenda for BWP face-to-face meeting to be held 15-17 February 2016** (EMA/CHMP/BWP/19300/2015)

Action: For information

The CHMP noted the agenda.

Scope: **Final minutes from face-to-face meeting held 9-11 November 2015** (EMA/CHMP/BWP/749788/2015)

Action: For information

The CHMP noted the minutes.

14.3.4. Central Nervous System Working Party (CNSWP)

Scope: **Guideline on the clinical investigation of medicines for the treatment of Alzheimer's disease and other dementias** (EMA/CHMP/539931/2014)

Action: For adoption for 6-months consultation

The CHMP adopted the guideline for 6-months public consultation. The guideline aims to provide guidance for the evaluation of any medicinal product for treatment across the AD continuum. In addition, development strategies for disease prevention are addressed. The usefulness of combination therapy targeting multiple pathophysiological mechanisms and their corresponding study designs are discussed.

Scope: **Overview of comments received on Guideline on clinical investigation of medicinal products for the treatment of Amyotrophic Lateral Sclerosis (ALS)** (EMA/CHMP/131550/2015)

Action: For information

The CHMP noted the overview of comments received.

14.3.5. International Council on Harmonisation (ICH)

Scope: **ICH guideline E18 on genomic sampling and management of genomic data - Step 3**

Action: For adoption for public consultation

The CHMP adopted the guideline for 4-months public consultation.

Scope: **ICH guideline E14: The clinical evaluation of QT/QTc interval prolongation and proarrhythmic potential for non-antiarrhythmic drugs (R3) - Step 4 questions and answers**

Action: For adoption

The CHMP adopted the guideline.

14.3.6. Vaccines Working Party (VWP)

Scope: Nomination of a core member in replacement of Kari Lankinen.

Nomination will be postponed until April CHMP to be handled at the same time as the other vacancies.

Nominations will be considered collectively.

Action: For adoption

Scope: Call for nomination for 2 more core members to replace Michael Pfleiderer and Stefania Salmaso

Expertise sought: Immunology, clinical trials for vaccines, virology/microbiology, quality (liaison with BWP), pharmacoepidemiology. Timelines: nominations should be put forward until the 8th of April 2016.

Action: For information

The CHMP noted the call.

14.3.7. Quality Working Party (QWP)

Chair: Jean-Louis Robert

Scope: **Revised mandate, objectives and rules of procedure for the joint CHMP/CVMP Quality Working Party**

Action: For adoption

The CHMP adopted the revised mandate, objectives and rules of procedure for the joint CHMP/CVMP Quality Working Party.

Scope: **Guideline on the sterilisation of the medicinal product, active substance, excipient and primary container**

Action: For adoption for public consultation

The CHMP adopted the guideline for 6-month public consultation. The guideline provides guidance on the documentation expected for sterile products in the quality dossier for a marketing authorisation application or a variation application for a medicinal product, (quality dossier), and the selection of appropriate methods of sterilisation for sterile products.

Scope: **Q/A on sterilisation of primary packaging**

Action: For adoption

The CHMP adopted the Q&A.

14.3.8. Biosimilar Medicinal Products Working Party (BMWP)

Scope: **Workshop on immunogenicity assessment of biotechnology derived therapeutic proteins to be held on 9 March 2016**

Action: For information

Draft agenda

The CHMP noted the information on the workshop. The workshop is held to discuss the draft CHMP/Biosimilar Medicinal Products Working Party (BMWP) guideline on immunogenicity assessment of biotechnology-derived therapeutic proteins. Participants will include experts from the BMWP, the Biostatistics Working Party (BWP), other regulatory authorities and stakeholders who provided comments on the draft guideline as well as specifically invited interested parties.

14.3.9. Oncology Working Party (ONCWP)

Scope: **Work plan for the CHMP Oncology Working Party for 2016** (EMA/CHMP/707548/2015)

Action: For adoption

The CHMP adopted the Work Plan 2016.

