24 July 2015
EMA/CHMP/502563/2015
Procedure Management and Committees Support Division

Committee for medicinal products for human use (CHMP)

Minutes of the meeting on 22-25 June 2015

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

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 held 22-25 June 2015.

1.2. Adoption of agenda

CHMP agenda for 22-25 June 2015.

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 18-21 May 2015.

The CHMP adopted the minutes.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. - guanfacine - EMEA/H/C/003759

treatment of ADHD

Scope: Oral explanation
Action: Oral explanation was held on Tuesday 23 June 2015 at 10.00

List of outstanding issues adopted on 26.03.2015. List of questions adopted on 24.07.2014. Report from SAG Psychiatry meeting held on 1 June 2015. The SAG report addressed the observed efficacy on symptoms of ADHD, which, even though seemingly modest, has been considered by the SAG as clinically relevant in itself. SAG pointed out that safety is a concern (sedation/somnolence, cardiovascular effects, BMI increase) with this medicinal product and that caution should apply as for every medication intended for children. The SAG considered that there is no specific ADHD population that can be described in details or would benefit exclusively from guanfacine as first line treatment. Therefore, treatment with stimulants has to be considered as first line treatment due the high efficacy. However, SAG agreed that although stimulants are considered in therapeutic guidelines and in clinical practice to be the first choice for pharmacological treatment for ADHD, the use of guanfacine should not necessarily be restricted to second or third line treatment. There may be cases indeed where stimulant would not be the most appropriate treatment due for example to specific clinical features of the patients (e.g. comorbidities such as tics, weight

loss or insomnia) or clear contraindications of stimulants.
An Oral Explanation was held on Tuesday 23 June 2015 at 10.00. Participation of patient representatives.
The applicant's presentation focused on the safety profile of the product in comparison with other available medicinal products and on the indication wording.

2.1.2. Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739

CSL Behring GmbH; treatment of lung disease

Scope: Oral explanation and opinion

Action: Oral explanation was held on Wednesday 24 June 2015 at 9.00.

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

List of outstanding issues adopted on 23.04.2015, 26.03.2015, 20.11.2014. List of questions adopted on 25.04.2014.

An oral explanation was held on Wednesday 24 June 2015 at 9.00.

The applicant's presentation focused on GCP issues.

See 3.1.9

2.1.3. Heparesc - human heterologous liver cells - Orphan - ATMP - EMEA/H/C/003750

Cytonet GmbH&Co KG; treatment of urea cycle disorders (UCD)

Scope: Oral explanation and opinion

Action: Oral explanation was held on Tuesday 23 June 2015 at 16.00.

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

List of outstanding issues adopted on 26.03.2015, 18.12.2014. List of questions adopted on 25.04.2014.

An Oral Explanation was held on Tuesday 23 June 2015 at 16.00. The presentation by the applicant focused on the overall benefit / risk of the product.

See 3.1.11

2.1.4. Kanuma - sebelipase alfa - Orphan - EMEA/H/C/004004

Synageva BioPharma Ltd; treatment of enzyme replacement therapy (ERT)

Scope: Opinion or Oral Explanation

Action: Possible oral explanation to be held on Wednesday 24 June 2015 at 11.00

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

List of questions adopted on 23.04.2015.

The CHMP agreed that no oral explanation as needed at this time.

See 3.1.5

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

2.4.1. Adrenaline auto injectors (EMEA/H/A-31/1398)

Rapporteur: Alar Irs, Co-Rapporteur: Robert James Hemmings,

Scope: Opinion or possible oral explanation

Article 31 triggered by the MHRA due to the lack of robust evidence that the devices deliver the adrenaline intramuscularly in all patients.

Action: Possible oral explanation to be held on Wednesday 24 June 2015

List of outstanding issues adopted on 26.02.2015 and 25.09.2014. Ad-hoc expert group meeting held on 23 January 2015.

The CHMP agreed that no oral explanation is needed at this time.

See 10.6.1

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Aripiprazole Sandoz - aripiprazole - EMEA/H/C/004008

SANDOZ GmbH; treatment of schizophrenia and treatment and prevention of manic episodes in bipolar I disorder

Scope: Opinion

Action: For adoption

Hybrid application (Article 10(3) of Directive No 2001/83/EC); Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Abilify

List of outstanding issues adopted on 26.03.2015. List of questions adopted on 20.11.2014.

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. Docetaxel Hospira UK Limited - docetaxel - EMEA/H/C/003925

HOSPIRA UK LIMITED; treatment of breast cancer, non small cell lung cancer, prostate cancer, metastatic gastric adenocarcinoma and head and neck cancer

Scope: Opinion

Action: For adoption

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

List of outstanding issues adopted on 21.05.2015, 26.03.2015. List of questions adopted on 23.10.2014.

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. Duloxetine Zentiva - duloxetine - EMEA/H/C/003935

Zentiva, k.s.; Treatment depressive disorder, diabetic neuropathic pain, anxiety disorder, treatment depressive disorder, diabetic neuropathic pain, anxiety disorder

Scope: Opinion

Action: For adoption

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

List of outstanding issues adopted on 23.04.2015. List of questions adopted on 22.01.2015.

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.

3.1.4. FARYDAK - panobinostat - Orphan - EMEA/H/C/003725

Novartis Europharm Ltd; treatment of multiple myeloma

Scope: Opinion

Action: For adoption

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

List of outstanding issues adopted on 26.03.2015. List of questions adopted on 25.09.2014.

The Committee discussed the final wording of the indication and 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 panobinostat is a new active substance, as claimed by the applicant.

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

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

The Committee noted the letter of recommendation dated 25.06.2015.

The summary of opinion was circulated for information.

The CHMP adopted the assessment report on similarity .

3.1.5. Kanuma - sebelipase alfa - Orphan - EMEA/H/C/004004

Synageva BioPharma Ltd; treatment of enzyme replacement therapy (ERT)

Scope: Possible Oral explanation / Opinion, BWP Report

Action: For adoption

See also 2.1.4

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

List of questions adopted on 23.04.2015.

The members discussed the post-authorisation measures concerning the development of *in-vitro* neutralising antibodies and the development of an assay for detecting the antibodies.

The CHMP agreed that no Oral Explanation was needed at this time.

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 sebelipase alfa is a new active substance, as claimed by the applicant.

Sebelipase alfa is the first recombinant product expressed in transgenic chicken (*Gallus gallus)* and purified from egg white of transgenic hens.

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 Committee noted the letter of recommendation dated 24.06.2015.

The summary of opinion was circulated for information.

The Committee adopted the BWP report.

3.1.6. Odomzo - sonidegib - EMEA/H/C/002839

Novartis Europharm Ltd; treatment of basal cell carcinoma (BCC)

Scope: Opinion

Action: For adoption

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

List of outstanding issues adopted on 23.04.2015. List of questions adopted on 25.09.2014.

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 sonidegib phosphate is a new active substance, as claimed by the applicant.

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

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

The summary of opinion was circulated for information.

3.1.7. Pregabalin Accord - pregabalin - EMEA/H/C/004024

Accord Healthcare Limited; treatment of epilepsy and generalised anxiety disorder (GAD),

Scope: Opinion

Action: For adoption

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

List of outstanding issues adopted on 21.05.2015. List of questions adopted on 18.12.2014.

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.

3.1.8. Raxone - idebenone - Orphan - EMEA/H/C/003834

Santhera Pharmaceuticals (Deutschland) GmbH; treatment of Leber's Hereditary Optic Neuropathy (LHON)

Scope: Opinion

Action: For adoption

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

List of outstanding issues adopted on 21.05.2015, 26.02.2015. List of questions adopted on 25.09.2014.

