22 July 2016
EMA/CHMP/498012/2016
Procedure Management and Committees Support Division

Committee for medicinal products for human use (CHMP)

Minutes for the meeting on 20-23 June 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) June 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 20-23 June 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.

1.2. Adoption of agenda

CHMP agenda for 20-23 June 2016

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 23-26 May 2016.

The CHMP adopted the minutes.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. - miglustat - EMEA/H/C/004016

treatment of Gaucher disease

Scope: Oral explanation

Action: Oral explanation to be held on 21 June 2016 at 16:00

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

An oral explanation was held on 21 June 2016 at 16:00.

See 3.2.6 Initial applications; Day 180 list of outstanding issues

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

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

MAH: PTC Therapeutics International Limited,

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus,

Scope: Oral explanation, Type II variation

"Update of sections 4.4, 4.6, 4.7, 4.8, and 5.1 of the SmPC and Annex II in order to reflect the result from the submitted study TC124-GD-020-DMD object of SOB 001. The Package Leaflet and the RMP are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some minor editorial changes throughout the Product information."
Request for Supplementary Information adopted on 01.04.2016.

Scope: Oral explanation, Renewal of Marketing Authorisation
Request for Supplementary Information adopted on 28.04.2016.

Action: Oral explanation to be held on Tuesday 21 June 2016 at 10:00.

Participation of patients' representatives

An oral explanation was held on Tuesday 21 June 2016 at 10:00.

See also 9.1.5 Post-authorisation issues

2.4. Referral procedure oral explanations

2.4.1. Alkem Laboratories Limited, India - EMEA/H/A-31/1436

Rapporteur: Harald Enzmann, Co-Rapporteur: Greg Markey,

Scope: Opinion

Article 31 procedure triggered by BfArM concerning studies performed by Alkem Laboratories, Department of Bioequivalence, C-17/7, MIDC Industrial estate, Taloja, Dist. Raigad – 410 208, India between March 2013 and March 2015, following critical GCP deficiencies reported during an inspection performed by BfArM and IGZ in 2015.

Action: Oral explanation to be held on 21 June 2016 at 14:30.

List of questions adopted on 01.04.2016.

An oral explanation was held on 21 June 2016 at 15:30.

See also 10.6.1. Referral under article 31

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Aerivio Spiromax - fluticasone propionate / salmeterol - EMEA/H/C/002752

Teva B.V.; treatment of asthma and COPD

Scope: Opinion

Action: For adoption

Hybrid application (Article 10(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 01.04.2016. 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.

3.1.2. Airexar Spiromax - fluticasone propionate / salmeterol - EMEA/H/C/004267

Teva B.V.; treatment of asthma and COPD

Scope: Opinion

Action: For adoption

Hybrid application (Article 10(3) of Directive No 2001/83/EC), Duplicate of Aerivio Spiromax

List of Outstanding Issues adopted on 01.04.2016. 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.

3.1.3. Atazanavir Mylan - atazanavir - EMEA/H/C/004048

MYLAN S.A.S.; treatment of HIV-1

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 28.04.2016, 28.01.2016, 22.10.2015. List of Questions adopted on 21.05.2015.

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 summary of opinion was circulated for information.

3.1.4. Cinqaero - reslizumab - EMEA/H/C/003912

Teva Pharmaceuticals Limited; treatment of asthma and elevated blood eosinophils who are inadequately controlled on inhaled corticosteroids

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 28.04.2016. 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.

Furthermore, the CHMP considered that reslizumab is new active substances, 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 23 June 2016.

The summary of opinion was circulated for information.

The CHMP adopted the BWP report.

3.1.5. Nordimet - methotrexate - EMEA/H/C/003983

Nordic Group B.V.; treatment of active rheumatoid arthritis; severe, active juvenile idiopathic arthritis; severe recalcitrant disabling psoriasis

Scope: Opinion

Action: For adoption

Hybrid application (Article 10(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 28.04.2016. List of Questions adopted on 17.12.2015.

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.

3.1.6. Zalmoxis - allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - Orphan - ATMP - EMEA/H/C/002801

MolMed SpA; treatment in haploidentical haematopoietic stem cell transplantation

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 01.04.2016, 28.01.2016, 26.03.2015. List of Questions adopted on 24.07.2014.

The CHMP was updated on the discussions from the June 2016 CAT meeting. The CHMP discussed the specific obligations to complete post-authorisation measures for the conditional marketing authorisation and endorsed these.

The Committee adopted a positive opinion based on the opinion taken by the CAT at their June 2016 meeting and CAT opinion adopted via written procedure recommending the granting of a conditional marketing authorisation by majority (27 positive out of 30) together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) is a new active substance, as claimed by the applicant.

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

The divergent position (Sol Ruiz, Arantxa Sancho Lopez, Joseph Emmerich) was appended to

the opinion.

The CHMP noted the letter of recommendation dated 16 June 2016.

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

The summary of opinion was circulated for information.

The CHMP adopted the BWP report and assessment report on similarity.

3.2. Initial applications; Day 180 list of outstanding issues

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

treatment of HIV-1 infection

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 25.02.2016.

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.

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

treatment of type 2 diabetes mellitus

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 25.02.2016.

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.

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

treatment of breast cancer

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 17.12.2015.

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.

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

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

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 28.01.2016.

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.

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

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

Scope: 2nd Day 180 list of outstanding issue

Action: For adoption

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

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.

3.2.6. - miglustat - EMEA/H/C/004016

treatment of Gaucher disease

Scope: Oral explanation

Action: Oral explanation to be held on 21 June 2016 at 16:00.

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

An oral explanation was held on 21 June 2016 at 16:00.

The CHMP adopted a 2nd list of outstanding issues.

The CHMP agreed to the request by the applicant for an extension of clock stop with a specific timetable.

See also 2.1.1 Pre-authorisation procedure oral explanations

3.3. Initial applications; Day 120 list of questions

3.3.1. - paclitaxel - Orphan - EMEA/H/C/004154

Oasmia Pharmaceutical AB; treatment of ovarian cancer

Scope: Day 120 list of questions

Action: For adoption

Request for extension of timeframe permitted to respond to Day 120 questions 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 agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions.

