20 July 2016
EMA/PDCO/436533/2016
Procedure Management and Committees Support Division

Paediatric Committee (PDCO)

Minutes for the meeting on 22-24 June 2016

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

22 June 2016, 08:30- 19:00, room 3A

23 June 2016, 08:30- 19:00, room 3A

24 June 2016, 08:30- 13:00, room 3A

Disclaimers

Some of the information contained in this set of minutes 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 PDCO Committee meeting reports (after the PDCO Opinion is adopted), and on the Opinions and decisions on paediatric investigation plans webpage (after the EMA Decision is issued).

Of note, this set of minutes is a working document primarily designed for PDCO members and the work the Committee undertakes.

Further information with relevant explanatory notes can be found at the end of this document.

Note on access to documents

Some documents mentioned in the minutes 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. Introductions

1.1. Welcome and declarations of interest of members, alternates and experts

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some meeting participants in upcoming discussions as included in the pre-meeting list of participants and restrictions.

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

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 23 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. Adoption of agenda

The agenda was adopted with amendments.

1.3. Adoption of the minutes

The minutes were adopted with amendments and will be published on the EMA website.

2. Opinions

Disclosure of some information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

2.1. Opinions on Products

2.1.1. Semaglutide - EMEA-001441-PIP02-15

Novo Nordisk; Treatment of Type 2 Diabetes Mellitus / Treatment of Type 2 Diabetes Mellitus

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO adopted a positive opinion.

2.1.2. Eculizumab - Orphan - EMEA-000876-PIP06-15

Alexion Europe SAS; Prevention of graft rejection following solid organ transplantation / Prevention of acute antibody-mediated rejection in sensitized recipients after kidney transplantation

Day 120 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO concluded that all issues have been addressed and resolved satisfactorily.
The Committee granted a waiver for eculizumab in children from birth to less than 1 year of age.
The PDCO adopted a positive opinion.

2.1.3. EMEA-001776-PIP01-15

Boehringer Ingelheim International GmbH; Treatment of Active Psoriatic Arthritis, Treatment of Crohn's disease, Treatment of plaque psoriasis, Treatment of Ankylosing Spondylitis, Treatment of Asthma / not available at present, Treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years, who are candidates for systemic therapies

Day 120 opinion

Immunology-Rheumatology-Transplantation / Dermatology / Pneumology - Allergology / Gastroenterology-Hepatology

Summary of committee discussion:

The applicant's proposal was considered acceptable. A positive opinion was adopted.

2.1.4. 3-[[5-chloro-1-[3-(methylsulfonyl)propyl]-1H-indol-2-yl]methyl]-1-(2,2,2-trifluoroethyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridine-2-one - EMEA-001838-PIP01-15

Janssen-Cilag International NV; Treatment of respiratory tract disease caused by human respiratory syncytial virus (RSV) / Treatment of respiratory tract disease caused by human RSV

Day 120 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO's view expressed at day 90 were re-discussed and endorsed.
The PDCO adopted a positive opinion accordingly.

2.1.5. Cabotegravir - EMEA-001418-PIP02-15

ViiV Healthcare UK Limited; Prevention of human immunodeficiency virus (HIV-1) infection / Cabotegravir is to be indicated in combination with safer sex practices for PrEP to reduce the risk of HIV-1 acquisition in sexually active adolescents at high risk, from 12 to < 18 years of age

Day 120 opinion

Infectious Diseases

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee the PDCO adopted a favourable opinion for cabotegravir in the condition of Prevention of HIV-1 infection.

2.1.6. Quizartinib - Orphan - EMEA-001821-PIP01-15

Daiichi Sankyo Europe GmbH; Acute myeloid leukaemia / For the treatment of paediatric patients aged from 1 month to less than 18 years of age with newly diagnosed FLT3-ITD(+) AML, For the treatment of paediatric patients aged from 1 month to less than 18 years of age with relapsed or refractory FLT3-ITD(+) AML after failure of front line intensive chemotherapy regimen, in combination with standard chemotherapy

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO continued on 23 June 2016 the discussion of the proposal for a modified paediatric investigation plan for the oral FLT3 inhibitor quizartinib for treatment of (FLT3 mutant) acute myeloid leukaemia (AML), taking into account comments by the applicant on a draft of the Opinion. All issues had been resolved and the Committee agreed the paediatric development.

2.1.7. andexanet alfa - EMEA-001902-PIP01-15

Portola Pharma UK Limited; Prevention of factor Xa inhibitor associated haemorrhage, Treatment of factor Xa inhibitor associated haemorrhage / (as above), For the reversal of anticoagulation due to direct and indirect factor Xa inhibitors in patients experiencing an acute major bleeding event or requiring urgent surgery.

Day 120 opinion

Other

Summary of committee discussion:

The committee adopted a positive opinion.