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 **under exceptional circumstances** 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 Committee noted the letter of recommendation dated 20.06.2015.

The summary of opinion was circulated for information.

3.1.9. Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739

CSL Behring GmbH; treatment of lung disease

Scope: Opinion

Action: For adoption

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

List of outstanding issues adopted on 23.04.2015, 26.03.2015, 20.11.2014. List of questions adopted on 25.04.2014.

See 2.1.2

An oral explanation was held on Wednesday 24 June 2015 at 9.00.

The applicant's presentation focused on GCP issues.

The Committee discussed the issues identified in a GCP inspection of the pivotal studies and their possible impact on the study data. The CHMP considered the findings not having a significant impact on the study data.

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.

3.1.10. Strensiq - asfotase alfa - Orphan - EMEA/H/C/003794

Alexion Europe SAS; treatment of paediatric-onset hypophosphatasia

Scope: Opinion

Action: For adoption

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

List of outstanding issues adopted on 21.05.2015, 26.03.2015. List of questions adopted on 20.11.2014.

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 **under exceptional circumstances** by consensus together with the CHMP assessment report and translation timetable.

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

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

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

The Committee noted the letter of recommendation dated 24.06.2015.

The summary of opinion was circulated for information.

3.1.11. Heparesc - human heterologous liver cells - Orphan - ATMP - EMEA/H/C/003750

Cytonet GmbH&Co KG; treatment of urea cycle disorders (UCD)

Scope: Opinion

Action: For adoption

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

List of outstanding issues adopted on 26.03.2015, 18.12.2014. List of questions adopted on 25.04.2014.

See 2.1.3

The Committee was informed that the CAT had recommended by consensus the refusal of a marketing authorisation for Heparesc. The CAT opinion and assessment report were circulated for information.

An Oral Explanation was held on Tuesday 23 June 2015 at 16.00. The presentation by the applicant focused on the overall benefit / risk of the product.

The Committee questioned the validity of the 13C ureagenesis assay and the clinical relevance of the observed changes. Furthermore uncertainty was expressed on the efficacy data and methodological issues in the conducted studies.

The CHMP adopted a negative opinion by consensus, based on the negative opinion adopted by the CAT, together with the assessment report.

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

The refusal question and answers document was circulated for information.

3.2. Initial applications; Day 180 list of outstanding issues

3.2.1. - cobimetinib - EMEA/H/C/003960

treatment of metastatic melanoma

Scope: Day 180 list of outstanding issue

Action: For adoption

List of questions adopted on 22.01.2015.

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

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

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

Orphan Europe S.A.R.L.; treatment of cystinosis
Scope: Day 180 list of outstanding issue
Action: For adoption
List of questions adopted on 22.01.2015.
The Committee was reminded of the status of this application and its remaining outstanding issues,
The CHMP adopted a list of outstanding issues with a specific timetable.

3.2.3. - talimogene laherparepvec – ATMP - EMEA/H/C/002771

Treatment of adults with melanoma that is regionally or distantly metastatic
Scope: Day 180 list of outstanding issues, BWP Report
Action: For adoption
List of questions adopted on 22.01.2015
The Committee was reminded of the status of this application and its remaining outstanding issues.
Furthermore the CHMP noted that the CAT agreed to consult the SAG Oncology together with the list of questions to the experts. The CHMP adopted an additional question to the SAG and to the applicant. The Committee adopted the BWP Report.
The CHMP noted the list of outstanding issues with a specific timetable as adopted by the CAT during their June Plenary meeting.

3.2.4. - pemetrexed - EMEA/H/C/004011

in combination with cisplatin is indicated for the treatment malignant pleural mesothelioma and non-samll cell lung cancer

Scope: Day 180 list of outstanding issue

Action: For adoption

List of questions adopted on 26.02.2015.

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

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

3.2.5. - glycerol phenylbutyrate - Orphan - EMEA/H/C/003822

Horizon Therapeutics Limited; treatment of patients with urea cycle disorders
Scope: Day 180 list of outstanding issue
Action: For adoption
List of questions adopted on 23.10.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues,
The CHMP adopted a list of outstanding issues with a specific timetable.

3.2.6. - insulin human - EMEA/H/C/003858

treatment of diabetes
Scope: Day 180 list of outstanding issue
Action: For adoption
List of questions adopted on 23.10.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues, The CHMP adopted a list of outstanding issues with a specific timetable.
The Committee adopted the BWP Report.

3.3. Initial applications; Day 120 list of questions

3.3.1. - amlodipine / valsartan - EMEA/H/C/004037

treatment of essential hypertension

Scope: Day 120 list of questions

Action: For adoption

The Committee noted the issues identified in this application.

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

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

Insmed Limited; treatment of Pseudomonas aeruginosa lung infection/colonisation in cystic fibrosis patients, treatment of nontuberculous mycobacterial lung infection.
Scope: Day 120 list of questions and revised timetable on similarity assessment
Action: For adoption
The Committee noted 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 with a specific timetable. The CHMP adopted the timetable for the assessment report of similarity.

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

treatment in exocrine pancreatic insufficiency
Scope: Day 120 list of questions, BWP Report
Action: For adoption
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions The Committee adopted the BWP Report.

3.3.4. - carfilzomib - Orphan - EMEA/H/C/003790

Amgen Europe B.V.; treatment of multiple myeloma
Scope: Day 120 list of questions
Action: For adoption
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions

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

Santen Oy; treatment of chronic non-infectious uveitis of the posterior segment of the eye

Scope: Day 120 list of questions

Action: For adoption

The Committee noted the issues identified in this application.

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

3.3.6. - pemetrexed - EMEA/H/C/004109

Treatment of malignant pleural mesothelioma and non-small cell lung cancer.

Scope: Day 120 list of questions

Action: For adoption

The Committee noted the issues identified in this application.

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

3.3.7. - glycopyrronium bromide - EMEA/H/C/003883

treatment of sialorrhoea

Scope: Day 120 list of questions

Action: For adoption

The Committee noted 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. - recombinant l-asparaginase - EMEA/H/C/002661

combination therapy for B/T cell lymphoblastic leukaemia (ALL) or B/T cell lymphoblastic lymphoma (LBL)

Scope: Letter from the applicant dated 5 June 2015 requesting an extension of clock stop to submit the responses to the D180 list of outstanding issues

Action: For adoption

List of outstanding issues adopted 21.05.2015. List of questions adopted on 25.04.2014.

The CHMP agreed to the request by the applicant for an extension of clock stop to submit the responses to the D180 list of outstanding issues together with a specific timetable.

3.4.2. - susoctocog alfa – Orphan - EMEA/H/C/002792

Baxter AG; treatment of acquired hemophilia

Scope: Report from the BPWP

Action: For adoption

The CHMP adopted the report from the BPWP

3.4.3. - human autologous spheroids of matrix– associated chondrocytes for transplantation – ATMP - EMA/H/C/0002736

Treatment is eligible for single as well as multiple adjacent defects. Cartilage defects of the knee, hip, elbow, shoulder and ankle joints were treated successfully. In a few cases, defect sizes between 11 and 23 cm^2 were treated successfully. The product is indicated for adults and adolescents with a closed epiphyseal growth plate cancer.

Action: for information

Rapporteurs' updated joint feasibility analysis for clock stop extension. At its April 2014 meeting, the CAT/CHMP agreed to a clock stop extension. Based on the progress report provided by the company outlining completed recruitment the CAT confirmed the clock extension.

