20 November 2015
EMA/CHMP/771530/2015
Procedure Management and Committees Support Division

Committee for medicinal products for human use (CHMP)

Minutes for the meeting on 19-22 October 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 to be held 19-22 October 2015.

1.2. Adoption of agenda

CHMP agenda for 19-22 October 2015.

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 21-24 September 2015.

The CHMP adopted the minutes.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

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

treatment of diabetes

Scope: Oral explanation

Action: An Oral explanation was held on Tuesday 20 October 2015 at 9.00.

List of Outstanding Issues adopted on 25.06.2015. List of Questions adopted on 23.10.2014.

The Committee noted the issues related to the application.

The Committee adopted the BWP report.

2.2. Re-examination procedure oral explanations

2.2.1. 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: An Oral explanation was held on Tuesday 20 October 2015 at 14.00.

List of Outstanding Issues adopted on 21.05.2015, 18.12.2014. List of Questions adopted on 25.04.2014.

See also 3.5.1

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Imlygic - talimogene laherparepvec - ATMP - EMEA/H/C/002771

Amgen Europe B.V.; treatment of adults with melanoma that is regionally or distantly metastatic

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 24.09.2015 and 25.06.2015. List of Questions adopted on 22.01.2015.

The members were updated on the discussions at CAT and were informed that the CAT adopted a positive opinion by majority (22 positive out of 23 votes) at their October CAT meeting.

The CHMP reflected on the wording of the indication as well as the Annex II conditions.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (29 positive out of 30 votes) together with the CHMP assessment report and translation timetable.

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

The divergent position (Johann Lodewijk Hillege) was appended to the opinion.

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 and the EMA press release were circulated for information.

3.2. Initial applications; Day 180 list of outstanding issues

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

treatment of HIV-1

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.05.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted a list of outstanding issues with a specific timetable.

3.2.2. - caspofungin - EMEA/H/C/004134

treatment of invasive candidiasis and invasive aspergillosis

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.07.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted a list of outstanding issues with a specific timetable.

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

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

Scope: 2nd Day 180 list of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 24.09.2015 and 25.06.2015. List of Questions adopted on 22.01.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted a 3rd list of outstanding issues with a specific timetable.

3.2.4. - lopinavir / ritonavir - EMEA/H/C/004025

treatment of human immunodeficiency virus (HIV-1) infected adults, adolescents and

children above the age of 2 years.

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.05.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted a list of outstanding issues with a specific timetable.

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

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

Scope: 2nd Day 180 list of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 24.09.2015. List of Questions adopted on 25.06.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted a 2nd list of outstanding issues with a specific timetable.

3.2.6. - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982

vaccination against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and invasive diseases caused by Haemophilus influenzae typeb (Hib)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.05.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted a list of outstanding issues with a specific timetable.

The Committee adopted BWP report.

3.2.7. - pitolisant - Orphan - EMEA/H/C/002616

BIOPROJET PHARMA; treatment of narcolepsy

Scope: 2nd Day 180 list of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 21.05.2015. List of Questions adopted on 25.09.2014.

The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted a 2nd list of outstanding issues with a specific timetable.

3.2.8. - lesinurad - EMEA/H/C/003932

treatment of hyperuricaemia

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.05.2015.

The Committee was reminded of the status of this application and its remaining outstanding issues.
The Committee adopted a list of outstanding issues with a specific timetable.

3.3. Initial applications; Day 120 list of questions

3.3.1. - fluticasone propionate / salmeterol xinafoate -EMEA/H/C/002752

treatment of asthma and COPD

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.2. - fluticasone propionate / salmeterol xinafoate - EMEA/H/C/004267

treatment of asthma and COPD

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

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

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions .

The Committee adopted the BWP report.

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

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

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions .

3.3.5. - osimertinib - EMEA/H/C/004124

Non-small-cell lung cancer (NSCLC)

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

Amicus Therapeutics UK Ltd; Treatment of patients with Fabry disease

Scope: Day 120 list of questions,

Action: For adoption

The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

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

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application,
The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

Intercept Italia s.r.l; treatment of primary biliary cirrhosis

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.9. - pemetrexed - EMEA/H/C/003895

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

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.10. - zonisamide - EMEA/H/C/004127

treatment of epilepsy

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

3.4.1. - Albutrepenonacog Alfa - Orphan - EMEA/H/C/003955

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

Action: For adoption

List of Questions adopted on 24.09.2015.

3.4.2. - methotrexate - EMEA/H/C/003756

treatment of rheumatological and dermatological diseases

Scope: Letter from the applicant requesting an extension of clock stop to respond to Day 120 list of questions adopted on 23 July 2015.

Action: For discussion

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to Day 120 list of questions adopted on 23 July 2015 with a specific timetable.

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

NPS Pharma Holdings Limited; treatment of hypoparathyroidism

Scope: Letter from the applicant dated 16 October 2015 requesting an extension of clock stop to respond to Day 180 list of outstanding issues adopted on 24 September 2015.

Action: For adoption

Day 180 list of outstanding issues adopted 24.09.2015. List of Questions adopted on 26.03.2015. SAG to be held on 24 November 2015.

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

3.4.4. - enoxaparin sodium - EMEA/H/C/003795

prophylaxis of thromboembolic disorders of venous origin

Scope: Revised timetable

Action: For adoption

The CHMP adopted a revised timetable.

3.4.5. - enoxaparin sodium - EMEA/H/C/004264

prophylaxis of thromboembolic disorders of venous origin

Scope: Revised timetable

Action: For adoption

The CHMP adopted a revised timetable.

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

treatment of moderate to severe plaque psoriasis

Scope: Letter from the applicant requesting an extension to the clock stop to respond to the list of questions adopted on 24.09.2015

Action: For adoption

List of Questions adopted on 24.09.2015.

The CHMP agreed to the request by the applicant for an extension to the clock stop to

respond to the list of questions adopted on 24.09.2015 with a specific timetable.

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

3.5.1. 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: An Oral explanation was held on Tuesday 20 October 2015 at 14.00.

Report from ad-hoc expert group held on 6 October 2015.

See also 2.2.1.

The committee noted the report from ad-hoc expert group. The ad-hoc expert group was in the opinion that it was difficult to conclude from the data presented that there is sufficiently conclusive evidence of efficacy. The experts found the medicine very interesting and promising, but are not convinced by the evidence seen for the current application.

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.

The company's presentation focused on case reports, which provided evidence suggestive for efficacy in a small number of patients. The company explained the patients' subgroup in which positive B/R could be justified. The company proposed to conduct a post-approval registry study covering all treated patients as a possible option to provide further relevant data and to allow continuous review of the benefit/risk ratio.