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

treatment of complicated skin and soft-tissue infections

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. - olaratumab - Orphan - EMEA/H/C/004216

Accelerated assessment

Eli Lilly Nederland B.V.; treatment of soft tissue sarcoma

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 similarity assessment report

The CHMP adopted the BWP report.

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

treatment of moderate to severe active rheumatoid arthritis (RA)

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 agreed to consult the Safety Working Party (SWP) and adopted a list of questions to SWP.

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

bene-Arzneimittel GmbH; treatment of Interstitial Cystitis

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application. Furthermore SAG involvement was considered necessary.

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

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

chronic hepatitis B in adults

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

for the treatment of hyperkalaemia

Scope: Letter from the applicant dated 8 June 2016 requesting an extension of clock stop to respond to the List of Questions adopted on 28.04.2016.

Action: For information

List of Questions adopted on 28.04.2016.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 28.04.2016.

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

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

Scope: Letter from the applicant dated 14 June 2016 requesting an extension of clock stop to respond to the List of Outstanding Issues adopted on 19.11.2015.

Action: For discussion

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

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Outstanding Issues adopted on 19.11.2015.

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

treatment of HIV-1

Scope: Letter from the applicant dated 16 June 2016 requesting an extension of clock stop to respond to the List of Outstanding Issues adopted on 26.05.2016.

Action: For adoption

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

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Outstanding Issues adopted on 26.05.2016.

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

APEIRON Biologics AG; treatment of neuroblastoma

Scope: Letter from the applicant dated 13 June 2016 requesting an extension of clock stop to respond to the List of Outstanding Issues adopted on 26.05.2016.

Action: For adoption

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

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Outstanding Issues adopted on 26.05.2016.

3.4.5. - dimethyl fumarate - EMEA/H/C/002157

treatment of moderate to severe plaque psoriasis in adults in need of systemic drug therapy, treatment of plaque psoriasis

Scope: Letter from the applicant dated 14 June 2016 requesting an extension of clock stop to respond to the list of questions adopted on 28.04.2016.

Action: For adoption

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the list of questions adopted on 28.04.2016.

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

GMP-Orphan SA; Wilson's disease

Scope: Letter from the applicant dated 2 June 2016 requesting an extension of clock stop to respond to the list of questions adopted on 28.04.2016.

Action: For adoption

List of Questions adopted on 28.04.2016

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the list of questions adopted on 28.04.2016.

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

3.5.1. Ninlaro - ixazomib - Orphan - EMEA/H/C/003844

Takeda Pharma A/S; multiple myeloma

Scope: Appointment of re-examination rapporteurs, draft timetable, SAG involvement, call for nominations of experts

Action: For discussion

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

Opinion adopted on 26 May 2016.

Letter from the applicant dated 6 June 2016 requesting a re-examination of the Opinion adopted on 26 May 2016 and consultation of Scientific Advisory Group.

The CHMP appointed re-examination Rapporteur and re-examination Co-Rapporteur.

The CHMP agreed to consult a SAG and adopted the draft timetable.

The CHMP noted the call for nominations of experts for Ninlaro SAG Oncology meeting.

Nominations of experts in multiple myeloma to be sent by 25 July 2016.

3.5.2. Sialanar - glycopyrronium bromide - PUMA - EMEA/H/C/003883

Proveca Limited; Symptomatic treatment of sialorrhoea (chronic pathological drooling) in children and adolescents aged 3 to <18 years with neurological disorders.

Scope: Call for nomination of experts to ad-hoc expert group, list of questions to ad-hoc expert group

Request for nomination of experts to ad-hoc expert group with the following expertise:

- Experts in Paediatric Palliative Medicine
- Paediatric neurologists
- General paediatricians who may follow such patients regularly and may have experience with the treatment of this condition.

Action: For adoption

Opinion adopted on 28.04.2016.

The CHMP noted the call for additional experts. The CHMP adopted the list of experts and the list of questions to this group.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. - drisapersen - Orphan - EMEA/H/C/003846

BioMarin International Limited; treatment of Duchenne muscular dystrophy (DMD)

Scope: Letter from the applicant dated 31 May 2016 informing of the decision to withdraw the MAA application.

Action: For information

The CHMP noted the withdrawal letter.

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

Insmed Limited; treatment of Mycobacterium avium Complex (MAC) lung disease in adults.

Scope: Letter from the applicant dated 8 June 2016 informing of the decision to withdraw the MAA application.

Action: For information

The CHMP noted the withdrawal letter.

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

treatment of postmenopausal osteoporosis

Scope: Letter from the applicant dated 27 May 2016 informing of the decision to withdraw the MAA application.

Action: For information

The CHMP noted the withdrawal letter.

3.7.4. - docetaxel - EMEA/H/C/004086

treatment of breast cancer, non-small cell lung cancer, prostate cancer, gastric adenocarcinoma, head and neck cancer

Scope: Letter from the applicant dated 6 June 2016 informing of the decision to withdraw the MAA application

Action: For information

The CHMP noted the withdrawal letter.

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. Keytruda - pembrolizumab - EMEA/H/C/003820/X/0001/G

Merck Sharp & Dohme Limited

Rapporteur: Daniela Melchiorri,

Scope: "To introduce concentrate for solution for infusion (25 mg/mL) as additional pharmaceutical form for Keytruda"

Action: For adoption

List of Outstanding Issues adopted on 01.04.2016. List of Questions adopted on 17.12.2015.

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

No items

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

Amgen Europe B.V.

Rapporteur: Pieter de Graeff, PRAC Rapporteur: Kimmo Jaakkola

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

Communication from the applicant dated 22 June 2016 requesting an extension of clock stop to respond to the list of questions adopted on 26.05.2016.

Action: For adoption

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

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the list of questions adopted on 26.05.2016.

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

No items

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

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

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

Otsuka Pharmaceutical Europe Ltd

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

Action: For adoption

Request for Supplementary Information adopted on 25.02.2016, 24.09.2015.