3.4.4. - p. falciparum circumsporozoite protein fused with hepatitis b surface antigen (rts), and combined with hepatitis b surface antigen (s) in the form of non-infectious virus-like particles (vlps) produced in yeast cells (saccharomyces cerevisiae) by recombinant dna technology - (EMEA/H/W/002300)

indicated for active immunisation against malaria

Scope: List of experts for the SAG Vaccines meeting, taking place on 26th June 2015

Action: For adoption

The CHMP adopted the list of experts for the SAG Vaccines.

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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. Norvir - ritonavir - EMEA/H/C/000127/X/0127

AbbVie Ltd.; the treatment of HIV-1 infection

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

Scope: The MAH applies for a line extension of a new oral powder formulation of Norvir (ritonavir) as a replacement for the currently marketed Norvir oral solution for a more suitable ritonavir formulation for the paediatric population.

Action: For adoption

List of outstanding issues adopted on 26.03.2015. List of questions adopted on 23.10.2014.

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

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

4.3.1. REVOLADE - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/X/0022/G

Novartis Europharm Ltd
Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Dolores Montero Corominas
Scope: "Extension of indication for paediatric (age 1 year and above) chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients who had an insufficient response to other treatments (e.g. corticosteroids, immunoglobulins).
Grouping with the line extension for one new tablet strength (12.5mg) and a new Powder for Oral Suspension formulation (25mg).
The Type II variation and the Extension are grouped within this Application. This grouping is justified, as one of the variations in the group is an extension of the marketing authorisation (Annex III of Commission Regulation (EC) No 1234/2008 of November 2008). Agreed justification. 120 day TT follws Line extension."
Action: For adoption
The Committee discussed the issues identified in this application and concluded that there is a need to clarify a number of quality, non-clinical and clinical issues.
The Committee adopted a request for supplementary information with a specific timetable.
The CHMP adopted the assessment report on similarity.

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

4.4.1. Suboxone - buprenorphine / naloxone - EMEA/H/C/000697/X/0029

RB Pharmaceuticals Ltd.

Rapporteur: Martina Weise

Scope: "Line extension application to add 12mg/3mg and 16mg/4mg sublingual tablets.", Clockstop extension requested to respond to LoOI, .

Letter from the applicant dated 19 June 2015 requesting an extension of clock stop to submit the responses to the list of outstanding issues

List of outstanding issues adopted on 21.05.2015

Action: For adoption

The CHMP agreed to the request by the applicant or an extension of clock stop to submit the responses to the list of outstanding issues together with a specific timetable

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. Adcetris - brentuximab vedotin - Orphan - EMEA/H/C/002455/II/0025

Takeda Pharma A/S

Rapporteur: Pieter de Graeff, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include new indication for Adcetris (ADCETRIS is indicated for the treatment of adult patients at increased risk of relapse or progression following ASCT"). as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application. The CHMP discussed the efficacy data in relation to the safety. The Committee agreed to seek clarification on the benefit/risk in the proposed extension of indication with specific focus on the target population.

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

5.1.2. 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
The Committee discussed the issues identified in this application, which were related to clinical efficacy and RMP. It was agreed that the wording of the SmPC needs to be adapted according to the issues identified.
The Committee adopted a request for supplementary information with a specific timetable.

5.1.3. Cosentyx - secukinumab - EMEA/H/C/003729/II/0001/G

Novartis Europharm Ltd

Rapporteur: Tuomo Lapveteläinen, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension of Indication to include new indication for Cosentyx "treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate as monotherapy or in combination with methotrexate (MTX)".
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, and 5.2 of the SmPC are updated in order to update the safety and efficacy information. The Package Leaflet is updated in accordance. Furthermore, minor editorial changes have been introduced throughout the PI and updated RMP has been also submitted."

Action: For adoption

The Committee discussed the issues identified in this application. The discussion focused on the dosing scheme and the significant clinical benefit in relation to the request for 1 year marketing protection.

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

5.1.4. Cosentyx - secukinumab - EMEA/H/C/003729/II/0002

Novartis Europharm Ltd

Rapporteur: Tuomo Lapveteläinen, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension of indication to add new indication for Cosentyx 'treatment of severe active ankylosing spondylitis in adults who have responded inadequately to conventional therapy'. Consequently SmPC sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, and 5.2 have been revised to include new efficacy and safety information. The Package Leaflet and RMP have been updated accordingly." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

The Committee discussed the issues identified in this application. The discussion mainly concerned the posology (maintenance dose to be used after the loading period).

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

The CHMP agreed by consensus to the request for an additional 1 year of market protection.

5.1.5. CYRAMZA - ramucirumab - Orphan - EMEA/H/C/002829/II/0004

Eli Lilly Nederland B.V.

Rapporteur: Pieter de Graeff, Co-Rapporteur: Kolbeinn Gudmundsson, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include a new indication for Cyramza, in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil), for the treatment of adult patients with metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin and a fluoropyrimidine.
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated.
The Package Leaflet is updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to correct minor editorial mistakes."

Action: For adoption

The Committee discussed the issues identified in this application. The CHMP looked at the efficacy data in relation to the safety. The Committee agreed to seek clarification on the benefit/risk in the proposed extension of indication with specific focus on subgroups.

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

5.1.6. Edurant - rilpivirine - EMEA/H/C/002264/II/0017/G

Janssen-Cilag International N.V.

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include treatment of ARV treatment-naïve paediatric patients aged 12 to <18 years of age based on the results of the 48-week data of study TMC278-TiDP38-C213 (PAINT), undertaken to evaluate the pharmacokinetics, safety/ tolerability, and efficacy of RPV 25 mg qd in combination with an investigator-selected background regimen containing 2
nucleoside (nucleotide) reverse transcriptase inhibitors (NRTIs) in this adolescent population.
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly.
A revised RMP version 6.0 was included as part of this application."

Action: For adoption

The Committee discussed the issues identified in this application. The discussion was mainly on the possible development of resistance in relation to low adherence.

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

5.1.7. Eylea - aflibercept - EMEA/H/C/002392/II/0021

Bayer Pharma AG

Rapporteur: Pierre Demolis, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Arnaud Batz

Scope: "Extension of Indication to include a new indication for adult for the treatment of

visual impairment due to myopic choroidal neovascularisation (myopic CNV).
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 are updated. The Package Leaflet is updated in accordance.
In addition, some editorial changes are proposed in section 5.1 of the SmPC, in the Annex II and in the PL."

Action: For adoption

The Committee discussed the issues identified in this application. The members noted that the clinical trial conducted in support of the extension of indication exclusively included Asian patients, with no data on the EU population available. The Committee discussed the ethnical insensitivity analysis of aflibercept in Asians and Caucasians provided by the MAH. The members concluded that the study data could be extrapolated to the EU population, but further information on some observed heterogeneity between Asians and non-Asians in the responses to aflibercept treatment should be provided by the MAH. The MAH was furthermore asked to present plans to better understand drug use in myopic CNV patients compared to other indications including frequency of injections in European clinical practice.

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

5.1.8. Humira - adalimumab - EMEA/H/C/000481/II/0137

AbbVie Ltd.
Rapporteur: Kristina Dunder, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga
Scope: "The Marketing authorisation holder (MAH) applied for a new indication for the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adult patients, including treatment of inflammatory lesions and prevention of worsening of abscesses and draining fistulas. Consequently, the MAH proposed the update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC. The Package Leaflet was proposed to be updated in accordance.
Action: For adoption
Request for supplementary information adopted on 26.02.2015.
The Committee confirmed that all issues previously identified in this application had been resolved.
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.