The Committee discussed the approval under exceptional circumstances.

The CHMP adopted a negative opinion based on the negative opinion adopted by the CAT recommending the refusal of a marketing authorisation by majority (18 negative out of 30 votes) together with the Assessment Report.

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

The divergent position (Agnes Gyurasics, Andrea Laslop, Bruno Sepodes, Daniela Melchiorri, David Lyons, Dimitrios Kouvelas, Ivana Pankuchova, Jean-Louis Robert, Mila Vlaskovska, Nevenka Trsinar, Panayiotis Triantafyllis, Viola Macolic Sarinic) was appended to the opinion.

The refusal question and answers document was circulated for information.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. Veraseal - human fibrinogen / human thrombin - EMEA/H/C/003914

Instituto Grifols, S.A.; supportive treatment for improvement of haemostasis and as a suture support in vascular surgery

Scope: Withdrawal of initial marketing authorisation, Q & A

Action: For information

List of Outstanding Issues adopted on 24.09.2015. List of Questions adopted on 26.02.2015.

The CHMP noted the withdrawal of the marketing authorisation application.

The withdrawal question and answers document was circulated for information.

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

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

4.1.1. Emend - aprepitant - EMEA/H/C/000527/X/0049/G

Merck Sharp & Dohme Limited; prevention of nausea and vomiting in cancer chemotherapy

Rapporteur: Filip Josephson, Co-Rapporteur: Pieter de Graeff, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “The MAH has submitted a type II variation classified as C.I.6 to extend the indication for chemotherapy-induced nausea and vomiting (CINV) in adults to paediatric patients (12 to 17years) for the 80mg and 125mg hard capsules. SmPC section 4.2 and 5.3 of the 165mg hard capsule label, which is consequential to the outcome of this grouped procedure, will be updated under the scope of type II variation classified as C.I.6.
In addition to this, an application for an addition of a new pharmaceutical form (powder for oral suspension) has been submitted for 125mg strength as part of this grouping.
The MAH has also submitted a type II variation classified as C.I.4 to reflect the paediatric results for prevention of post-operative nausea and vomiting (PONV) in the clinical sections of 40mg hard capsules label, thus updating sections 5.1 and 5.2 of the SmPC.
The Package Leaflet has been proposed to be updated accordingly.”

Action: For adoption

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

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.

4.1.2. Zostavax - shingles (herpes zoster) vaccine (live) - EMEA/H/C/000674/X/0085

Sanofi Pasteur MSD SNC

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: “Addition of the route of administration "intramuscular" for all presentations.”

Action: For adoption

List of Questions adopted on 21.05.2015.

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

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

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

The summary of opinion was circulated for information

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

No items

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

No items

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

No items

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

Request for Supplementary Information adopted on 25.06.2015.

The Committee discussed the issues identified in this application. The discussion mainly focused on the clinical efficacy and the outcome seen for progression free survival versus overall survival. Furthermore the safety profile was discussed in relation to the drop-out rate of the clinical trial.

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

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

Novartis Europharm Ltd

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Doris Stenver

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

Action: For adoption

The Committee discussed the issues identified in this application. The discussions mainly focused on benefit/risk of the maintenance therapy with particular focus on overall survival

outcome and the safety profile. Furthermore the wording of the indication was discussed.

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

The CHMP adopted the Assessment Report on similarity

5.1.3. Avastin - bevacizumab - EMEA/H/C/000582/II/0086

Roche Registration Ltd

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Doris Stenver

Scope: "Extension of indication to extend the use of Avastin in combination with erlotinib for the first line treatment of patients with unresectable advanced, metastatic or recurrent non-squamous NSCLC with EGFR activating mutations. As a consequence sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are proposed to be updated. The Package Leaflet and RMP are updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application. The discussion focused on the baseline data of patients and any possible effect on the trial outcome.

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

5.1.4. 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 in the treatment alone or in combination with methotrexate (MTX) of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate; 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 and RMP have been updated accordingly. Furthermore, the due of the final report for the psoriasis registry in the RMP has been amended and minor editorial changes have been introduced throughout the PI."

Action: For adoption

Request for Supplementary Information adopted on 25.06.2015.

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

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

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

The summary of opinion was circulated for information.

5.1.5. 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 in the treatment of 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

Request for Supplementary Information adopted on 25.06.2015.

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

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

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

The summary of opinion was circulated for information.

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

5.1.6. Cubicin - daptomycin - EMEA/H/C/000637/II/0053/G

Novartis Europharm Ltd

Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams

Scope: “Extension of indication to extend the age range for the indication "complicated skin and soft-tissue infections" (cSSTI), to include paediatric patients from 1 to 17 years of age; as a consequence, sections 4.1, 4.2, 4.4, 5.1, 5.2 and 6.6 of the Cubicin SmPC are amended. The Package Leaflet is updated accordingly. Moreover, the updated RMP version 9.1 has been agreed.”

Action: For adoption

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

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

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

The summary of opinion was circulated for information.

5.1.7. 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

Request for Supplementary Information adopted on 25.06.2015.

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

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

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

The summary of opinion was circulated for information.

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

Boehringer Ingelheim International GmbH

Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption

The Committee discussed the issues identified in this application. The CHMP mainly discussed the wording of the indication and some efficacy and safety analysis aspects. Furthermore the members elaborated on the request for an additional 1 year market protection.

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

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

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

Bristol-Myers Squibb Pharma EEIG

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

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

Action: For adoption

The Committee discussed the issues identified in this application. The members discussed appropriate sub-group of patients and the optimum cut-off value for PD-L1 as a predictor of response.

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

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

Bristol-Myers Squibb Pharma EEIG

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

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

Action: For adoption

The Committee discussed the issues identified in this application. The main focus was on the benefit /risk of the product in combination with ipilimumab in comparison with the monotherapy. The Committee discussed the validity of the biomarker as well as the most appropriate patient population.

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

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

Celgene Europe Limited

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

Scope: "Extension of Indication to add treatment of adult patients with relapsed and/ or refractory mantle cell lymphoma (MCL). As a consequence, SmPC sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and Package Leaflet. A revised version of the RMP (version 25.0) was provided as part of this application."

Action: For adoption

Request for Supplementary Information adopted on 23.07.2015, 26.03.2015.

The Committee discussed the issues identified in this application. The discussions focused on some clinical aspects in relation to the clinical outcome data in patients with high and low tumour burden. Furthermore the members went through the risk management plan.

The Committee adopted 3rd Request for Supplementary Information with a specific timetable.

5.1.12. 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

Request for Supplementary Information adopted on 25.06.2015.

The Committee discussed the issues identified in this application. The discussion mainly focused on the wording of the indication.