14.3.10. 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

The CHMP discussed the reflection paper. The reflection paper intends to provide guidance on how to assess cardiovascular safety profile of a new product for the treatment of cardiovascular and metabolic diseases. The CHMP discussed the scope of the paper. Further discussions will be held in February CHMP. Members were invited to express their views meanwhile in writing.

Scope: **Draft Guideline on clinical investigation of medicinal products for the treatment of chronic heart failure** (EMA/CHMP/47656/2015 Rev 2)

Action: For adoption for 6-months public consultation

The CHMP adopted the guideline for 6-months public consultation. The scope of the guideline was restricted to the development of medicinal products for the treatment of patients with chronic heart failure including those in the post-acute phase of heart failure. The guideline is intended to assist applicants during the development phase and for guidance only.

Nomination of Bart van der Schueren as new observer from Belgium

Action: For adoption

The CHMP adopted the new observer.

14.3.11. Safety Working Party (SWP)

Nomination of Petre Cojocaru as new alternate for Romania

Action: For adoption

The CHMP adopted the new alternate.

14.3.12. Blood Products Working Party (BPWP)

Guideline on core SmPC for human plasma derived and recombinant coagulation factor VIII products (EMA/CHMP/BPWP/1619/1999 Rev 2)

Action: For adoption

The CHMP adopted the guideline. The guideline describes the information to be included in the Summary of Product Characteristics (SmPC) for human plasma derived and recombinant coagulation factor VIII products, which are indicated for use in the treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency).

Guideline on the clinical investigation of recombinant and human plasma-derived factor VIII products (EMA/CHMP/BPWP/144533/2009 Rev 1)

Action: For adoption

The CHMP adopted the guideline. The guideline describes the information to be documented when an application for a marketing authorisation for recombinant or human plasma-derived factor VIII products is made for use in treatment and prevention of bleeding in patients with haemophilia A. The guidance covers clinical investigations to be conducted pre- and post-marketing authorisation. Guidance is also provided for authorised products where a significant change in the manufacturing process has been made.

Draft Guideline on the core SmPC for Human Anti-D Immunoglobulin for Intramuscular Use (EMA/CHMP/BPWP/29205/2005 Rev 2)

Action: For adoption for public consultation

The CHMP adopted the guideline for 3-months public consultation. The guideline describes the information to be included in the SmPC for a human anti-D immunoglobulin for intramuscular use. With respect to the previous version, this Core SmPC has been adapted to the current QRD template. The method of administration for overweight patients has been specified.

Draft Guideline on the Core SmPC for Human Anti-D Immunoglobulin for Intravenous Use (EMA/CHMP/BPWP/319619/2005 Rev 2)

Action: For adoption for public consultation

The CHMP adopted the guideline for 3-months public consultation. The guideline describes the information to be included in SmPC for a human anti-D immunoglobulin for intravenous use. With respect to the previous version, this Core SmPC has been adapted to the current QRD template. The method of administration has been clarified for intravenous products that also have dosage recommendation for intramuscular use, in particular for obese patients.

14.3.13. Biostatistics Working Party (BSWP)

Nomination of 2 core members following resignation of Marco Massari and Peter Volkers

Action: For adoption

The CHMP noted the nominations received and appointed the proposed new core members: Christian Gartner (AT) and Jörg Zinserling (DE).

14.3.14. Excipients Drafting Group (ExcpDG)

Scope: Election of Chair and Vice-chair of the ExcpDG

Action: For adoption

The CHMP elected Dominique Masset as chair and Laivi Saaremäel as vice-chair of the excipients drafting group.

14.3.15. Respiratory Drafting Group (RDG)

Scope: **Nomination of core members to the Respiratory drafting group**

Establishment of the core members of the Respiratory Drafting Group, convened to provide assistance to the CHMP with revision of the guidelines on clinical development of medicinal products for the treatment of cystic fibrosis and orally inhaled medicinal products.

Action: For adoption

The CHMP nominated David Lyons (IE), Janet Schriever (DE) and Hanneke van der Woude (NL) as new core members to the RDG.