The Committee discussed the issues identified in this application. The members discussed the available clinical data and noted the limited data in 13 – 14 year olds. The members discussed whether an extrapolation to this age group was seen appropriate. The Committee also looked at data concerning weight gain and requested further clarification on this.

The Committee noted the report from the Central Nervous System Working Party.

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

5.1.2. Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0020

Biofrontera Bioscience GmbH

Rapporteur: Harald Enzmann,

Scope: "Extension of Indication to include treatment of actinic keratosis of mild to moderate severity on the face and scalp (Olsen grade 1 to 2) and of field cancerization based on the phase III clinical study ALA-AK-CT007. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in the SmPC and Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 01.04.2016.

The Committee discussed the issues identified in this application, which were related to higher recurrence and incidence rates of (non)melanoma cancer.

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

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

Novartis Europharm Ltd

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

Scope: Opinion / Request for Supplementary Information, report from SAG-Oncology

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

Action: For adoption

Request for Supplementary Information adopted on 26.05.2016, 28.04.2016, 25.02.2016, 22.10.2015. SAG Oncology meeting was held on 14 April 2016. Oral explanation held on 24 May 2016.

The CHMP noted the report from SAG-Oncology via written procedure on the findings in the high-risk subgroup.

The CHMP considered that there was uncertainty about the importance of the observed effect on progression-free survival associated with Arzerra. The findings on progression-free survival were not supported by other measures such as overall survival or a significant improvement in patients' quality of life.

The CHMP considered that the use of Arzerra for maintenance treatment should be seen in the

context of its side effects. Common side effects of Arzerra included infusion reactions, neutropenia (low levels of neutrophils, a type of white blood cell) and upper respiratory tract infections (nose and throat infections). The CHMP considered that the data were not sufficient to conclude that maintenance treatment with Arzerra is of more benefit than no treatment.

The CHMP adopted a negative opinion by majority (23 negative out of 30 votes) recommending the refusal of the variation to the terms of the marketing authorisation together with the Assessment Report.

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

The divergent position (Sinan B. Sarac, David Lyons, Harald Enzmann, Jan Mueller-Berghaus, Nela Vilceanu, Outi Maki-Ikola, Radka Montoniova) was appended to the opinion.

The refusal question and answers document was circulated for information.

The CHMP adopted the CHMP assessment report on similarity for Arzerra.

5.1.4. Arzerra - ofatumumab - Orphan - EMEA/H/C/001131/II/0045/G

Novartis Europharm Ltd

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

Scope: "Extension of indication to include the combination of Arzerra with fludarabine and cyclophosphamide or in combination with bendamustine for the treatment of adult patients with relapsed CLL.
As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2, 6.6 and 9 of the SmPC are updated. The Package Leaflet and the RMP (v.13) are updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application.

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

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

AstraZeneca AB

Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard

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

Action: For adoption

Request for Supplementary Information adopted on 01.04.2016, 19.11.2015.

The Committee discussed the issues identified in this application.

The Committee adopted a 3rd request for supplementary information with a specific timetable.

5.1.6. Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0067

GlaxoSmithKline Biologicals

Rapporteur: Daniel Brasseur, PRAC Rapporteur: Jean-Michel Dogné

Scope: "Extension of Indication to include prevention against premalignant anal lesions and anal cancer as of 9 years of age for Cervarix.
As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the RMP (v.11.0) including the new indication."

Action: For adoption

Request for Supplementary Information adopted on 01.04.2016, 19.11.2015, 25.06.2015.

The CHMP discussed the available data and whether the vaccination of boys/adolescents prior to sexual debut was justified, considering that the incidence of anal cancer in the overall population is very low.

The CHMP adopted a positive opinion by majority (29 positive out of 31 votes) together with the CHMP Assessment Report and translation timetable.

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

The divergent position (Pieter de Graeff, Agnes Gyurasics) was appended to the opinion

The summary of opinion was circulated for information.

5.1.7. Ilaris - canakinumab - EMEA/H/C/001109/II/0043

Novartis Europharm Ltd

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

Scope: "Extension of Indication to amend the Systemic Juvenile Idiopathic Arthritis (SJIA) indication to include treatment of active Still's disease including Adult-Onset Still's Disease (AOSD) in patients aged 2 years and older who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids. 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 updated accordingly. In addition, the MAH took the opportunity to bring the annexes in line with the latest QRD template. An updated RMP version 10 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 01.04.2016.

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

Boehringer Ingelheim International GmbH

Rapporteur: Pieter de Graeff, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Dolores Montero Corominas

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

Action: For adoption

Request for Supplementary Information adopted on 25.02.2016.

The Committee discussed the issues identified in this application. The main discussions related to the wording of the indication in particular on the proposed separate cardiovascular prevention indication. Another point of discussion was the use in patients with moderate renal insufficiencies as well as the safety profile.

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

5.1.9. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0007

Merck Sharp & Dohme Limited

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

Scope: "Extension of Indication to include a new indication for Keytruda in second line Non-Small Cell Lung Cancer (NSCLC). As a consequence, sections 4.1, 4.2 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 28.04.2016.

The Committee summarised the available clinical data and finalised the wording of several SmPC sections.

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.

5.1.10. Nevanac - nepafenac - EMEA/H/C/000818/II/0032

Alcon Laboratories (UK) Ltd

Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension of indication to include the indication 'reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients' also for the 3 mg/ml strength based on data from the phase III studies C-12-067 and C-12-071. 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 updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in SmPC and to update the annexes in line with the latest QRD template. An updated RMP version 7 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 01.04.2016.

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.

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

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of Indication to include the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL):
- after autologous stem cell transplant (ASCT) and treatment with brentuximab vedotin, or
- after at least two prior therapies in patients who are not candidates for ASCT,
for OPDIVO as monotherapy.
As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the proposed new indication, add a warning that patients with active autoimmune disease and symptomatic interstitial lung disease were excluded from clinical trials of cHL, and update the safety and pharmacodynamic information. The Package Leaflet is updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 10.0.
Moreover, the updated RMP version 5.0 has been submitted"

Action: For adoption

The Committee discussed the issues identified in this application. The main focus of the discussion related to the efficacy data and the wording of the indication. Particularly for

patients who are not considered for autologous stem cell transplant further data was required to a thorough assessment.