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

5.1.13. Volibris - ambrisentan - Orphan - EMEA/H/C/000839/II/0041

Glaxo Group Ltd

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Radka Montoniová, PRAC Rapporteur: Dolores Montero Corominas

Scope: “Extension of indication for the treatment of pulmonary arterial hypertension (PAH), in adult patients of WHO Functional Class (FC) II to III including use in combination treatment; as a consequence sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. A warning related to the increase in peripheral oedema and anemia with the combination therapy is introduced in section 4.4. Section 4.8 is updated accordingly to include updated frequencies of ADRs observed in the AMBITION study and with a new ADR introduced (sudden hearing loss) in case of use in combination therapy. The Package Leaflet is updated in accordance. In addition, the annex II is updated with a minor change in the key messages to healthcare professionals and also in line with the latest version of the QRD template. A change to the list of local representatives is also introduced in the Package Leaflet.

Action: For adoption

Request for Supplementary Information adopted on 24.09.2015, 23.07.2015, 26.03.2015.

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

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

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

The summary of opinion was circulated for information.

5.1.14. Xalkori - crizotinib - EMEA/H/C/002489/II/0024

Pfizer Limited

Rapporteur: Pierre Demolis, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Corinne Fechant

Scope: “Extension of Indication to add first-line treatment of adults with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) based on the results of the pivotal Study A8081014; a multinational, multicenter, randomized, open-label, Phase 3 study comparing the efficacy and safety of crizotinib to first-line chemotherapy (pemetrexed/cisplatin or pemetrexed/carboplatin) in patients with previously untreated ALK-positive advanced non-squamous NSCLC, as well as updated safety results from Studies A8081001, A8081005 and A8081007. As a result sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement minor editorial and QRD-template related changes in the SmPC, Annex II and Package Leaflet. A revised RMP version 6.2 was agreed during the procedure.”

Action: For adoption

Request for Supplementary Information adopted on 23.07.2015, 26.03.2015.

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

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

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

The summary of opinion was circulated for information.

5.1.15. Zutectra - human hepatitis b immunoglobulin - EMEA/H/C/001089/II/0024

Biotest Pharma GmbH

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to Prevention of hepatitis B virus (HBV) re-infection in HBsAg and HBV-DNA negative patients at least one week – instead of the approved at least 6 months - after liver transplantation for hepatitis B induced liver failure.
As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly.
An updated RMP has been provided."

Action: For adoption

Request for Supplementary Information adopted on 23.07.2015.

The Committee discussed the issues identified in this application. The discussions mainly concerned methodological issues with the comparability exercise to assess the contribution of the IV treatment to plasma levels.

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

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

Gilead Sciences International Ltd

Rapporteur: Kristina Dunder, PRAC Rapporteur: Rafe Suvarna

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

Action: For adoption

The Committee discussed the issues identified in this application. The discussion was mainly related to the observed results in progression free survival and a comparison to results from previous clinical studies.

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

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

No items

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

No items

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. - abaloparatide - H0004157

treatment of osteoporosis in postmenopausal women

Scope: Request for an Accelerated Assessment

Action: For adoption

Letter from the company requesting an accelerated assessment

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

8.1.2. - bezlotoxumab - H0004136

prevention of Clostridium difficile infection (CDI) recurrence in adult patients receiving antibiotic therapy for CDI

Scope: Request for an Accelerated Assessment

Action: For adoption

Letter from the company dated 21 September 2015 requesting an accelerated assessment

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

The CHMP noted the tentative accelerated timetable.

8.1.3. - Cabozantinib - H0004163

treatment of renal cell carcinoma

Scope: Request for an Accelerated Assessment

Action: For adoption

Letter from the company dated 27 August 2015 requesting an accelerated assessment

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

The CHMP noted the tentative accelerated timetable.

8.1.4. - inotuzumab ozogamicin - H0004119 - Orphan

Pfizer Limited, treatment of relapsed or refractory b cell Acute Lymphoblastic Leukaemia

Scope: Request for an Accelerated Assessment

Action: For adoption

Letter from the company requesting an accelerated assessment

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

8.1.5. - Sofosbuvir / Velpatasvir - H0004210

treatment of genotype 1-6 chronic hepatitis C virus (HCV) infection in adults

Scope: Request for an Accelerated Assessment

Action: For adoption

Letter from the company requesting an accelerated assessment

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

The CHMP noted the tentative accelerated timetable.

8.1.6. - Venetoclax - Orphan - H0004106

AbbVie Ltd., treatment of adult patients with chronic lymphocytic leukaemia in the presence of 17p deletion

Scope: Request for an Accelerated Assessment

Action: For adoption

Letter from the company dated 5 October 2015 requesting an accelerated assessment

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

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Antiretroviral medicinal products: Ziagen - Abacavir – EMEA/H/C/000252/LEG 089.1; Kivexa -abacavir, lamivudine – EMEA/H/C/000581/LEG 045.1; Trizivir - abacavir, lamivudine, zidovudine - EMEA/H/C/000338/LEG 090.1; Reyataz - atazanavir– EMEA/H/C/000494/LEG 080.1; Prezista - darunavir - EMEA/H/C/000707/LEG 070.1; Stocrin - efavirenz – EMEA/H/C/000250/LEG 071.1, Sustiva - efavirenz – EMEA/H/C/000249/LEG 080.1; Atripla - efavirenz, emtricitabine, tenofovir disoproxil - EMEA/H/C/000797/LEG 040.1; Stribild - elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil - EMEA/H/C/002574/LEG 014.1; Emtriva - emtricitabine - EMEA/H/C/000533/LEG 049.2; Truvada - emtricitabine, tenofovir disoproxil –EMEA/H/C/000594/LEG 043.1; Eviplera - emtricitabine, rilpivirine, tenofovir disoproxil –EMEA/H/C/002312/LEG 031.1; Intelence - etravirine – EMEA/H/C/000900/LEG 048.1; Telzir -fosamprenavir - EMEA/H/C/000534/LEG 076.1; Crixivan - indinavir –EMEA/H/C/000128/LEG 039.1; Epivir - lamivudine - EMEA/H/C/000107/LEG 052.1, Lamivudine VIIV (Art 58) – lamivudine - EMEA/H/W/000673/LEG 007.1; Combivir - lamivudine, zidovudine - EMEA/H/C/000190/LEG 038.1; Aluvia - lopinavir, ritonavir - (Art 58) - EMEA/H/W/000764/LEG 031.1, Kaletra - lopinavir, ritonavir - EMEA/H/C/000368/LEG 118.1; Viramune - nevirapine - EMEA/H/C/000183/LEG 061.1; Edurant - rilpivirine – EMEA/H/C/002264/LEG 026.1; Norvir - ritonavir - EMEA/H/C/000127/LEG 049.1;