5.1.9. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0027

Vertex Pharmaceuticals (U.K.) Ltd.
Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Miguel-Angel Macia
Scope: "Extension of indication for Kalydeco to include the treatment of cystic fibrosis in patients aged 18 years and older who have a R117H mutation in the CFTR gene. Consequently, changes are proposed to sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and to the Package Leaflet."
Action: For adoption

Request for supplementary information adopted on 26.02.2015, 23.10.2014.
The Committee discussed the issues identified in this application. The Committee discussed whether the indication can be extended to children and adolescents and what kind of information can be included in the SmPC in this respect. The Committee agreed that indication should be revised and SmPC changes are needed.
The Committee adopted a 3rd request for supplementary information with a specific timetable.

5.1.10. Levemir - insulin detemir - EMEA/H/C/000528/II/0070

Novo Nordisk A/S
Rapporteur: Jens Heisterberg
Scope: "Update of sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to extend the clinical use of Levemir in children from 2 years to 1 year of age.
The Package Leaflet is updated accordingly."
Action: For adoption
Request for supplementary information adopted on 26.03.2015.
The Committee confirmed that all issues previously identified in this application had been resolved.
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.
The CHMP considered that the PSUR cycle for Levemir should be changed from 3-yearly to yearly.

5.1.11. Nplate - romiplostim - Orphan - EMEA/H/C/000942/II/0051

Amgen Europe B.V.

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

Scope: "Extension of Indication to include second line treatment of all non-splenectomised patients (including those without a contraindication to surgery). As a consequence, section 4.1 of the SmPC has been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in Croatia and Italy in the Package Leaflet."

Action: For adoption

The Committee discussed the issues identified in this application. The discussion focused on the benefit/risk in the applied indication considering the heterogeneous population of non-splenectomized patients. The Committee agreed to request further information on the benefit/risk in the different subgroups.

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

5.1.12. Perjeta - pertuzumab - EMEA/H/C/002547/II/0010

Roche Registration Ltd;
Rapporteur: Christian Schneider, Co-rapporteur: Daniela Melchiorri, PRAC Rapporteur: Doris Stenver;
Scope: "Extension of indication to include the use of pertuzumab in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence.
As a consequence, update of sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC. In addition, the MAH took the opportunity to make a correction in sections 2 and 6.6 of the SmPC regarding the dose contained in 1 ml of solution after dilution.
The Package Leaflet is updated in accordance."
Action: For adoption
Request for supplementary information adopted on 21.05.2015, 18.12.2014.
The Committee confirmed that all issues previously identified in this application had been resolved.
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. Rebetol - ribavirin - EMEA/H/C/000246/II/0074

Merck Sharp & Dohme Limited
Rapporteur: Joseph Emmerich
Scope: "Change of the indication of Rebetol to reflect that ribavirine is indicated in the treatment of hepatitis C in combination with other medicinal products and remove reference to the peginterferon used (2a or 2b) in line with the PRAC recommendation in the PSUR assessment (EMEA/H/C/PSUSA/000100007/201307). As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.7, 4.8, 4.9 and 5.1 of the SmPC are updated. The package leaflet is updated accordingly."
Action: For adoption
Request for supplementary information adopted on 26.03.2015, 23.10.2014.
The Committee discussed the issues identified in this application, which were related to updates in the SmPC and PL of the product according to the CHMP requests on content and QRD included in the product information.
The Committee adopted a 3rd request for supplementary information with a specific timetable.

5.1.14. REVOLADE - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0020

Novartis Europharm Ltd

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

Scope: "Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to add a new indication on the treatment of adult patients with severe aplastic anaemia (SAA) who have

had an insufficient response to immunosuppressive therapy. The package leaflet is updated accordingly. In addition, the MAH has corrected the acronym used for full blood counts (FBC) in the SmPC, Annex II and PL."

Action: For adoption

Request for supplementary information adopted on 26.02.2015.

The Committee discussed the issues identified in this application. The main discussions focused on the wording of the indication and it was agreed to consult the MAH on this issue.

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

5.1.15. REVOLADE - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0023

Novartis Europharm Ltd

Rapporteur: Arantxa Sancho-Lopez, Co-Rapporteur: Greg Markey, Scope: "Extension of Indication to extend the use of Revolade to non-splenectomized patients.
As a consequence, section 4.1 of the SmPC is updated. The Package Leaflet is updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application. The discussion focused on the benefit/risk in the applied indication considering the heterogeneous population of non-splenectomized patients. The Committee agreed to request further information on the benefit/risk in the different subgroups.

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

The CHMP adopted the assessment report on similarity.

5.1.16. Stayveer - bosentan - EMEA/H/C/002644/II/0011

Marklas Nederlands BV

Rapporteur: Pierre Demolis, PRAC Rapporteur: Arnaud Batz

Scope: "Update of SmPC sections 4.2, 4.5, 4.6, 4.8, 5.1, 5.2 and 5.3 to reflect non-clinical and clinical data generated in studies conducted according to the agreed Paediatric Investigation Plan for bosentan (EMEA-000425-PIP02-10-M04) in line with the recently approved application II-66 for Tracleer (bosentan). The Annex II and the Package Leaflet have been updated accordingly. Further, the MAH took the opportunity to make editorial changes in the SmPC and to update the contact details of the local representatives in the Package Leaflet. In addition, taking into account the new data in the paediatric population, an updated version of the RMP (version 7) aligned with RMP version 7 for Tracleer was provided."

Action: For adoption

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

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 CHMP noted the letter of recommendation dated 22.06.2015.

The summary of opinion was circulated for information.

5.1.17. Tysabri - natalizumab - EMEA/H/C/000603/II/0077

Biogen Idec Ltd
Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: "Extension of Indication to include new indication for Tysabri.
As a consequence, sections 4.1 and 4.4 of the SmPC are updated in order to provide physicians with more options for treating RRMS patients with high disease activity who fail an initial disease modifying therapy (DMT). Consequential changes to sections 4.2, 4.3, 5.1 and Package Leaflet in Sections 2 and 3 are also proposed."
Action: For adoption
The Committee discussed the issues identified in this application, which were related to major safety issues (insufficient safety dataset) and several efficacy questions had been raised. The Committee noted the major safety concern - the possible increase in the frequency of progressive multifocal leukoencephalopathy (PML) events due to the sequential use of new disease-modifying therapies with immunosuppressive activity and Tysabri. It is at present not known if the risk minimization measures proposed by the MAH to prevent the potential additive negative effect on PML occurrence will be efficacious, and as such cannot be considered to resolve the safety concern.
The Committee adopted a request for supplementary information with a specific timetable.

5.1.18. Voncento - human coagulation factor viii / human von willebrand factor - EMEA/H/C/002493/II/0008/G

CSL Behring GmbH;

Rapporteur: Pieter de Graeff, Co-rapporteur: Greg Markey, PRAC Rapporteur: Sabine Straus;

Scope: "Extension of indication to include prophylactic treatment of patients with Von Willebrand Disease (VWD); in addition, the product information has been updated to provide data on the treatment of paediatric patients with VWD. As a consequence, sections 4.1, 4.2, 4.4, 4.9, 5.1 and 5.2 of the SmPC have been updated. The package leaflet is updated accordingly. Moreover, the MAH took the opportunity to correct the manufacturing sites addresses in Annex II and to make editorial changes to the product information."

Action: For adoption

Request for supplementary information adopted on 21.05.2015, 18.12.2014.

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

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)

7.1.1. Daclatasvir compassionate use - EMEA/H/K/0003867/OTH/0001

Daclatasvir for the use in combination with sofosbuvir +/- ribavirin, for genotype 1 adult patients at a high risk of decompensation or death within 12 months if untreated

Action: For adoption

Assessment report

The CHMP adopted the Development Safety Update Report (DSUR) assessment report.