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

5.1.12. RoActemra - tocilizumab - EMEA/H/C/000955/II/0057

Roche Registration Limited

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of Indication to include the treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with methotrexate (MTX) for the RoActemra subcutaneous formulation; as a consequence, section 4.1 of the SmPC is updated. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in the SmPC and Package Leaflet. Moreover, the MAH took the opportunity to update the contact details of the local representative in Germany in the Package Leaflet. Further, the updated RMP version 18.1 has been agreed.

Action: For adoption

Request for Supplementary Information adopted on 01.04.2016.

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.

5.1.13. 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

Request for Supplementary Information adopted on 28.04.2016, 28.01.2016.

The members discussed the available data also taking the agreed PIP waiver into account. The Committee looked at the safety data and considered that there was no significant difference in the number of hypoglycaemias between the young age treatment groups. Furthermore the CHMP considered the use of premixed insulin appropriate in children below the age of 6 years

in combination with a close monitoring of hypoglycaemia in the paediatric population. Some members raised concern on the indication in children from 2 years to less than 6 years due to the possibility of hypoglycaemia also referring to international treatment guidelines.

The CHMP adopted a positive opinion by majority (27 positive out of 31 votes) together with the CHMP Assessment Report and translation timetable.

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

The divergent position (Jean-Louis Robert, Jacqueline Genoux-Hames, Alar Irs, Agnes Gyurasics) was appended to the opinion.

The summary of opinion was circulated for information.

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

Teva B.V.

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

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

Action: For adoption

The Committee discussed the issues identified in this application. The discussions concerned the environmental risk assessment.

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

5.1.15. Zontivity - vorapaxar - EMEA/H/C/002814/II/0005

Merck Sharp & Dohme Limited

Rapporteur: Greg Markey, PRAC Rapporteur: Carmela Macchiarulo

Scope: "Extension of Indication to include treatment of patients with symptomatic Peripheral Arterial Disease (PAD) and 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 accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of local representative in Luxembourg in the Package Leaflet. Furthermore, the PI is brought in line with the QRD template version 9.1. Moreover, revised RMP version 2.4 has been agreed."

Action: For adoption

Request for Supplementary Information adopted on 01.04.2016, 17.12.2015.

The CHMP discussed the wording of the indication and agreed on it.

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.

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

No items

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. - andexanet alfa - H0004108

For adult patients treated with a direct or indirect factor Xa (FXa) inhibitor when reversal of anticoagulation is needed in situations such as: in life-threatening or uncontrolled bleeding; for emergency surgery/urgent procedures

Scope: Letter from the company dated 12 May 2016 requesting an accelerated assessment.

Action: For adoption

Briefing note and Rapporteurs' recommendation on the request for accelerated assessment. 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. - masitinib mesylate - H0004398

Treatment of adults with Amyotrophic Lateral Sclerosis

Scope: Letter from the company dated 24 May 2016 requesting an accelerated assessment

Action: For adoption

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

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.

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

Action: For information

The CHMP noted the list of applications received.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 8 recommendations for eligibility to PRIME: 2 were granted and 6 were denied. The individual outcomes are listed in PRIME Monthly Report on EMA website.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. InductOs - Dibotermin Alfa - EMEA/H/C/000408

Medtronic BioPharma B.V., Rapporteur: Pieter de Graeff, Co-Rapporteur: Outi Mäki-Ikola,

Scope: Update from GMP inspection

Action: For information

The CHMP noted an update on the GMP inspection.

9.1.2. Revatio - sildenafil - EMEA/H/C/000638/II/0073

MAH: Pfizer Limited, Rapporteur: Pieter de Graeff,

Scope: Opinion

"Following the availability of powder for oral suspension formulation and following the request of CHMP, update of sections 4.2, 6.3, 6.4 and 6.6 of Revatio 20mg film-coated tablets SmPC and section 4.2 of Revatio 10mg powder for oral suspension to delete information related to the extemporaneously prepared oral suspension. The film-coated tablet PL is updated accordingly."

Request for Supplementary Information adopted on 26.05.2016.

Action: For adoption

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.

9.1.3. Xarelto - Rivaroxaban - EMEA/H/C/000944 – follow up of 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 AF Trial and International Normalized Ratio (INR) device

Action: For discussion

Follow up of previous assessment completed in January 2016.

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

9.1.4. Selincro – Nalmefene - EMEA/H/C/002583

H. Lundbeck A/S, indicated for the reduction of alcohol consumption

Rapporteur: Martina Weise, Co-Rapporteur: Patrick Salmon, PRAC Rapporteur: Martin Huber, PRAC Co-Rapporteur: Almath Spooner

Scope: Update on recent publication in journal 'Addiction' by N. Fitzgerald et al.

Action: For discussion

The CHMP noted the publication in the journal 'Addiction', raising some issues with the clinical trials on which the authorisation is based. The Committee discussed the data and having taken into account the divergent position at time of positive opinion, concluded that the recent literature reports do not contain new information that would necessitate a re-evaluation of the benefit/risk ratio of Selincro.

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

MAH: PTC Therapeutics International Limited,

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus,

Scope: Oral explanation, Type II variation

"Update of sections 4.4, 4.6, 4.7, 4.8, and 5.1 of the SmPC and Annex II in order to reflect the result from the submitted study TC124-GD-020-DMD object of SOB 001. The Package Leaflet and the RMP are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some minor editorial changes throughout the Product information."
Request for Supplementary Information adopted on 01.04.2016.

Scope: Oral explanation, Renewal of Marketing Authorisation
Request for Supplementary Information adopted on 28.04.2016.

Action: Oral explanation to be held on Tuesday 21 June 2016 at 10:00.