2.1.8. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with lentiviral vector that encodes for the human ARSA cDNA sequence - Orphan - EMEA-001765-PIP02-15

GlaxoSmithKline Trading Services Limited; Metachromatic leukodystrophy (MLD) / For the treatment of metachromatic leukodystrophy (MLD)

Day 120 opinion

Other

Summary of committee discussion:

The PDCO adopted a positive Opinion at day 120.

2.1.9. Hydrochlorothiazide / Amlodipine / Ramipril - EMEA-001942-PIP01-16

Adamed Sp. z o.o.; Treatment of hypertension

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed.
Based on the assessment of this application and further discussions at the Paediatric Committee the PDCO agrees with the applicant's request for a waiver.

2.1.10. Rosuvastatin / Amlodipine - EMEA-001935-PIP01-16

Adamed Sp. z o.o.; Treatment of angina and dyslipidaemia, Treatment of concomitant hypertension and dyslipidemia, Treatment of essential hypertension in patients who are estimated to have a high risk for a first cardiovascular event

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The PDCO discussed at D60 the waiver application for procedure EMEA-001935-PIP01-16, regarding the fixed dose combination of rosuvastatin and amlodipine.

2.1.11. Lusutrombopag - EMEA-001905-PIP01-15

Shionogi Limited; Treatment of thrombocytopenia

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO agrees with the applicant's request for a waiver.
The PDCO emphasises that the granting of a waiver for the condition mentioned above

should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.2. Opinions on Compliance Check

The following compliance checks have been put up for discussion and the members of the PDCO have been invited to comment on issues of possible non-compliance

2.2.1. Human Fibrinogen - EMEA-C1-001208-PIP01-11-M02

Octapharma Pharamzeutika Produktionsges.m.b.H; Treatment of congenital fibrinogen deficiency

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The applicant is deemed compliant on all relevant key elements in the opinion. A letter of partial compliance was adopted.

2.2.2. semaglutide - EMEA-C1-001441-PIP01-13

Novo Nordisk A/S; Treatment of type 2 diabetes mellitus

Day 30 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO discussed the compliance request on 23 June 2016.
The following completed non-clinical studies were checked for compliance. It was considered that these are compliant with the latest Agency's Decision (P/0095/2015) of 08 May 2015.
The PDCO finalised on 24 June 2016 this partially completed compliance procedure.

2.2.3. solithromycin - EMEA-C1-001581-PIP01-13-M02

Triskel EU Services, Ltd; Treatment of tularaemia

Day 30 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO finalised on 24-June-2016 this partially completed compliance procedure and considered that the completed study is not compliant with the latest Agency's Decision (P/0119/2016) of 28 April 2016. The PDCO concluded that this partially completed compliance procedure is negative.

2.2.4. Octenidine Dihydrochloride - EMEA-C1-001514-PIP01-13

Cassella-med GmbH & Co. KG; Treatment of upper respiratory tract infections

Day 30 opinion

Oto-rhino-laryngology

Summary of committee discussion:

The PDCO discussed the completed study and considered that this is compliant with the latest Agency's Decision (P/0093/2016) of 22 March 2016.
The PDCO finalised on 24 June 2016 this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be completed until this date.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Recombinant human beta-glucuronidase - Orphan - EMEA-001540-PIP01-13-M01

Ultragenyx UK Limited; ICD-10: E76.2, Mucopolysaccharidosis type 7 (MPS 7) / Treatment of Mucopolysaccharidosis 7 (MPS 7)

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, and the clarifications they provided between D30 and D60, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0151/2014 of 13 June 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.2. elobixibat - EMEA-001484-PIP01-13-M01

Elobix AB; Constipation

Day 60 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0053/2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.3. turoctocog alfa - EMEA-000428-PIP01-08-M03

Novo Nordisk A/S; Hereditary Factor VIII Deficiency / Treatment and prophylaxis of bleeding in patients with Haemophilia A (congenital Factor VIII deficiency)

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO re-discussed this modification on 22-24 June 2016.
The PDCO assessed the answers that the applicant provided to the Committee's questions and found them satisfactory.
Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0091/2013 of 29 April 2013).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.4. Adalimumab - EMEA-000366-PIP05-12-M02

AbbVie Limited; Non-infectious uveitis

Day 60 opinion

Immunology-Rheumatology-Transplantation / Ophthalmology / Dermatology / Gastroenterology-Hepatology

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted. The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0094/2016 of 18-March 2016). The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.5. (3-((4-Benzoyl-1-piperazinyl)(oxo)acetyl)-4-methoxy-7-(3-methyl-1H-1,2,4-triazol-1-yl)-1H-pyrrolo[2,3-c]pyridin-1-yl)methyl dihydrogen phosphate, 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) - EMEA-001687-PIP01-14-M01

Bristol-Myers Squibb International Corporation; Treatment of human immunodeficiency virus [HIV-1] infection / Treatment of multi-drug resistant HIV-1 infection as part of a combination therapy in paediatric patients aged 2 years to <18 years, who have no more than 2 remaining available fully active antiretroviral therapies

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0258/2015 of 30/10/2015).