Applicants: AbbVie Ltd (Kaletra, Norvir), Boehringer Ingelheim International GmbH (Aptivus, Viramune), Bristol-Myers Squibb Pharma EEIG (Reyataz, Sustiva, Zerit), Bristol-Myers Squibb and Gilead Sciences Ltd.(Atripla), Gilead Sciences International Ltd.(Emtriva, Eviplera, Stribild, Truvada, Tybost, Viread), Janssen-Cilag International N.V.(Edurant, Intelence, Prezista), Merck Sharp & Dohme Ltd (Crixivan, Isentress, Stocrin), Roche Registration Ltd. (Invirase), ViiV Healthcare UK Limited (Celsentri, Combivir, Epivir, Lamivudine Viiv, Kivexa, Telzir, Trizivir, Ziagen)

PRAC Rapporteur (lead): Qun-Ying Yue; PRAC Co-Rapporteur: Isabelle Robine; Julie Williams

Scope: Class labelling revision on lipodystrophy and lactic acidosis, Communication

Action: For adoption

The Committee discussed the warning about lipodystrophy and lactic acidosis and noted the current evidence.

The Committee agreed that the general warning about lipodystrophy will be removed for HIV medicines and a specific warning related to loss of subcutaneous fat will remain for medicines containing zidovudine, stavudine, and didanosine. In line with current evidence, the class warning about lactic acidosis is being removed for nucleoside and nucleotide analogue medicines, with exception of products containing zidovudine, stavudine and didanosine.

The CHMP agreed with the PRAC advice. The CHMP agreed to the communication plan. The EMA press release was circulated for information.

9.1.2. Cellcept - mycophenolate mofetil- EMEA/H/C/000082/II/0121

Roche Registration Ltd, prophylaxis of acute transplant rejection

Rapporteur: Rafe Suvarna,

Scope: Update of sections 4.3, 4.4 and 4.6 of the SmPC in order to add a contraindication for pregnant women unless there is no suitable alternative treatment to prevent transplant rejection, and update the safety information related to pregnancy. The Patient Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the PI in line with the latest QRD template version.
The requested variation proposed amendments to the Summary of Product Characteristics, Annex II and Package Leaflet.

Action: For adoption

Request for Supplementary Information adopted on 24.09.2015, 25.06.2015, 26.03.2015.

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

The Committee adopted a positive opinion by consensus together with the CHMP

assessment report and Translation timetable.

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

The CHMP agreed to the wording of the DHPC and communication plan.

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

Biogen Idec Ltd, Treatment of adult patients with relapsing remitting multiple sclerosis

Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber,

Scope: Opinion

Action: For adoption

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 26.02.2015, 23.04.2015, 23.07.2015, 24.09.2015. SAG Neurology held on 11 June 2015. Oral explanation held on 22.09.2015.

The Committee discussed the possible options for SmPC wording.

The Committee agreed on the measures in order to minimize the risk of PML: a complete blood count should be performed before starting treatment with Tecfidera, and every 3 months during treatment. Additionally, a baseline MRI should be available (usually within 3 months) as a reference. If during treatment the levels of lymphocytes drop to very low levels for more than 6 months, the doctor should consider stopping Tecfidera. If treatment is continued, patients should be closely monitored.

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.

9.1.4. Fluenz Tetra - (A/California/7/2009 (H1n1)Pdm09-Like Strain (A/California/7/2009, Medi 228029),A/Texas/50/2012 (H3n2)-Like Strain (A/Texas/50/2012, Medi 237514),B/Brisbane/60/2008 (Victoria Lineage)-Like Strain (B/Brisbane/60/2008, Medi 228030),B/Massachusetts/2/2012 (Yamagata Lineage)-Like Strain (B/Massachusetts/2/2012, Medi 237751)) - EMEA/H/C/002617

MedImmune LLC, Prophylaxis of influenza in individuals 24 months to less than 18 years

Rapporteur: Daniel Brasseur, Co-Rapporteur: Karsten Bruins Slot

Action: For discussion

The CHMP noted the information.

9.1.5. Gilenya - fingolimod - EMEA/H/C/002202/II/0037

Novartis Europharm Ltd, treatment of multiple sclerosis

Rapporteur: Pierre Demolis, PRAC Rapporteur: Isabelle Robine,

Scope: Opinion or Request for supplementary information
"Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information to include additional warning and guidance on PML. The Package Leaflet is updated accordingly."

Action: For adoption

The Committee discussed the issues identified in this application. The CHMP discussed the wording of section 4.4 and 4.8 in relation to PML. See also discussions on PML for Tecfidera (9.1.3).

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

Post-meeting note: The final Request for Supplementary Information was adopted via written procedure on 30 October 2015.

9.1.6. Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0006

AbbVie Ltd., In combination with other medicinal products for the treatment of chronic hepatitis C in adults

Rapporteur: Filip Josephson,

"Update of sections 4.5 and 5.2 of the SmPC to indicate that paritaprevir is eliminated predominantly via biliary excretion as recommended by the CHMP in the Post Authorisation Measure MEA 002."

Action: For adoption

The members discussed the available data for this variation and agreed that the absorption and extrapolation to steady state has not been addressed sufficiently to support the proposed changes to the product information.

The CHMP was informed that the MAH does not request an oral explanation.

The CHMP adopted a negative opinion by consensus recommending the refusal of the variation.

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

9.1.7. Xarelto - Rivaroxaban - EMEA/H/C/000944

Bayer Pharma AG , prevention of venous thromboembolism (VTE), prevention of venous thromboembolism (VTE), prevention of stroke and systemic embolism

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

Scope: Update on ROCKET trial.

Action: For discussion

The CHMP noted the update on the ROCKET trial and the communication document.

9.1.8. Xofigo - radium-223 - EMEA/H/C/002653

Bayer Pharma AG, treatment of castration-resistant prostate cancer

Rapporteur: Harald Enzmann, Co-Rapporteur: Daniela Melchiorri,

Follow up on update of the Product Information to correct the radioactivity of the drug product solution contained in the vial from 1000 kBq/mL to 1100 kBq/mL at reference date and of the patient dose from 50 kBq/kg body weight to 55 kBq/kg body weight as a result of the change of the National Institute of Standards and Technology primary reference standard used to quantify the radioactivity of radium-223 (variation EMEA/H/C/2653/II/11)

Scope: Xofigo second DHPC on NIST implementation (follow up from variation EMEA/H/C/2653/II/11 and from first DHPC on NIST implementation adopted by CHMP in March 2015)

Action: For adoption

The CHMP agreed to the wording of a DHPC letter.