Participation of patients' representatives

The CHMP noted the report from the SAG Neurology. The SAG expressed a view that the results of the clinical study 020 are considered negative although some experts highlighted that some positive trends were observed and no new safety concerns were raised. The experts saw the variability of the results inherent to the tests themselves but also identified some methodological issues. The experts agreed that the proposed subgroup of patients represents a more sensitive part of the population but doubts on the way of how the subgroup was identified and also their clinical relevance were raised. The SAG gave advice on the identification of the proposed subgroup in clinical practice. In addition the experts gave recommendations on additional clinical trials and highlighted that no alternative treatment exists for those patients seeing a benefit from Translarna.

An oral explanation was held on Tuesday 21 June 2016 at 10:00. The oral explanation concentrated on the results from study TC124-GD-020-DMD with specific focus on the efficacy

data.

The members discussed the clinical data from study 020 also in relation to previous study results and the possible impact on the benefit/risk of the product. Views questioning the efficacy of the product were raised although case reports on positive effects were noted. The absence of treatment options and no major safety concerns were taken into account during the discussions. The different regulatory possibilities were debated. The CHMP agreed to the proposal by the MAH to submit a draft study protocol for further discussion.

See also 2.3.1 Post-authorisation procedure oral explanations

10. Referral procedures

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

No items

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

No items

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

Altergon Italia srl

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Joseph Emmerich,

RMS: UK, CMS: CZ, FR, SK

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

Scope: PKWP response to CHMP question on diclofenac

Disagreements regarding the demonstration of bioequivalence in the fed state.

Action: For adoption

The CHMP adopted the report from the PKWP on the bioequivalence for generic diclofenac products.

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: Opinion or List of outstanding Issues

Action: For adoption

List of outstanding Issues adopted 28.01.2016 and 28.04.2016.

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

Submission of responses: 05.07.2016

Re-start of the procedure: 06.07.2016

Joint assessment report circulated to CHMP: 11.07.2016

Comments: 13.07.2016

Updated joint assessment report circulated to CHMP: 15.07.2016

List of outstanding issues or CHMP opinion: July 2016 CHMP

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

Lundbeck group of companies and associated companies

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

Scope: Opinion or List of Outstanding Issues

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

Action: For adoption

List of outstanding issues adopted on 01.04.2016.

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

Submission of responses: 01.09.2016

Re-start of the procedure: 15.09.2016

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 28.09.2016

Comments: 03.10.2016

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 06.10.2016

CHMP LoOI/CHMP opinion: October 2016 CHMP

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

10.6.1. Alkem Laboratories Limited, India - EMEA/H/A-31/1436

Rapporteur: Harald Enzmann, Co-Rapporteur: Greg Markey,

Scope: Opinion

Article 31 procedure triggered by BfArM concerning studies performed by Alkem Laboratories, Department of Bioequivalence, C-17/7, MIDC Industrial estate, Taloja, Dist. Raigad – 410 208, India between March 2013 and March 2015, following critical GCP deficiencies reported during an inspection performed by BfArM and IGZ in 2015.

Action: For adoption

List of questions adopted on 01.04.2016.

An oral explanation was held on 21 June 2016 at 15:30. During the oral explanation, the company described the GCP inspection findings and bioequivalence data for 2 products (riluzole and cefuroxime).

The Committee discussed the data presented by the Alkem during the oral explanation and concluded that for riluzole, in absence of reliably proven bioequivalence, currently the efficacy and safety of the medicinal product has not been established and suspension of MA is recommended. For Cefuroxime axetil, the overall study outcome demonstrated bioequivalence of Cefuroxime tablets manufactured by Alkem vs. the EU reference medicinal product.

The CHMP adopted an opinion by consensus, recommending that

- the marketing authorisation applications for Ibuprofen Orion do not satisfy the criteria for authorisation
- the marketing authorisations for Riluzole Alkem should be suspended
- the inspection findings should not preclude the granting of the marketing authorisations for Cefuroxime Ingen Pharma
- the marketing authorisations should be maintained for:
    - Cefuroxime Krka
    - Cefuroxime Alkem

The CHMP assessment report was adopted.

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

The CHMP noted the EMA question-and-answer document.

See also 2.4.1. Referral procedure oral explanations

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

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

Scope: Opinion or List of outstanding issues

Action: For adoption

The CHMP discussed the wording of the indication in light with the available data. The main discussion focused on the wording of the indication and the line of treatment.

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

Submission of responses: 04.08.2016

Re-start of the procedure: 18.08.2016

Rapporteur/co-rapporteur joint assessment reports circulated to CHMP: 31.08.2016

Comments: 05.09.2016

Updated Rapporteur/co-rapporteur joint assessment reports circulated to CHMP: 08.09.2016

CHMP opinion: September 2016 CHMP

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 Graeff, Scope: List of outstanding issues

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

Action: For adoption

List of Questions adopted 28 January 2016.

The CHMP discussed several parts of the SmPC, in particular section 4.2 and 4.3.

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

Submission of responses: 04.08.2016

Re-start of the procedure: 18.08.2016

Rapporteur/co-rapporteur joint assessment reports circulated to CHMP: 31.08.2016

Comments: 05.09.2016

Updated Rapporteur/co-rapporteur joint assessment reports circulated to CHMP: 08.09.2016

CHMP opinion: September 2016 CHMP

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

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

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

Article 31 triggered by the EC

Letter from the European Commission dated 17 June notifying of official referral under Article 31 and its grounds.

The Committee noted the letter from the European Commission dated 17 June notifying of official referral under Article 31 and its grounds.

The CHMP appointed Nithyanandan Nagercoil as Rapporteur (interest level 3) and David Lyons as Co-Rapporteur (interest level 2). The declarations of interest forms of the Rapporteurs have been checked with regard to their involvement in the concerned products and no conflicts of interest have been identified.

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

Submission of responses: 01.07.2016

Re-start of the procedure: 04.07.2016

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 08.07.2016

Comments: 13.07.2016

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 15.07.2016

CHMP LoOI or CHMP opinion: July 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

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

Action: For information

The CHMP noted the June 2016 Early Notification System.