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. – Elotuzumab - Orphan - H0003967

Bristol-Myers Squibb Pharma EEIG, Treatment of multiple myeloma in combination with lenalidomide and dexamethasone in patients who have received one or more prior therapies

Scope: Request for an accelerated review

Action: For adoption

Rapporteurs' accelerated assessment briefing note

Letter from the company dated 18 May requesting an accelerated review.

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

8.1.2. Drisapersen Sodium - H0003846

Treatment of Duchenne Muscular Dystrophy (exon 51 mutation specific)

Scope: Request for an accelerated review

Action: For adoption

Rapporteurs' accelerated assessment briefing note

Letter from the company dated 18 May requesting an accelerated review.

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

8.1.3. - Begelomab - Orphan - H0004144

ADIENNE S.r.l. S.U., indicated for the treatment of steroid resistant acute Graft-versus-Host Disease (GvHD) in adult patients who underwent allogeneic haematopoietic progenitor cell transplantation (HPCT) and received a standard immunosuppressive regimen

Scope: Request for an accelerated review

Action: For adoption

Letter from the company dated 4 May 2015 requesting an accelerated review.

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.

8.1.4. - Elbasvir\Grazoprevir - H0004126

Grazoprevir, a hepatitis C virus (HCV) NS3/4A protease inhibitor, in combination with

elbasvir, a HCV NS5A inhibitor, is indicated for the treatment of chronic hepatitis C (CHC) Genotypes 1, 4, and 6 infection

Scope: Request for an accelerated review

Action: For adoption

Letter from the company dated 5 June 2015 requesting an accelerated review.

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

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Pradaxa - dabigatran etexilate –EMEA/H/C/000829; Xarelto – Rivaroxaban – EMEA/H/C/000944; Eliquis – Apixaban – EMEA/H/C/002148; Lixiana – Edoxaban – EMEA/H/C/002629

Boehringer Ingelheim International GmbH (Pradaxa), Bayer Pharma AG (Xarelto), Bristol-Myers Squibb / Pfizer (Eliquis), Daiichi Sankyo Europe GmbH (Lixiana)
Lead Rapporteur: Jens Heisterberg,
Rapporteurs: Joseph Emmerich, Rafe Suvarna, Kristina Dunder, Martina Weise, Pieter de Graeff, Concepcion Prieto Yerro,
Scope: New oral anticoagulants - LEGs
Action: For discussion
The CHMP noted the overview of characteristics in currently authorised NOACs and discussed further actions to be taken.
CHMP was of the view that there is a need to shed further light on the utility of implementing limited or targeted PK or PD measurements in the clinical use of the new oral anticoagulants for more individualised dosing. In addition, compound-specific questions were raised.
CHMP agreed to liaise with all concerned MAHs to obtain further data and information and agreed on a further LOQ to MAHs. CHMP also agreed to obtain expert's opinion on the topic through a public expert workshop planned for Q4 2015 (date to be confirmed).
All MAHs will receive the LOQs following the CHMP meeting this week. It was agreed to inform PRAC and to come back to this topic.

9.1.2. Kolbam - Cholic Acid - Orphan - EMEA/H/C/002081

ASK Pharmaceuticals GmbH, treatment of inborn errors of primary bile acid synthesis

Rapporteur: Robert James Hemmings, Co-Rapporteur: Patrick Salmon

Scope: Update on licensing status

Action: For discussion

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

"Case T-452/14 – CTRS v Commission – Judgement of 11 June 2015 by which the General

Court annuls the Commission Implementing Decision C(2014) 2375 of 4 April 2014 granting, in exceptional circumstances, marketing authorisation under Regulation (EC) No 726/2004 of the European Parliament and of the Council for 'Cholic Acid FGK — cholic acid', an orphan medicinal product for human use, as amended by Commission Implementing Decision C(2014) 6508 of 11 September 2014 transferring and amending the marketing authorisation granted in exceptional circumstances by Decision C(2014) 2375 for 'Kolbam — cholic acid', an orphan medicinal product for human use".

The Committee noted the update.

9.1.3. Mysimba - Naltrexone/Bupropion – EMEA/H/C/003687/ANX 001

Orexigen Therapeutics Ireland Limited, indicated for the management of obesity

Rapporteur: Jens Heisterberg, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Martin Huber,

Scope: PASS protocol review, Request for supplementary information, PRAC advice

PRAC consultation on a PASS protocol for a multicentre, randomised, double-blind, placebo-controlled, phase 4 study to assess the effect of naltrexone extended release (ER) /bupropion ER on the occurrence of major adverse cardiovascular events (MACE) in overweight and obese subjects

Action: For adoption

The CHMP discussed the PRAC report including a request for supplementary information. Most of the PRAC recommendations were included in the CHMP list of questions. Feedback on the CHMP discussion will be given to the PRAC.

9.1.4. CellCept - Mycophenolate Mofetil,Mycophenolate Mofetil Hydrochloride - EMEA/H/C/000082

Roche Registration Ltd, prophylaxis of acute transplant rejection
Rapporteur: Rafe Suvarna, Co-Rapporteur: Patrick Salmon,
Scope: ANSM communication on the teratogenic risks associated with mycophenolates
Action: For discussion
Complete application (stand-alone) - Council Directive 81/851/EEC
The Committee was informed about the planned communication by the French agency ANSM related to the teratogenic risks of mycophenolates, when using mycophenolate-containing medicines during pregnancy. The outcome of this evaluation (to determine whether to update the advice for patients and healthcare professionals in the medicine's product information) from PRAC is expected in September 2015. Lines to take will be circulated.

9.1.5. TECFIDERA - Dimethyl Fumarate - EMEA/H/C/002601/WS0689/G; NAPs included in WS: Fumaderm, Fumaderm Intial

MAH: Biogen Idec Ltd, treatment of multiple sclerosis

Rapporteur: Martina Weise, Co-Rapporteur: Robert James Hemmings,

Scope: “Update of sections 4.4 of the SmPC in order to add a recommendation to consider interruption of treatment in patients with low lymphocyte counts (<0.5 x 109/L) persisting for more than six months and to monitor lymphocyte counts until recovery. Update of section 4.8 of the SmPC with information on observed low lymphocyte counts in clinical studies with tecfidera and PML (Progressive multifocal leukoencephalopathy) occurrence in the setting of severe and prolonged lymphopenia. Furthermore, the due dates of two commitments as part of the RMP have been revised.” Request for supplementary information adopted on 23.04.2015, 26.02.2015.

Report from SAG Neurology held on 11 June 2015

Action: For discussion

The CHMP noted the report from the SAG. The SAG advised on risk factors for developing PML as well as on parameters to be studied on the potential risks of lymphopenia and PML. Furthermore the SAG commented on monitoring algorithms to minimise the risk of developing PML for patients with MS and psoriasis receiving fumarates/ dimethylfumarate. For patients switching from natalizumab to dimethylfumarate, the SAG recommended a high vigilance for the first 6 months. The experts supported further investigation on the posology for patients experiencing lymphopenia in view of efficacy and safety.

9.1.6. Rotarix - human rotavirus, live attenuated - EMEA/H/C/000639/II/0062

GlaxoSmithKline Biologicals S.A.,
Rapporteur: Daniel Brasseur, PRAC Rapporteur: Jean-Michel Dogné,
Scope: Opinion, VWP Report
“To submit the final report of genetic stability study EPI-ROTA-014 VS BE – 112560 that addresses the Post-Approval Measure ME2 005.2 in which the MAH commits to monitor for the potential occurrence of genetic drifts and shifts in the vaccine strain in post-marketing settings.” Request for supplementary information adopted on 24.07.2014, 20.03.2014.