9.1.9. ChondroCelect - characterised viable autologous cartilage cells expanded ex vivo expressing specific marker proteins – EMEA/H/C/000878

TiGenix NV, Repair of single symptomatic cartilaginous defects

CAT Rapporteur: Egbert Flory, CAT Co-Rapporteur: Tiina Palomaeki, CHMP Coordinators: Jan Mueller Berghaus and Outi Maki-Ikola,

Scope: Revision of post authorisation measures

Action: For information

The CHMP was informed about discussions at the October 2015 CAT meeting on the revision of post authorisation measures: the MAH cannot conduct the randomised controlled trial, which is included in the RMP. They propose to enlarge the ongoing non-interventional study to include patients with large lesions.

9.1.10. Pravafenix - fenofibrate / pravastatin - EMEA/H/C/001243/R/0020

Laboratoires SMB s.a., treatment of mixed dyslipidaemia

Rapporteur: Joseph Emmerich, Co-Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Corinne Fechant,

Scope: Renewal

Action: For discussion

The CHMP agreed to the recommendation from the PRAC not to request an additional 5 year renewal

9.1.11. AML and cut-off age

Scope: AML and cut-off age

Action: For discussion

The CHMP discussed this issue.

10. Referral procedures

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

10.1.1. Inductos - Dibotermin alfa – EMEA/H/A-20/1422/C/0408/0082

Medtronic BioPharma B.V., treatment of anterior lumbar spine fusion and tibia fracturesRapporteur: Pieter de Graeff, Co-Rapporteur: Outi Mäki-Ikola,

Scope: Opinion
Non-GMP compliance of a manufacturing site

Action: For adoption

The CHMP adopted an opinion by consensus recommending the suspension of Inductos together with condition(s) for lifting the suspension of the marketing authorisation. The CHMP also adopted the assessment report.

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

The CHMP agreed to the EMA public health communication.

10.1.1. CERVARIX - Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed)
GARDASIL, SILGARD - Human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed)
GARDASIL 9 - Human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/A-20/1421

MAH(s): GlaxoSmithKline Biologicals S.A. (Cervarix), Sanofi Pasteur MSD SNC (Gardasil, Gardasil 9), Merck Sharp & Dohme Limited (Silgard)

PRAC Rapporteur: Julie Williams; PRAC Co-rapporteurs: Jean-Michel Dogné, Qun-Ying Yue

Scope: List of Questions to SAG Vaccines held 21 October 2015

Review to further clarify the safety profile of human papillomavirus vaccines following notification by the European Commission of a referral under Article 20 of Regulation (EC) No 726/2004, based on pharmacovigilance data. The questions were related to the safety profile of human papillomavirus vaccines in relation to the available data regarding complex regional pain syndrome (CRPS) and postural orthostatic tachycardia syndrome (POTS).

Action: For adoption by written procedure

The Committee adopted the List of Questions to SAG Vaccines held 21 October 2015 by written procedure.

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

No items

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

No items

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

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

Biocodex Benelux SA/NV

Rapporteur: TBC, Co-Rapporteur: TBC,

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

Scope: List of questions and timetable, appointment of (Co)Rapporteur

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

Action: For adoption

The CHMP noted the letter from the Federal agency for medicines and health products in Belgium dated 2 October 2015 notifying of an official referral under Article 29(4) and its grounds.

The CHMP appointed Daniel Brasseur 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: 02.10.2015

Start of procedure: October 2015 CHMP

List of questions: 22.10.2015

Submission of responses: 07.01.2016

Re-start of the procedure: 28.01.2016

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 10.02.2016

Comments: 15.02.2016

Updated rapporteur/co-rapporteur assessment reports circulated to CHMP: 18.02.2016

List of outstanding issues or CHMP opinion: February 2016 CHMP

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

UAB VVB

Rapporteur: TBC, Co-Rapporteur: TBC,

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

Scope: List of questions and timetable, appointment of (Co)Rapporteur

Action: For adoption

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

The Committee discussed the procedural aspects of the referral and proposed list of questions to the applicant, which were related to clinical superiority over the orphan-designated medicinal product Tobi Podhaler.

The CHMP appointed Romaldas Maciulaitis (interest level 2) and Piotr Fiedor as Co-Rapporteur (interest level 1).

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

Notification: 09.10.2015

Start of procedure (CHMP): October 2015 CHMP

List of Questions: 22.10.2015

Submission of responses: 17.12.2015

Re-start of the procedure: 31.12.2015

Rapporteur and co-rapporteur assessment reports circulated to CHMP: 13.01.2016

Comments: 18.01.2016

Updated Rapporteur and co-rapporteur assessment report(s) circulated to CHMP:

21.01.2016

List of outstanding issues / CHMP opinion: January 2016 CHMP

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

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

MAH: Janssen-Cilag group of companies and associated companies

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

Scope: Revised timetable

Letter from the MAH dated 7 October 2015 requesting a 2-month extension of timeframe to submit responses to the List of Questions adopted on 24 September 2015.

Action: For information

The CHMP agreed to the request by the applicant for an additional 2-month clock stop and adopted an amended timetable.

Start of procedure (CHMP): September 2015 CHMP

Submission of responses: 01.12.2015

Re-start of the procedure: 21.12.2015

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 13.01.2016

Comments: 18.01.2016

Updated rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 21.01.2016

List of outstanding issues or CHMP opinion: January 2016 CHMP

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

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

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

Scope: List of questions and timetable

Harmonisation exercise for Etopophos and associated names

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

Action: For adoption

Note: The Rapporteurs were appointed by CHMP in October 2014

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

Notification: 14 October 2015

Start of procedure (CHMP): October 2015 CHMP

List of Questions: 22.10.2015

Submission of responses: 14.01.2016

Re-start of the procedure: 28.01.2016

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 10.02.2016

Comments: 15.02.2016 CHMP

Updated rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 18.02.2016

List of outstanding issues/ CHMP opinion: February 2016 CHMP

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

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

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

Scope: List of questions and timetable

Harmonisation exercise for Vepesid and associated names

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

Action: For adoption

Note: The Rapporteurs were appointed by CHMP in October 2014

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

Notification: 14 October 2015

Start of procedure (CHMP): October 2015 CHMP

List of Questions: 22.10.2015

Submission of responses: 14.01.2016

Re-start of the procedure: 28.01.2016

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 10.02.2016

Comments: 15.02.2016 CHMP

Updated rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 18.02.2016

List of outstanding issues/ CHMP opinion: February 2016 CHMP

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

No items

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)

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

MAH: Gedeon Richter Plc Group of companies

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

Scope: List of questions and timetable, appointment of (Co)Rapporteur

Action: For adoption

The CHMP noted the letter from the MHRA in UK dated 5 October 2015 notifying of an official referral under Article 13(1) and its grounds.