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

No items

13.2. Innovation Task Force briefing meetings

No items

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

Request from EDQM for EMA scientific Opinion under Art. 57 (1)J of Regulation (EC) No 726/2004

Action: For information

Update on procedure

The CHMP noted the update.

Request from the European Commission for an EMA scientific Opinion under Article 57

Action: For information

Update on procedure

The CHMP noted the update.

13.4. Nanomedicines activities

4th TC on the IPRF Nano Working Group on 6 July 2016

Action: For information

Agenda

The CHMP noted the agenda.

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. CHMP Seating plan during Slovakian presidency 1 July - 31 December 2016

Action: For information

The CHMP noted the new seating plan under the Slovakian EU presidency.

14.1.2. General update on the procedural handling of GMP inspection issues

Action: For information

Postponed to July ORGAM.

14.1.3. Revision of Procedure for nomination and appointment of co-opted members in CHMP, CVMP and HMPC

Action: For adoption

Postponed to July ORGAM.

14.1.4. New procedure for 107q PASS Results - early involvement of CHMP

CHMP sponsor: Johann Hillege,

Action: For information

Postponed, will be adopted via written procedure.

14.1.5. New timetable proposal for type II variations involving the PRAC

Action: For discussion

Background document

Postponed to July ORGAM.

14.1.6. Follow-up actions from the CHMP Strategic Review and Learning meeting in Utrecht

Action: For information

The CHMP discussed the follow up actions from the meeting in Utrecht as well as previous Presidency meetings and agreed the way forward for those actions.

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 06-09 June 2016

Action: For information

The CHMP noted the Summary of recommendations and advice.

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

Action: For adoption

The CHMP adopted the List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 16-17 June 2016
Action: For information

The CHMP noted the draft minutes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 30 May- 2 June 2016

Action: For information

The CHMP noted the report from the HMPC meeting.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at June 2016 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 22-24 June 2016

Action: For information

The CHMP noted the report.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 14-16 June 2016

Action: For information

The CHMP noted the report.

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 20-22 June 2016

Action: For information

The CHMP noted the report.

Scope: PKWP response to the CMDh letter dated 21 April 2016 regarding administration of crushed/disintegrated tablets

Action: For adoption

The CHMP adopted the PKWP response.

Scope: PKWP response to the CMDh letter dated 22 April 2016 regarding low dose acetylsalicylic acid gastro-resistant formulations in fixed dose combinations with substitution indication

Action: For adoption

The CHMP adopted the PKWP response.

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

14.3.1. Scientific Advice Working Party (SAWP)

Scope: Report from the SAWP meeting held on 6-9 June 2016. Table of conclusions

Action: For information

Scope: 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. Name Review Group (NRG)

Scope: Endorsement of NRG recommendation **Action:** For discussion

The members were reminded of potential name related issues. The CHMP endorsed the NRG recommendation.

Table of Decisions of the NRG plenary meeting held on 1 June 2016

Action: For adoption

The CHMP adopted the NRG report.

14.3.3. Biosimilar Medicinal Product Working Party (BMWP)

Chair: Christian Schneider / Martina Weise

Scope: Call for nomination of a new Chairperson following end of mandate in September 2016

Action: For information

Nominations should be sent by 31 July 2016.
Candidates should submit a brief résumé in support of their candidature. Election is going to take place at the September 2016 CHMP Plenary meeting.

14.3.4. European Medicines Agency Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP)

Scope: Appointment of CHMP representatives (1 member and 1 alternate) to the PCPWP

Action: For adoption

The CHMP appointed Concepcion Prieto Yerro and Harald Enzmann as CHMP representatives to the PCPWP.

14.3.5. European Medicines Agency Human Scientific Committees' Working Party with Healthcare Professionals' Organisations (HCPWP)

Scope: Appointment of CHMP representatives (1 member and 1 alternate) to the HCPWP

Action: For adoption

The CHMP appointed Fátima Ventura as CHMP representative to the HCPWP.

14.3.6. Biologics Working Party (BWP)

Draft agenda for BWP face-to-face meeting to be held 11-13 July 2016 (EMA/CHMP/BWP/377241/2016)

Action: For information

The CHMP noted the draft agenda.

Final minutes from face-to-face meeting held 18-20 April 2016 (EMA/CHMP/BWP/281453/2016)

Action: For information

The CHMP noted the final minutes.

Reflection paper on viral safety of plasma-derived medicinal products with respect to Hepatitis E virus (EMA/CHMP/BWP/723009/2014)

Action: For adoption

The CHMP adopted the reflection paper. The reflection paper discusses the key questions raised during the EMA Workshop on Viral safety of plasma-derived medicinal products with respect to Hepatitis E virus (held on 28-29 October 2014).

Scope: Revised "Guideline on the requirements for quality documentation concerning biological investigational medicinal products in clinical trials" (EMA/CHMP/BWP/534898/2008)

Action: For adoption for 6-months public consultation

The CHMP adopted the guideline for 6-months public consultation. The guideline addresses the specific documentation requirements on the biological, chemical and pharmaceutical quality of IMPs containing biological / biotechnology derived substances. The guideline lists, as regards to documentation on the biological, chemical and pharmaceutical quality of the IMP, examples of modifications which are typically considered as 'substantial'.

14.3.7. Vaccines Working Party (VWP)

Scope: Call for nomination for a new chairperson following resignation of Michael Pfleiderer

Action: For information

Nominations should be sent by 31 July 2016

Candidates should submit a brief résumé in support of their candidature. Election is going to take place at the September 2016 CHMP Plenary meeting.

The CHMP noted the information.

14.3.8. Blood Products Working Party (BPWP)

Scope: Final agenda of WP meeting held face-to-face on 2-3 June 2016 (EMA/CHMP/BPWP/344525/2016)

Action: For information

The CHMP noted the final agenda.

Scope: Final minutes of WP meeting held by TC on 3 March 2016 (EMA/CHMP/BPWO/170164/2016)

Action: For information

The CHMP noted the final minutes.

Scope: Election of new vice-chair

The CHMP elected Karri Penttilä as vice-chair to BPWP.