Action: For discussion

The CHMP adopted the VWP report.

The PRAC recommendation endorsing the VWP report and a request for supplementary information was noted. The CHMP was in agreement in principle; however members should make comments if applicable via their PRAC representatives.

9.1.7. Picato - ingenol mebutate - EMEA/H/C/002275/II/0012

Leo Pharma A/S

Rapporteur: Robert James Hemmings,
Scope: Opinion or request for supplementary information
“Update sections 4.2, 4.8 and 5.1 to provide new efficacy and safety data supporting a labelling update that introduces repeat treatment of Picato gel (150 mcg/g and 500 meg/g), based on Trial LP0041-22. The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor linguistic amendments.”

Request for supplementary information adopted on 23.04.2015.

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 members were in agreement with the CHMP recommendation.

10. Referral procedures

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

10.1.1. Canagliflozin – INVOKANA- EMEA/H/C/002649; canagliflozin, metformin – VOKANAMET - EMEA/H/C/002656; dapagliflozin – FORXIGA - EMEA/H/C/002322; dapagliflozin, metformin – XIGDUO - EMEA/H/C/002672; empagliflozin - JARDIANCE - EMEA/H/C/002677; empagliflozin, metformin – SYNJARDY EMEA/H/C/003770

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

Rapporteurs: Martina Weise, Kristina Dunder, Filip Josephson, Agnes Gyurasics, Pieter de Graeff, Bart Van der Schueren, Daniela Melchiorri

Scope: Signal of diabetic ketoacidosis - start of Article 20 referral at PRAC

Action: For information

The CHMP noted the start of procedure at the PRAC.

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

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

Scope: Assessment timetable

Action: Adopted by written procedure

The CHMP adopted a revised timetable by written procedure:

Co-Rapporteur's assessment report: 26.06.2015

Lead Rapporteur's assessment report: 03.07.2015

Comments: 10.07.2015

CHMP discussion/revision of the interim CHMP AR as applicable: July 2015 CHMP

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. IOGOL and associated names soft capsules, 25 / 50 mg - diclofenac epolamine - EMEA/H/A-29/1414)

Regiomedica GmbH
Rapporteur: Martina Weise, Co-Rapporteur: Concepcion Prieto Yerro,
Scope: List of outstanding issues
Disagreements regarding the demonstration of bioequivalence with the reference product
Action: For adoption
RMS: DE, CMS: AT, BE, CZ, EL, ES, HU, IT, PL, SK, UK, Decentralised procedure number: DE/H/3633/002-003/DC
The Committee discussed the difference in Cmax between the test and reference product. Some members expressed their view, that differences in Cmax values are small and not expected to affect efficacy or safety of the test product in the proposed indication / posology since conditions of total systemic absorption are very similar. However, some members were of the opinion that lower Cmax of the test product may have a clinically relevant impact on the efficacy, and therefore B/R was considered non-approvable.
The food impact on the absorption of the medicinal product was also discussed, and the decrease in Cmax when taken with food was highlighted, casting doubts on the efficacy of Iogol when administered with food. Therefore some of the members were of the view that the proposed method of administration of the test product reflecting this difference, which is also different to that of the reference product, should be justified.
The CHMP adopted a list of outstanding issues with a specific timetable:
Adoption list of outstanding issues: 25.06.2015 CHMP
Submission of responses: 03.08.2015
Re-start of the procedure: 25.08.2015
Rapporteur and co-rapporteur assessment reports circulated to CHMP: 09.09.2015
Comments: 14.09.2015

10.5. Oral Explanation / CHMP opinion: September 2015 CHMP Harmonisation - Referral procedure under Article 30 of Directive 2001/83/EC

10.5.1. Amoxil - amoxicillin - EMEA/H/A-30/1372

GlaxoSmithKline

Rapporteur: Robert James Hemmings, Co-Rapporteur: Concepcion Prieto Yerro,

Scope: Opinion or List of outstanding issues

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

Action: For adoption

List of questions adopted on 25.07.2013. List of outstanding issues adopted 25.04.2014,

23.10.2014, 26.02.2015.

The Committee confirmed that all issues previously identified in this referral had been resolved.

The CHMP adopted an opinion by consensus recommending changes to the SmPCs, labelling and package leaflets. The 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.

10.5.2. Clenil and associated names - Beclometasone dipropionate - EMEA/H/A-30/1418

Chiesi group of companies and associated companiesScope: Appointment of Rapporteurs, list of questions and timetable
Harmonisation exercise for Clenil and associated names (beclometasone dipropionate). The review was triggered by Italy due to the need to harmonise the product information across all Member States, including the therapeutic indication, the target populations and the posology recommendations.
Action: For adoption
The CHMP noted the letter from AIFA in Italy dated 19 June 2015 notifying of the official referral under Article 30
The CHMP appointed Daniela Melchiorri as Rapporteur (interest level 1) and Martina Weise as Co-Rapporteur (interest level 2).
The CHMP adopted a list of questions with a specific timetable.
Notification: 19.06.2015
Start of procedure: June 2015 CHMP
Adoption of list of questions: 25.06.2015
Submission of responses: 10.09.2015
Re-start of the procedure: 24.09.2015
Rapporteur and co-rapporteur assessment reports circulated to CHMP: 07.10.2015
CHMP member comments: 12.10.2015
Updated rapporteur and co-rapporteur assessment reports circulated to CHMP: 15.10.2015
Adoption of list of outstanding issues / CHMP opinion: October 2015 CHMP

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

10.6.1. Adrenaline auto injectors (EMEA/H/A-31/1398)

Rapporteur: Alar Irs, Co-Rapporteur: Robert James Hemmings,

Scope: Opinion or possible oral explanation

Article 31 triggered by the MHRA due to the lack of robust evidence that the devices deliver the adrenaline intramuscularly in all patients.

Action: For adoption

List of outstanding issues adopted on 26.02.2015 and 25.09.2014. Ad-hoc expert group meeting held on 23 January 2015.

See 2.4.1

The Committee was reminded of previous discussions and noted the PRAC advice. The members discussed the proposed PK/PD studies to assess the influence of different factors on distribution, exposure and activity of adrenaline when administered via the different auto-injector devices and to what extent the protocols from the different MAHs should be harmonised. The Committee considered slightly different protocols as acceptable. Furthermore the members agreed on a recommendation for patients to carry 2 pens at all times in light of uncertainties in whether a single administration would suffice for any given episode. In addition other changes to the product information and risk minimisation measures were discussed and agreed.

The CHMP concluded that the benefit-risk balance for adrenaline auto-injectors remains favourable subject to the agreed changes to the product information and the agreed additional risk minimisation measures.

The Committee adopted a positive opinion recommending by consensus that the marketing authorisations for these medicinal products should be varied. The CHMP also adopted the assessment report and translation timetable.

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

The CHMP agreed to the EMA public health communication.

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 2015 Early Notification System on Envisaged CHMP Recommendations for Regulatory Action (based on Identified Safety Concerns) Accompanied by Communication to the General Summary of recommendations and advice of PRAC meeting held on 08-11 June 2015.

Action: For information

11.1.1. Gilenya - Fingolimod Hydrochloride - EMEA/H/C/002202

Novartis Europharm Ltd, treatment of multiple sclerosis

Rapporteur: Pierre Demolis, Co-Rapporteur: Filip Josephson,

Scope: Signal of occurrence of one case of progressive multifocal leukoencephalopathy (PML) without prior natalizumab use

Report SAG/ad hoc expert advisory group for fingolimod held 11 June 2015.