The CHMP appointed Rafe Suvarna as Rapporteur (interest level 1) and Daniela Melchiorri as Co-Rapporteur (interest level 1).

The Committee discussed the list of questions to be addressed: whether levonorgestrel 3mg

would be a suitable form of emergency contraception for patients taking concomitant enzyme inducers that are unwilling or unable to use non-hormonal methods, such as a Cu IUD.

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

Notification: 01.10.2015

Start of the procedure (CHMP): October 2015 CHMP

List of questions: 22.10.2015

Submission of responses: 14.01.2016

Re-start of the procedure: 28.01.2016

Rapporteur/co-rapporteur assessment reports circulated to CHMP: 10.02.2016

Comments: 15.02.2016

Updated rapporteur/co-rapporteur assessment reports circulated to CHMP: 18.02.2016

List of outstanding issues /CHMP opinion: February 2016 CHMP

11. Pharmacovigilance issue

11.1. Early Notification System

October 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 05-08 October 2015.

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Action: For information

13.2. Innovation Task Force briefing meetings

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

13.2.1. ITF Briefing Meeting

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

13.2.3. 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. Discussion of CHMP co-opted member expertise

Action: For discussion

The CHMP discussed the area of expertise of the 5th CHMP co-opted member. Please send nominations for a co-opted member with expertise in one of the following areas - Statistics and methodology, Epidemiology, Geriatrics and/or Pharmacology, The election is planned for the December 2015 CHMP.

14.1.2. Updated Assessment Report templates

The Assessment Report templates for annual re-assessments and annual renewals have been updated to align them with the newly implemented process for 5 year renewals.

Furthermore the specific section "3.5. Special populations: the elderly" has been introduced in the CHMP D80 AR for issues specific to the elderly

Action: For adoption

The CHMP noted the information on updated Assessment Report templates. Template for annual re-assessments and annual renewals have been updated to align them with the newly implemented process for 5 year renewals: Single Joint Assessment Report which evolves from submission to final opinion will be introduced. The intention is to start using the updated template from the end of the year. Comments on the revised templates (if any) should be provided in writing by the November CHMP meeting.

The CHMP adopted updated AR template on Special populations: the elderly. The CHMP agreed to a pilot with about 10 Rapporteur Assessment Reports.

14.1.3. Draft Scientific Guideline on Post-authorisation efficacy studies (PAES)

Action: For adoption and for 3-months public consultation

It was previously introduced to CHMP in July 2015 for comments.

The aim of this draft is to provide scientific guidance for MAHs and NCAs on the general need for such studies including within the scope of Delegated Regulation (EU) No 357/2014, on general methodological considerations, on specific situations and on study conduct. Following its adoption by the EMA Scientific Committees the draft guidance will be released for public consultation in Q4 2015.

The CHMP adopted the draft guideline for 3-months public consultation.

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

Scope: Reflection paper on a proposal to enhance early dialogue to facilitate accelerated assessment of priority medicines (PRIME)

Action: For adoption and for 2-months public consultation

The CHMP adopted the reflection paper for 2-months public consultation. The reflection paper describes proposed eligibility criteria and procedure, proposed support features and monitoring of development.

14.1.5. Strategic Review and Learning Meetings

Scope: Updated documents on organisational aspects

Action: For information

Principles for organisation of NCA hosted meetings

Responsibilities for confidentiality in NCA Hosted Meetings

Postponed to November ORGAM meeting.

14.1.6. Strategic review of the Article 58 procedure

Action: For discussion

The CHMP noted the presentation. The study results of Article 58 procedure were presented. The objectives of the study were: to understand awareness, experience and views of stakeholders of Article 58 and its influence on manufacturers' decisions to use the procedure and the wider landscape of alternative regulatory tools and pathways. The report makes a number of recommendations that will be considered by EMA and discussed by the Management Board in 2016, particularly in the context of the globalisation theme of the EU Medicines Agencies Network Strategy to 2020.

14.1.7. Concept paper on guideline on pregnancy and breastfeeding (GVP)

Product- or Population specific considerations III: pregnancy and breastfeeding

Action: For adoption

The CHMP adopted the internal concept paper.

14.1.8. DOAC - Direct oral anticoagulants – update on workshop to be held on 23 November 2015

Action: For information

Workshop programme

The CHMP agreed to the timetables for Pradaxa, Lixiana, Xarelto, Eliquis.

The CHMP noted the Workshop programme taking place on 23rd November 2015. Experts and stakeholders will be brought together to discuss the utility of PK and PD measurements in the clinical use of the direct oral anticoagulants.

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 05-08 October 2015

Action: For information

The CHMP noted the Summary of recommendations.

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

Action: For adoption

The CHMP adopted the document.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 15-16 October 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 28 September -1 October 2015

Action: For information

The CHMP noted the report.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at October 2015 PDCO

Action: For information

The CHMP noted the document.

Report from the PDCO meeting held on 7-9 October 2015

Action: For information

The CHMP noted the report.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 6-8 October 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 19-21 October 2015

Action: For information

The CHMP noted the report.

Question from CMDh to CHMP/PKWP on bioequivalence requirements for generics of amoxicillin and clavulanic acid

Action: For adoption

The CHMP agreed to this request to the PKWP.

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 5-8 October 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.

Scope**: Call for nomination of SAWP Member**

Dr Bertil Jonsson stepped down from the SAWP at the 5-8 October 2015 SAWP meeting. A

new SAWP member with expertise in haematology, oncology, infectious diseases is sought. The letter of candidacy together with CV should be sent. The election of a new SAWP Member will take place at November 2015 plenary meeting.

Action: For information

The CHMP noted the information.

14.3.2. Safety Working Party (SWP)

Scope: **Election of SWP Chair**

Action: For adoption

The CHMP re-elected Jan Willem van der Laan (NL) for the second mandate as chair of the SWP.

Scope: **Reflection paper on the use of methyl-and propylparaben as excipients in human medicinal products for oral use**

Action: For adoption

The CHMP adopted the reflection paper. The reflection paper addresses methyl- and propylparaben, as those are the parabens predominantly used in oral pharmaceutical formulations. Given the public concerns, the focus of this document is on possible endocrine-disrupting effects in humans.

Scope: Overview of comments received on the 'Reflection paper on the use of methyl- and propylparaben as excipients in human medicinal products for oral use' EMA/CHMP/SWP/272921/2012

Action: For information

The CHMP noted the overview of comments.

Scope: **Guideline on non-clinical local tolerance testing of medicinal products**

Action: For adoption

The CHMP adopted the guideline. The document provides guidance on the non-clinical local tolerance testing to support the clinical development and marketing authorisation of medicinal products for human use. Studies on impurities arising from the active substances or excipients present in the drug product or extracted or leached from a container closure system are not directly covered by the guideline.