Scope**: Call for further members.** Expertise required: respiratory disease, cystic fibrosis, orally inhaled medicinal products, asthma, COPD

All CHMP members are invited to submit nominations of experts

The CHMP noted the call for further members.

Scope**: Work Plan for 2016**

Discussion and adoption are expected in February 2016 CHMP.

14.3.16. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus / Nils Feltelius,

Update on the election of the RIWP WP Vice-Chair

14.3.17. Guideline Consistency Group (GCG)

The extension of deadline of the call for nomination. Expressions of interest for one additional member should be sent.

Action: For information

The CHMP noted the information.

14.4. Cooperation within the EU regulatory network

14.4.1. Antimicrobial Advice ad hoc expert group (AMEG) Colistin action plan 2016

Action: For discussion

The CHMP discussed the action plan. The action plan relates to the use of colistin in animals.

14.4.2. Letter from the European Commission on a definition for 'principal molecular structural features'

Scope: Update the CHMP on progress

Letter from the European Commission, requesting that a definition for 'principal molecular structural features' as referred to in Art 3(3)c of Reg (EC) No 847/2000 on similar active substance is developed by end of February 2016

Action: For discussion

The CHMP discussed the letter. Drafting group is working on this.

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

14.7.1. CHMP 2016 Work Plan

Action: For adoption

Letter from the European Commission dated 4 December 2015 regarding CHMP Work Plan.

The CHMP adopted the 2016 Work Plan. The CHMP noted the letter from the European Commission.

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. Information on the French trial

The Committee was updated by the French delegation on the serious adverse events during a French clinical trial.