Action: For discussion

The CHMP noted the report from the SAG. The SAG advised on risk factors for developing PML as well as on parameters to be studied on the potential risks of lymphopenia and PML. The experts agreed that further data was needed on the impact of T-helper and regulator cells on PML development. Furthermore the SAG commented on monitoring algorithms to minimise the risk of developing PML and their general applicability. No clear advice could be given on the fingolimod treatment strategy for high risk PML patients or patients diagnosed with PML.

11.1.2. Canagliflozin – INVOKANA- EMEA/H/C/002649; canagliflozin, metformin – VOKANAMET - EMEA/H/C/002656; dapagliflozin – FORXIGA - EMEA/H/C/002322; dapagliflozin, metformin – XIGDUO - EMEA/H/C/002672; empagliflozin - JARDIANCE - EMEA/H/C/002677; empagliflozin, metformin – SYNJARDY EMEA/H/C/003770

Outcome of PRAC discussion upon signal assessment adopted at the 08-11 June 2015 PRAC meeting.

Rapporteurs: Pieter de Graeff, Kristina Dunder and Martina Weise

Scope: Signal of diabetic ketoacidosis; PRAC recommendation of DHPC and its communication plan

Action: For adoption

The CHMP adopted the PRAC recommendation and the DHPC and its communication plan with some modifications.

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Action: For information

13.2. Innovation Task Force briefing meetings

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

13.2.1. ITF Briefing Meeting

Action: For adoption

The CHMP agreed to the ITF Briefing Meeting

13.2.2. ITF Briefing Meeting

Action: For adoption

The CHMP agreed to the ITF Briefing Meeting

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Strategic Review & Learning Meeting

Outcome and follow-up items from the Strategic review and learning Meeting under Latvian Presidency, Ljubljana, Slovenia held on 26-28 May 2015

Action: For information

Presentations from the meeting. The members agreed to the follow-up items resulting from the strategic review and learning meeting.

The CHMP noted the feedback on the programme of the Strategic review and learning meeting in Ljubljana.

14.1.2. CHMP plenary 17-20 August 2015 to be replaced by CHMP written procedure

Action: For adoption

Timetable for August 2015 written procedure

The CHMP adopted the timetable for the August 2015 written procedure.

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 08-11 June 2015

Action: For information

The Committee noted the report.

The members noted the Summary of recommendations and advices of the PRAC meeting.

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for June 2015

Action: For adoption

The EURD list was adopted.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 18-19 June 2015
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 4-7 May 2015
Action: For information
The CHMP noted the report.

Letter from HMPC concerning the toxicological assessment of pulegone/menthofuran and consequences for medicinal products containing menthae piperitae aetheroleum
Action: For Discussion
The CHMP agreed to consult the SWP.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at June 2015 PDCO
Action: For information
The CHMP noted the report

Report from the PDCO meeting held on 17-19 June 2015
Action: For information
The CHMP noted the report

PIP: Expected key elements and requirements for a new DTaP-containing combination vaccine
Answers to public comments and final document
Action: For adoption

The document defines the study outline that applicants should follow when preparing the PIP for a new diphtheria-tetanus-acellular pertussis (DTaP) containing combination vaccine (e.g. pentavalent, hexavalent, heptavalent), for a priming schedule and booster dose before 2 years of age. This document applies to new combinations with known DTaP antigens and components and to those vaccines in which additional antigen(s) were added while retaining the known antigens (e.g. by adding an additional pertussis component).
The CHMP adopted the document.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 16-18 June 2015
Action: For information

The CHMP noted the report.

14.2.6. CMDh

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 22-24 June 2015

Action: For information

The CHMP noted the report.

Letter from CMD(h) dated 29 May 2015 to CHMP (PKWP / MSWG) on biowaiver justification

Action: For discussion

Question to CHMP (PKWP / MSWG) on biowaiver justification

The CHMP agreed to consult the PKWP / MSWP

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

14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 1-3 June 2015. Table of conclusions

Action: For information

The CHMP noted the report.

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

14.3.2. Invented name issues

Table of Decisions of the NRG meeting held on 20 May 2015.

Action: For adoption

The CHMP adopted the Table of Decisions

14.3.3. Quality Working Party (QWP)

Q&A on complex manufacturing processes (EMA/CHMP/CVMP/QWP/390257/2015)
Action: For adoption
The CHMP adopted the Q&A document (What is understood by “manufactured by complex manufacturing processes” in change code B.II.b.4 (change in batch size of the finished product) or in change code B.II.b.1 (replacement or addition of a manufacturing site)? H+V).

14.3.4. Gastroenterology Drafting Group

Guideline on the evaluation of medicinal products for the treatment of chronic constipation (including opioid induced constipation) and for bowel cleansing

Action: For adoption

The guideline is intended to assist applicants during the development of products for the treatment of Chronic Constipation and the related fields of “Opioid Induced Constipation” and for the development of purgatives for the cleansing of the bowels in relation to procedures needing a clean bowel.

The CHMP adopted the guideline. The guideline will come into effect on 1 January 2016.

14.3.5. Biostatistics Working Party (BSWP)

Nomination of Mr Jiri Haman (CZ) as observer to Biostatistics Working Party

Action: For adoption

The CHMP noted the observer to the Biostatistics WP.

14.4. Cooperation within the EU regulatory network

None

14.5. Cooperation with International Regulators

None

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

None

14.7. CHMP work plan

14.7.1. CHMP Work Plan 2015 - update on activities

Action: **For information**

The CHMP noted the update on activities.

14.7.2. Planning and reporting

2015 initial MAA submissions with appointed Rapporteur

Q2-15 planning update

Action: For information

The CHMP noted the planning update.

14.8. Others

None

15. Any other business

15.1. Revision of the Accelerated Assessment guideline

Action: For discussion

The CHMP discussed the revision of the guideline. Members were invited to send comments on the revised guideline

15.2. Enhanced early dialogue to foster development and facilitate accelerated assessment

Action: For discussion

The CHMP noted the update on the enhanced early dialogue to foster development and facilitate accelerated assessment.

15.3. Patient involvement in benefit and risk assessment of medicinal products

Action: For discussion

The CHMP noted the presentation on the first pilot. The CHMP members will be invited to participate in the survey (a separate communication will be circulated to the members). The results will be updated and presented to the CHMP at their July meeting. The Committee was informed about a planned second larger pilot.

15.4. Committee update on CHMP/PRAC Liaison person for the PRAC-led variations

Action: For discussion

The members were informed about the new role of the CHMP/PRAC Liaison person. It was emphasized that this role has been established for administrative purposes only – as PRAC has responsibility producing assessment reports on specific variations (PRAC led variations), then CHMP member or alternate from the same member state is appointed as Liaison person for such variations. It was noted that the scientific responsibilities could be delegated to the PRAC Rapporteur.

15.5. Update of CHMP D210 AR template for initial marketing authorisation applications

Action: For adoption

The Summary of Proposed changes included the changes in following sections: Pharmacovigilance, Risk Management Plan, Product Information, Background information on the procedure. This information was circulated to the members in advance. In addition, another change was presented for section for recommendations, as QRD template version 9.1 was recently finalised and published (10/06/15). This change consists of an alignment of wording and guidance for conditions in AR template with wording for Annex II in QRD template version 9.1. It was discussed that Effects tables could potentially also be included in the AR template, in line with wording and location of the already updated Rapporteurs' report templates.

The Committee adopted the updated CHMP D210 AR template for initial marketing authorisation applications.