Scope: Overview of comments received on Draft guideline on non-clinical local tolerance testing of medicinal products' EMA/CHMP/SWP/2145/2000 Rev. 1

Action: For information

The CHMP noted the overview of comments.

Scope: **Concept paper on a proposal to limit the applicability of the CPMP/CVMP**

Note for Guidance on Limitations to the Use of Ethylene Oxide in the Manufacture of Medicinal Products to medicinal products for veterinary use

Action: For adoption

The CHMP adopted the concept paper. SWP is recommending to withdraw the Note for Guidance on Limitations to the Use of Ethylene Oxide in the Manufacture of Medicinal Products and replace the guidance provided for the limitation of ethylene oxide by the approach that is recommended for Class 1 impurities in ICH M7. This recommendation applies to medicinal products for human use only.

SWP final response to HMPC questions on Pulegone

Action: For adoption

The CHMP adopted the final response.

Scope: **Draft agenda of SWP virtual meeting on 27 October 2015**

Action: For information

The CHMP noted the draft agenda.

14.3.3. Quality Working Party (QWP)

Scope: **Question and answer on expression / declaration of potency in quantitative and qualitative composition for Vancomycin products**

Action: For adoption

The CHMP adopted the Q&A document.

Scope: **Response to the EDQM request for QWP opinion on new information on alkyl sulfonates**

Action: For adoption

The CHMP adopted the response.

Quality Working Party reviewed the article from Snodin et al. QWP acknowledges the scientific rationale in this article and that the formation of alkyl sulfonates is very low and very much depends on the reaction conditions. This makes the presence of these mutagenic impurities at toxicologically significant levels unlikely.

However, as the presence and formation of these alkyl sulfonates cannot be totally excluded, QWP proposes the following approach: MAHs should justify via Risk Assessment that alkyl sulfonates are not expected to be present for their product, which may be sufficient.

Depending on the outcome of this RA supportive analytical data might or might not be required.

Scope: **ICH Q3D Workshop in April 2016**

Action: For information

The CHMP noted the information.

14.3.4. Biologics Working Party (BWP)

Scope: **Draft agenda for BWP meeting to be held 9-11 November 2015**

Action: For information

The CHMP noted the draft agenda.

Scope: **Final minutes from meeting held 13-15 July 2015**

Action: For information

The CHMP noted the final minutes.

14.3.5. Blood Products Working Party (BPWP)

Scope: **Final Minutes of WP meeting held face-to-face-on 28-29 May 2015**

Action: For information

The CHMP noted the final minutes.

14.3.6. Cardiovascular Working Party

Scope: **Guideline on clinical investigation of medicinal products for prevention of venous thromboembolism (VTE) in non-surgical patients**

Action: for adoption for 6-month public consultation

The CHMP adopted the guideline for 6-month public consultation. The aim of the guideline is to provide guidance to industry when performing trials to develop medicinal products in the prevention of venous thromboembolism in non-surgical patients. The revised guideline does not deal with the development of medicinal products for prevention of long-term sequelae of VTE, such as post-phlebitic syndrome or chronic thromboembolic pulmonary hypertension.

Scope: **Final Minutes of WP meeting held by teleconference on 3 June 2015**

Scope: **Draft Table of Decisions of WP meeting held by on 30 September 2015**

Action: for information

The CHMP noted the final minutes and Draft Table of Decisions

14.3.7. Central Nervous System Working Party (CNSWP)

Scope: **Final Agenda of WP meeting held face-to-face teleconference on 7 October 2015**

Scope: **Final Minutes of WP meeting held by teleconference on 12 May 2015**

Scope: **Final Minutes of WP meeting held by teleconference on 12 June 2015**

Action: for information

The CHMP noted the documents.

14.3.8. Pharmacokinetics Working Party (PKWP)

Responses to CMDh question to CHMP (PKWP, SWP) regarding potential risk of longer half-life of acitretin

Action: For adoption

The CHMP adopted the responses to CMDh.

14.3.9. Excipients Drafting Group

Scope: Draft agenda of DG meeting to be held by teleconference on 4 or 5 November 2015

Action: For information

Postponed to November ORGAM

Scope: New mandate of the Excipient drafting group (ExcpDG)

Action: For adoption

Postponed to November ORGAM

Scope: Proposed new core members and Chair

Action: For discussion

Postponed to November ORGAM

14.3.10. Biostatistics Working Party (BSWP)

Scope: Nomination of new observer Barbara Bidzinska (PL)

Action: For adoption

Current membership list

New observer was adopted.

14.3.11. Asthma Guideline Drafting Group

Scope: **Guideline on the Clinical Investigation of Medicinal Products for the Treatment of Asthma (CHMP/EWP/2922/01 Rev. 1)**

Action: For adoption

The CHMP adopted the asthma guideline. The document is intended to provide guidance for the clinical development and evaluation of new medicinal products for the treatment of asthma. It should be considered as general guidance and should be read in conjunction with other European and ICH guidelines which may apply to this disease area and patient population.

14.3.12. CHMP-GCP inspectors working group

Scope: **Results of the analysis on the impact of GCP inspection findings on CHMP opinions**

Action: For discussion

The CHMP noted the presentation. The review showed that depending on the nature of the critical findings and the possibility to correct the issues revealed by the inspections, more applicants decided to withdraw their MAA following a triggered GCP inspection than following a routine inspection. It was emphasized that the good collaboration between assessors and GCP inspectors need to continue, as well as regular exchange of information on GCP inspections with other regulatory authorities.

14.3.13. EPAA Annual conference in Brussels (EP), 1st December 2015,

Chair: Sonja Beken/ Ellen-Margrethe Vestergaard

Scope: EMA representation

Sonja Beken will represent the EMA (CHMP/CVMP JEG 3Rs) at this meeting.

Action: For information

The CHMP noted the EMA representation.

14.3.14. Vaccines Working Party (VWP)

Scope: Draft agenda of VWP plenary meeting on 27-28 October 2015

Action: For information

The CHMP noted the draft agenda.

14.3.15. Biosimilar Medicinal products Working Party (BMWP)

Scope: Draft agenda of BMWP plenary meeting on 27-28 October 2015

Action: For information

The CHMP noted the draft agenda.

14.3.16. Infectious Diseases Working Party (IDWP)

Draft agenda of IDWP plenary meeting on 11-12 November 2015

Action: For information

The CHMP noted the draft agenda.

14.3.17. Invented name issues

Table of Decisions of NRG plenary meeting held on 30 September 2015

Action: For adoption.

The CHMP adopted the table of decisions.