14.3.9. Cardiovascular Working Party

Chair: Pieter de Graeff/Kristina Dunder

Scope: Concept paper on the need for revision of the Guideline on clinical investigation of medicinal products in the treatment or prevention of diabetes mellitus (EMA/317855/2016)

Action: For adoption for 3-months public consultation

The CHMP adopted the guideline for 3-months public consultation. The reason for a revision of the guideline is to update the section on cardiovascular safety to align it with the recently adopted Reflection paper on assessment of cardiovascular safety profile of medicinal products. Some additional changes to the guideline are proposed to be considered based on recent developments and queries from different stakeholders.

Scope: Guideline on clinical investigation of medicinal products in the treatment of lipid disorders (EMA/CHMP/748108/2013 rev 3)

Action: For adoption

The CHMP adopted the guideline. The guideline provides advice to applicants on the main regulatory requirements that are expected to be followed in the development of a medicinal product for treatment of lipid disorders associated with increased cardiovascular risk encountered in adult patients (i.e. lipid modifying agents). Lipid disorders in paediatric patients are addressed in a separate addendum.

Scope: Draft Guideline of medicinal products used in weight management (EMA/CHMP/311805/2014)

Action: For adoption

The CHMP adopted the guideline. The scope of the guideline is the development of pharmacological options for weight management. Specific recommendations on non-pharmacological options are out of scope of the guideline.

Overview of comments received (EMA/CHMP/76995/2015)

Action: For information

The CHMP noted the overview of comments.

Scope: Draft Guideline on clinical investigations of Medicinal Products in the treatment of Hypertension (EMA/CHMP/29947/2013)

Action: For adoption

The CHMP adopted the guideline. The aim of the 4th revision of the guideline is to unify the section of the Guideline on the collection of long-term safety data with the other relevant EMA guidelines of the treatment of cardiovascular or metabolic diseases.

Scope: Overview of comments received (EMA/CHMP/345847/2015)

Action: For information

The CHMP noted the overview of comments.

14.3.10. Central Nervous System Working Party (CNSWP)

Scope: Final minutes of WP meeting held by teleconference on 10 March 2016 (EMA/189345/2016)

Action: For information

The CHMP noted the final minutes.

14.3.11. Infectious Diseases Working Party (IDWP)

Scope: Call for nomination of a new Chairperson following end of mandate in September 2016

Action: For information

Nominations to be sent by 31 July 2016

Candidates should submit a brief résumé in support of their candidature.

The CHMP noted the information.

Scope: Guideline on the clinical evaluation of direct acting antivirals for the treatment of chronic hepatitis (EMEA/CHMP/EWP/30039/2008 Rev 1)

Action: For adoption for 6-month public consultation

The CHMP adopted the guideline for 6-month public consultation. Guidance is provided on the design of clinical studies considered to be of relevance for the evaluation of direct-acting anti-HCV compounds. The scope of the guideline reflects the experience with DAA in the field of drug development for the treatment of CHC. Sponsors planning modes of drug development that are not covered in this guideline, are advised to consult with EU Regulators early in the clinical development programme, and at least prior to initiating confirmatory studies.

Scope: Guideline on the use of pharmacokinetics and pharmacodynamics in the development of antimicrobial medicinal products (Doc ref: EMA/CHMP/594085/2015)

Action: For adoption

Postponed to July CHMP ORGAM.

Scope: Addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections to address the clinical development of new agents to treat disease due to Mycobacterium tuberculosis (EMA/CHMP/EWP/14377/2008 Rev 1) –

Action: For adoption for 6-months consultation

Postponed to July CHMP ORGAM.

14.3.12. Oncology Working Party

Scope: Call for nomination of a new Chairperson following end of mandate in September 2016

Action: For information

Nominations to be sent by 31 July 2016

Candidates should submit a brief résumé in support of their candidature.

The CHMP noted the information.

14.3.13. Biostatistics Working Party (BSWP)

Scope: Final minutes of BSWP meeting held by teleconference on 19 April 2016 (EMA/279984/2016)

Action: For information

The CHMP noted the final minutes.

Scope: Draft agenda of BSWP meeting to be held by teleconference on 14 June 2016 (EMA/380152/2016)

Action: For information

The CHMP noted the draft agenda.

Scope: Call for nomination for a new chairperson following resignation of David Jonathan Wright

Action: For information

Expertise sought: Candidates for the position should be professionally qualified senior assessors within the European regulatory network, with relevant expertise in the field of biostatistics. Experience in co-operation with EMA Committees, Working Parties and Working Groups would be of advantage.

Nominations should be sent by 31 July 2016.

Candidates should submit a brief résumé in support of their candidature. Election is going to take place at the September 2016 CHMP Plenary meeting.

The CHMP noted the information.

14.3.14. Radiopharmaceutical Drafting Group (RadDG)

Scope: Call for nomination of a new Chairperson following end of mandate in September 2016

Action: For information

Nominations to be sent by 31 July 2016

Candidates should submit a brief résumé in support of their candidature.

The CHMP noted the information.

14.3.15. Quality Working Party (QWP)

Chair: Jean-Louis Robert

Scope: ICH Q3D – implementation strategy

Action: For adoption for 1-month public consultation

The CHMP adopted the ICH Q3D – implementation strategy for 1 month public consultation. The purpose of the document is to describe the practical implementation of ICH Q3D Guideline for Elemental Impurities in the European context.

Scope: Question-and-answer on product specific active substance information

Action: For adoption

The CHMP adopted the Question-and-answer on product specific active substance information.

14.3.16. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus,

Scope: Guideline on the clinical investigation of medicinal products for the treatment of Axial Spondyloarthritis (CPMP/EWP/4891/03 Rev.1)

Rapporteur: Arantxa Sancho-Lopez

Action: For adoption for 6-month public consultation

The guideline was adopted for 6-month public consultation. Guidance is provided on the clinical development and evaluation of medicinal products for the systemic treatment of axial SpA, including both ankylosing spondylitis and non-radiographic axial SpA forms.