15.6. First draft of Scientific Guidance on Post-authorisation Efficacy Studies (PAES)

Action: For information

The CHMP noted the first draft of Scientific Guidance on Post-authorisation Efficacy Studies (PAES). This guidance is intended to provide scientific guidance for MAHs and for competent authorities regarding PAES in the EU on the general need for such studies, on general methodological considerations, on specific situations and on study conduct.

Comments from CHMP should be sent. The guideline will be put for 3 months public consultation after that (current planning for Q3/4 2015).

15.7. Feedback on Early Background Summaries

Action: For discussion

15.8. The Committee was informed about the pilot of the EMA early background summary. Feedback from the assessors will be collected by end of 2015. The comment was made to inform the assessors at an early stage of the assessment, for them to be able to complete the data in parallel to the assessment. Expertise of CHMP members and alternates

Action: For agreement

The members are asked to discuss and agree on the expertise required for the 5th co-opted member. The CHMP agreed on the area of expertise as epidemiology.

The election is planned for the September CHMP Plenary meeting. Nominations for a co-opted member with expertise in epidemiology should be sent

15.9. Report on benefit/risk project

The CHMP noted the update on the benefit/risk project, which resulted from a workshop to identify ways to improve the process of preparing the benefit/risk section in the assessment report. As next steps tools/training materials will be developed and the guidance will be updated. Lead member states have been identified for specific topics. Members were asked to provide any existing tools and training material on the topics.

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 22-25 June 2015 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	
Viola Macolić Šarinić	Member	Croatia	No interests declared	
Ana Dugonjić	Alternate	Croatia	No interests declared	
Panayiotis Triantafyllis	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No restrictions applicable to this meeting	
Radka Montoniová	Alternate	Czech Republic	No interests declared	
Jens Heisterberg	Member	Denmark	No restrictions applicable to this meeting	
Christian Schneider	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	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Pierre Demolis	Member (Vice-Chair)	France	No interests declared	
Joseph Emmerich	Alternate	France	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	
Melinda Sobor	Alternate	Hungary	No interests declared	
Hrefna Gudmundsdottir	Alternate	Iceland	No interests declared	
Patrick Salmon	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No interests declared	
Natalja Karpova	Alternate	Latvia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Romaldas Mačiulaitis	Member	Lithuania	No restrictions applicable to this meeting	
John Joseph Borg	Member	Malta	No interests declared	
Pieter de Graeff	Member	Netherlands	No interests declared	
Johann Lodewijk Hillege	Alternate	Netherlands	No interests declared	
Karsten Bruins Slot	Member	Norway	No interests declared	
Piotr Fiedor	Member	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Dinah Duarte	Alternate	Portugal	No interests declared	
Nela Vilceanu	Member	Romania	No interests declared	
Ivana Pankuchova	Alternate	Slovakia	No interests declared	
Stanislav Primožič	Member	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Arantxa Sancho-Lopez	Alternate	Spain	No interests declared	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Greg Markey	Member	United Kingdom	No interests declared	
Rafe Suvarna	Alternate	United Kingdom	No interests declared	
Robert James Hemmings	Co-opted member	United Kingdom	No restrictions applicable to this meeting	
Hubert Leufkens	Co-opted member	Netherlands	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	
Sabine Mayrhofer	Expert - in person*	Germany	No interest declared	
Patricia Diaz Ramos	Expert - in person*	Spain	No restrictions applicable to this meeting	
Mette Tranholm	Expert - in person*	Spain	No interest declared	
Valerie Lescrainier	Expert - in person*	Belgium	No interest declared	
Ulf Vigonius	Expert - in person*	Denmark	No participation in discussions, final deliberations and voting on:	5.1.1.Adcetris - brentuximab vedotin - Orphan - EMEA/H/C/002455/II/0025
Claire-Li Ding	Expert - in person*	France	No interest declared	
Cécile Dop	Expert - in person*	France	No interest declared	
Marc Martin	Expert - in person*	France	No interest declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Alexandre Moreau	Expert - in person*	France	No interest declared	
Mair Powell	Expert - in person*	United Kingdom	No interest declared	
Anna Hrabovska	Expert - in person*	Slovakia	No restrictions applicable to this meeting	
Leon Bongers	Expert - in person*	Netherlands	No interest declared	
Michelle Beharry	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Maria Jesús Fernández Cortizo	Expert - via telephone*	Spain	No interests declared	
Sinan B. Sarac	Expert - via telephone*	Denmark	No interests declared	
Kristina Bech Jensen	Expert - via telephone*	Denmark	No interests declared	
Paula Salmikangas	Expert - via telephone*	Finland	No interests declared	
Jorge Camarero Jiménez	Expert - via telephone*	Spain	No restrictions applicable to this meeting	
Elmer Schabel	Expert - via telephone*	Germany	No interests declared	
Ralf Sanzenbacher	Expert - via telephone*	Germany	No interests declared	
Egbert Flory	Expert - via telephone*	Germany	No interests declared	
Janet Schriever	Expert - via telephone*	Germany	No interests declared	
Michael Kölch	Expert - via telephone*	Germany	No restrictions applicable to this meeting	
Ingrid Wang	Expert - via telephone*	Norway	No restrictions applicable to this meeting	
Tamar Wohlfarth	Expert - via telephone*	Netherland	No restrictions applicable to this meeting	
Serge Bakchine	Expert - via telephone*	France	No restrictions applicable to this meeting	
Karri Penttilä	Expert - via telephone*	Finland	No interests declared	
Olli Tenhunen	Expert - via telephone*	Finland	No restrictions applicable to this meeting	
Kristiina Airola	Expert - via telephone*	Finland	No interests declared	
Mika Kastarinen	Expert - via telephone*	Finland	No interests declared	
Sabine Straus	Expert - via telephone*	Netherlands	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Maria Vanenburg	Expert - via telephone*	Netherlands	No interests declared	
Hendrik Kommerie	Expert - via telephone*	Netherlands	No interests declared	
Paolo Foggi	Expert - via telephone*	Italy	No interests declared	
Dolores Montero Corominas	Expert - via telephone*	Spain	No interests declared	
Representatives 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 give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

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

Oral explanations *(section 2)*

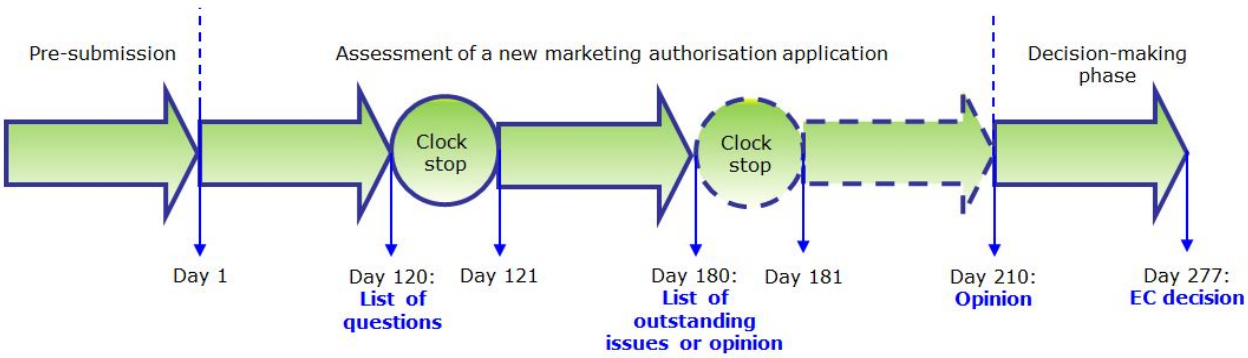
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

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

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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