14.4. Cooperation within the EU regulatory network

14.4.1. EMCDDA Risk Assessment meeting on α-PVP, 18 November 2015

Scope: EMA representation

Leon van Aerts will represent EMA at this meeting of the extended Scientific Committee.

Action: For information

The CHMP noted the EMA representation.

14.5. Cooperation with International Regulators

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

14.6.1. International Society for Stem Cell Research

Consolidated comments on the ISSCR's "Guidelines for Stem Cell Research and Clinical Translation" (EXT/601308/2015)

Action: For adoption

The CHMP adopted the consolidated comments on the draft guideline.

14.7. CHMP work plan

14.8. Planning and reporting

14.9. Others

15. Any other business

15.1. AOB topic

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 19- 22 October 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	
Maria Popova-Kiradjieva	Alternate	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	
Georgios Savva	Alternate	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Jens Heisterberg	Member	Denmark	No restrictions applicable to this meeting	
Sinan B. Sarac	Alternate	Denmark	No interests declared	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Kersti Oselin	Alternate	Estonia	No interests declared	
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	
Harald Enzmann	Member	Germany	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Dimitrios Kouvelas	Member	Greece	No interests declared	
George Aislaitner	Alternate	Greece	No interests declared	
Agnes Gyurasics	Member	Hungary	No interests declared	
Melinda Sobor	Alternate	Hungary	No interests declared	
Hrefna Gudmundsdottir	Alternate	Iceland	No interests declared	
David Lyons	Member	Ireland	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Patrick Salmon	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No interests declared	
Luca Pani	Alternate	Italy	No interests declared	
Natalja Karpova	Alternate	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No restrictions applicable to this meeting	
Rugile Pilviniene	Alternate	Lithuania	No interests declared	
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
Carola de Beaufort	Alternate	Luxembourg	No restrictions applicable to this meeting	
John Joseph Borg	Member	Malta	No interests declared	
Helen Vella	Alternate	Malta	No interests declared	
Pieter de Graeff	Member	Netherlands	No interests declared	
Johann Lodewijk Hillege	Alternate	Netherlands	No interests declared	
Karsten Bruins Slot	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No participation in final deliberations and voting on:	9.1.9. Xofigo - radium-223 -EMEA/H/C/002653
Piotr Fiedor	Member	Poland	No interests declared	
Aldona Paluchowska	Alternate	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Patricia Silva	Alternate	Portugal	No interests declared	
Nela Vilceanu	Member	Romania	No interests declared	
Dana Gabriela Marin	Alternate	Romania	No interests declared	
Jan Mazag	Member	Slovakia	No interests declared	
Ivana Pankuchova	Alternate	Slovakia	No interests declared	
Stanislav Primožič	Member	Slovenia	No interests declared	
Nevenka Tršinar	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Arantxa Sancho-Lopez	Alternate	Spain	No interests declared	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Greg Markey	Member	United Kingdom	No interests declared	
Rafe Suvarna	Alternate	United Kingdom	No interests declared	
Robert James Hemmings	Co-opted member	United Kingdom	No restrictions applicable to this meeting	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Jean-Louis Robert	Co-opted member	Luxembourg	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Patricia Diaz	Support	Spain	No restrictions	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ramos			applicable to this meeting	
Sabine Mayrhofer	Support	Germany	No interests declared	
Jorge Camarero Jiménez	Expert - in person*	Spain	No restrictions applicable to this meeting	
Jana Schweigertova	Expert - in person*	Slovakia	No restrictions applicable to this meeting	
Christophe Focke	Expert - in person*	Belgium	No interests declared	
Anna Maria Cassar	Observer	Malta	No interests declared	
Elaine Gatt Baldacchino	Observer	Malta	No interests declared	
Olli Tenhunen	Expert - via telephone*	Finland	No restrictions applicable to this meeting	
Karri Penttilä	Expert - via telephone*	Finland	No interests declared	
Paula Salmikangas	Expert - via telephone*	Finland	No interests declared	
Elisabeth Johanne Rook	Expert - in person*	Netherlands	No interests declared	
Cristel Loeb	Expert - in person*	Netherlands	No restrictions applicable to this meeting	
Walburga Lutkehermolle	Expert - via telephone*	Germany	No interests declared	
Cornelia Lipperheide	Expert - via telephone*	Germany	No interests declared	
Gabriele Schlosser-Weber	Expert - via telephone*	Germany	No interests declared	
Christine Greiner	Expert - via telephone*	Germany	No interests declared	
Henning Brohmann	Expert - via telephone*	Germany	No interests declared	
Clemens Mittmann	Expert - in person*	Germany	No interests declared	
Joerg Zinserling	Expert - via telephone*	Germany	No interests declared	
Brigitte Brake	Expert - in person*	Germany	No interests declared	
Carlo Pini	Expert - via telephone*	Italy	No restrictions applicable to this meeting	
Maria Wirz	Expert - in person*	Italy	No interests declared	
Vincent Gazin	Expert - in person*	France	No interests declared	
Joseph Lim	Expert - via telephone*	United Kingdom	No interests declared	
Marit Hystad	Expert - via telephone*	Norway	No interests declared	
Janice Cook	Expert - via telephone*	United Kingdom	No interests declared	
Mats Welin	Expert - via	Sweden	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
	telephone*			
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

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

17. Explanatory notes

The Notes 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)*

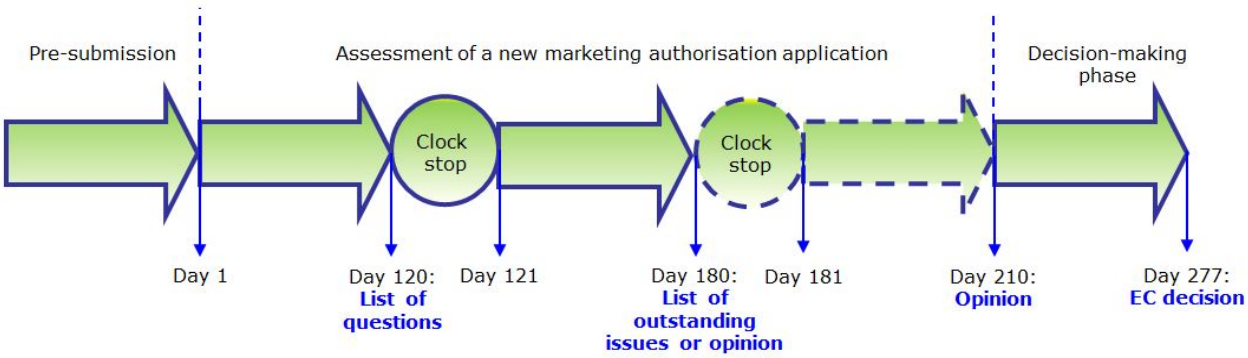
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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