16. List of participants

List of participants including any restrictions with respect to involvement of members/alternates/ experts following evaluation of declared interests for the 25-28 January 2016 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Daniel Brasseur	Member	Belgium	No interests declared	
Bart Van der Schueren	Alternate	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Ines Baotic	Member	Croatia	No restrictions applicable to this meeting	
Katarina Vučić	Alternate	Croatia	No interests declared	
Panayiotis Triantafyllis	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Jens Heisterberg	Member	Denmark	No restrictions applicable to this meeting	
Sinan B. Sarac	Alternate	Denmark	No interests declared	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Pierre Demolis	Member (Vice-Chair)	France	No interests declared	
Joseph Emmerich	Alternate	France	No interests declared	
Harald Enzmann	Member	Germany	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Dimitrios Kouvelas	Member	Greece	No interests declared	
George Aislaitner	Alternate	Greece	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Agnes Gyurasics	Member	Hungary	No interests declared	
Melinda Sobor	Alternate	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	Iceland	No interests declared	
David Lyons	Member	Ireland	No restrictions applicable to this meeting	
Daniela Melchiorri	Member	Italy	No interests declared	
Natalja Karpova	Alternate	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No restrictions applicable to this meeting	
John Joseph Borg	Member	Malta	No interests declared	
Pieter de Graeff	Member	Netherlands	No interests declared	
Johann Lodewijk Hillege	Alternate	Netherlands	No interests declared	
Karsten Bruins Slot	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No restrictions applicable to this meeting	
Piotr Fiedor	Member	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Patricia Silva	Alternate	Portugal	No interests declared	
Nela Vilceanu	Member	Romania	No interests declared	
Jan Mazag	Member	Slovakia	No interests declared	
Nevenka Tršinar	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Arantxa Sancho-Lopez	Alternate	Spain	No interests declared	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Greg Markey	Member	United Kingdom	No interests declared	
Nithyanandan Nagercoil	Alternate	United Kingdom	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Robert James Hemmings	Co-opted member	United Kingdom	No restrictions applicable to this meeting	
Koenraad Norga	Co-opted member	Belgium	No restrictions applicable to this meeting	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Jean-Louis Robert	Co-opted member	Luxembourg	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Ana Gutierrez	Expert - in person*	Spain	No interests declared	
Concepsion Payares	Expert - in person*	Spain	No restrictions applicable to this meeting	
Jorge Camarero Jiménez	Expert - in person*	Spain	No restrictions applicable to this meeting	
Mette Tranholm	Expert - in person*	Denmark	No interests declared	
Viola Macolic Sarinic	Expert - in person*	Croatia	No interests declared	
Krishna Prasad	Expert - via telephone*	United Kingdom	No restrictions applicable to this meeting	
Valentina Mantua	Expert - via telephone*	Italy	No restrictions applicable to this meeting	
Christian Schneider	Expert - via telephone*	Denmark	No interests declared	
Giuseppe Rosano	Expert - in person*	Italy	No interests declared	
Claudia Gramiccioni	Expert - via telephone*	Italy	No interests declared	
Lorenzo Montrasio	Expert - via telephone*	Italy	No interests declared	
Valérie Lescrainier	Expert - in person*	Belgium	No interests declared	
Bengt Ljungberg	Expert - in person*	Sweden	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Malin Filler	Expert - via telephone*	Sweden	No interests declared	
Sean Barry	Expert - via telephone*	Ireland	No restrictions applicable to this meeting	
Jonas Bergh	Expert - via telephone*	Sweden	No restrictions applicable to this meeting	
Barbara Spruce	Expert - via telephone*	United Kingdom	No restrictions applicable to this meeting	
Stefan Vieths	Expert - via telephone*	Germany	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Maaike van Dartel	Expert - via telephone*	The Netherlands	No interests declared	
Hanneke Van der Woude	Expert - via telephone*	The Netherlands	No interests declared	
Elisabeth Johanne Rook	Expert - via telephone*	The Netherlands	No interests declared	
Lieke Sandberg	Expert - via telephone*	The Netherlands	No interests declared	
Abidali Fazal	Expert - via telephone*	United Kingdom	No interests declared	
Sabine Lenton	Expert - via telephone*	United Kingdom	No interests declared	
Brigitte Mueller	Expert - via telephone*	Austria	No interests declared	
Karl Broich	Expert - via telephone*	Germany	No interests declared	
Jana Schweigertova	Expert - in person*	Slovakia	No restrictions applicable to this meeting	
Bertil Jonsson	Expert - via telephone*	Sweden	No interests declared	
Maarten Lagendijk	Expert - via telephone*	The Netherlands	No interests declared	
A representative from the European Commission attended the meeting				

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Meeting run with support from relevant EMA staff				

17. 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)*

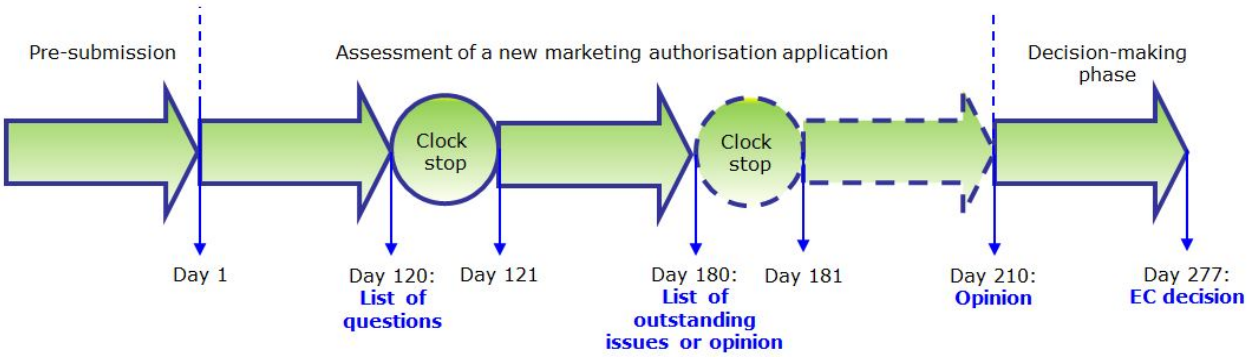
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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