14.3.17. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/ Alfredo Garcia-Arieta,

Scope: Nomination of Ewa Bałkowiec-Iskra as a PKWP observer

Action: For adoption

The CHMP appointed Ewa Bałkowiec-Iskra as observer to PKWP.

14.3.18. Safety Working Party (PKWP)

Scope: nomination of Leon van Aerts to represent EMA at the EMCDDA meeting taking place on 22nd July 2016

Action: For adoption

The CHMP agreed to nominate Leon Van Aerts in this role.

14.4. Cooperation within the EU regulatory network

No items

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

No items

14.8. Planning and reporting

14.8.1. New marketing authorisation applications for 2016 with appointed rapporteurs

Action: For information

The CHMP noted the report.

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Feedback from non-clinical and clinical experts on review of EU guidance on first-in-human clinical trials

Action: For discussion

The CHMP noted the feedback of the experts.

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 20-23 June 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	
Andrea Laslop	Member	Austria	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	
Radka Montoniová	Alternate	Czech Republic	No interests declared	
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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
Agnes Gyurasics	Member	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	
Juris Pokrotnieks	Member	Latvia	No restrictions applicable to this meeting	
Romaldas Mačiulaitis	Member	Lithuania	No restrictions applicable to this meeting	
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Pieter de Graeff	Member	Netherlands	No interests declared	
Johann Lodewijk	Alternate	Netherlands	No interests	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Hillege			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	
Aldona Paluchowska	Alternate	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
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 restrictions applicable to this meeting	
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 interests declared	
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	
Tereza Bazantova	Expert - in person*	Czech Republic	No restrictions applicable to this meeting	
Theis Moeslund Jensen	Expert - in person*	Denmark	No restrictions applicable to this meeting	
Jorge Camarero Jiménez	Expert - in person*	Spain	No restrictions applicable to this meeting	
Macarena Rodriguez Mendizabal	Expert - in person*	Spain	No interests declared	
Ana Alonso Gutierrez	Expert - in person*	Spain	No interests declared	
Alfredo García-Arieta	Expert - via telephone*	Spain	No interests declared	
Janet Mifsud	Expert - via telephone*	Malta	No restrictions applicable to this meeting	
Valérie Lescrainier	Expert - in person*	Belgium	No interests declared	
Carolien Versantvoort	Expert - via telephone*	Netherlands	No interests declared	
Jan Neuhauser	Expert - via telephone*	Austria	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Hanne Lomholt Larsen	Expert - in person*	Denmark	No interests declared	
Bernard Mooney	Observer, in person	Patient representative	No interests declared	
Elizabeth Vroom	Expert - in person*	Patient representative	No interests declared	
Paula Boudewina van Hennik	Expert - in person*	Netherlands	No interests declared	
Patrick Vrijlandt	Expert - in person*	Netherlands	No interests declared	
Ingrid Schellens	Expert - via telephone*	Netherlands	No interests declared	
Nieske Rodenhuis	Expert - via telephone*	Netherlands	No restrictions applicable to this meeting	
Violeta Stoyanova-Beninska	Expert - in person*	Netherlands	No interests declared	
Renee van Binsbergen	Expert - via telephone*	Netherlands	No interests declared	
Elina Rönnemaa	Expert - via telephone*	Sweden	No interests declared	
Ingrid Wang	Expert - via telephone*	Norway	No interests declared	
Carla Herberts	Expert - via telephone*	Netherlands	No interests declared	
Steven Teerenstra	Expert - via telephone*	Netherlands	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Aghadiuno Olaperi	Expert - via telephone*	United Kingdom	No interests declared	
Elisabeth Joanne Rook	Expert - via telephone*	Netherlands	No interests declared	
Karl Broich	Expert - via telephone*	Germany	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Olga Kholmanskikh	Expert - via telephone*	Belgium	No interests declared	
Jonas Bergh	Expert - via telephone*	Sweden	No restrictions applicable to this meeting	
Serge Bakchine	Expert - via telephone*	France	No restrictions applicable to this meeting	
Paula Salmikangas	Expert - via telephone*	Finland	No interests declared	
Representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

* Experts were only evaluated against the product(s) they have been invited to talk about.

17. Explanatory notes

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

Oral explanations *(section 2)*

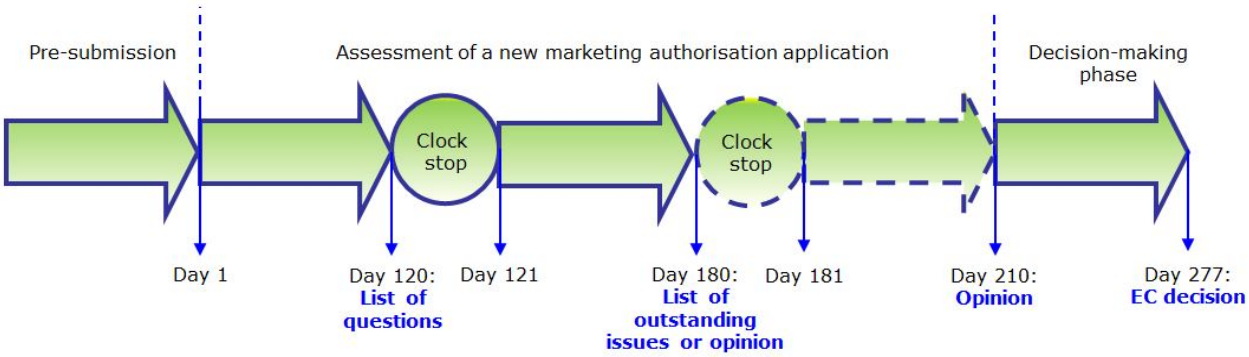
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

Extensions of marketing authorisations are applications for the change or addition of new strengths, formulations or routes of administration to existing marketing authorisations. Extension applications

follow a 210-day evaluation process, similarly to applications for new medicines (see figure above).

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

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

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

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

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

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

Re-examination procedures *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

This section lists referrals that are ongoing or due to be started at the plenary meeting. A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the EU. Further information on such procedures can be found

here.

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

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

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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