The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.6. Anidulafungin - EMEA-000469-PIP01-08-M06

Pfizer Limited; Treatment of invasive candidiasis

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO's view expressed at day 30 was re-discussed and endorsed. The committee also discussed the applicant's clarifications and considered them agreeable.
The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0091/2015 of 8 May 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.7. rilpivirine (as hydrochloride) - EMEA-000317-PIP01-08-M09

Janssen-Cilag International NV; Treatment of human immunodeficiency virus (HIV-1) infection / Rilpivirine is indicated in combination with other antiretroviral (ARV) medicinal products, for the treatment of human immunodeficiency virus (HIV-1) infection in ARV-naïve paediatric patients from 2 to less than 18 years with a baseline viral load below 100,000 HIV-1 RNA copies/mL

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The applicant's justification was considered sufficient and a positive opinion was adopted. Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted. The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0012/2016 of 29-Jan-2016). The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.8. Tenofovir alafenamide (as fumarate) - EMEA-001584-PIP01-13-M01

Gilead Sciences International Ltd.; Treatment of chronic hepatitis B / indicated for the treatment of chronic hepatitis B infection in paediatric patients aged 2 years and above.

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

This modification was discussed on D60. The applicant's responses to the issues raised on D30 were considered generally acceptable.
The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0209/2014).

The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.9. Brentuximab vedotin - Orphan - EMEA-000980-PIP01-10-M04

Takeda Pharma A/S; Treatment of Hodgkin lymphoma, Treatment of anaplastic large cell lymphoma / Treatment of paediatric patients with newly diagnosed, relapsed or refractory Hodgkin lymphoma (from 5 years of age), Treatment of paediatric patients with first and subsequent relapse or refractory systemic anaplastic large cell lymphoma (from 2 years of age)

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision. The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.10. Dinutuximab - Orphan - EMEA-001285-PIP01-12-M02

United Therapeutics Europe Limited; Neuroblastoma / Treatment of patients with high-risk neuroblastoma following myeloablative therapy and autologous stem cell rescue in combination with GM-CSF, IL-2, and isotretinoin.

Day 60 opinion

Oncology

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan and in line with the day 30 PDCO discussion, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0208/2013 of 03/09/2013).

2.3.11. vemurafenib - EMEA-000978-PIP01-10-M01

Roche Registration Limited; Treatment of melanoma

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO discussed the modification request for vemurafenib taking into account the applicant's additional information and proposal to replace the agreed PIP with a product-specific waiver.
Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/91/2011 of 08 April 2011).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.12. ivacaftor / lumacaftor - EMEA-001582-PIP01-13-M04

Vertex Pharmaceuticals (Europe) Limited; cystic fibrosis / Treatment of cystic fibrosis

Day 60 opinion

Other

Summary of committee discussion:

The PDCO's view expressed at day 30 was re-discussed and endorsed. The committee also endorsed the conclusions of the formulation working group.
In conclusion, the committee concluded that some, but not all proposed changes could be agreed and therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0185/2015 of 24/08/2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.13. Benralizumab - EMEA-001214-PIP01-11-M05

AstraZeneca AB; Asthma / Treatment of asthma

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

The PDCO's view expressed at day 30 was re-discussed and endorsed. The committee also discussed the applicant's clarifications and considers them acceptable.
Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0283/2015 of 27 November 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.14. budesonide - EMEA-001087-PIP02-12-M02

Vectura Limited; treatment of asthma

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

An oral explanation meeting was held with the applicant's representatives and an external expert on 23 June 2016.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0218/2013 of 6 September 2013).

The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.15. lurasidone hydrochloride - EMEA-001230-PIP01-11-M02

Sunovion Pharmaceuticals Ltd.; schizophrenia / schizophrenia

Day 60 opinion

Psychiatry

Summary of committee discussion:

The PDCO re-discussed the application including the additional information submitted after Day 30.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.16. Pneumococcal polysaccharide serotype 23F conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 19F conjugated to diphtheria toxoid / Pneumococcal polysaccharide serotype 18C conjugated to tetanus toxoid / Pneumococcal polysaccharide serotype 14 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 9V conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 7F conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 6B conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 5 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 1 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 4 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein - EMEA-000673-PIP01-09-M09

GlaxoSmithKline Biologicals S.A.; Disease caused by Streptococcus pneumoniae, Acute Otitis Media caused by Non-typeable Haemophilus influenzae / Disease caused by Streptococcus pneumoniae, Acute Otitis Media caused by Non-typeable Haemophilus influenzae

Day 60 opinion

Vaccines

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted. The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0270/2015 of 03 December 2015). The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.4. Opinions on Re-examinations

No items.

2.5. Finalisation and adoption of opinions

3. Discussion of applications

Disclosure of some information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.1. Discussions on Products D90-D60-D30

3.1.1. Cathine hydrochloride (D-Norpseudoephedrine hydrochloride) - EMEA-001909-PIP01-15

Treatment of obesity / Adjunct therapy for patients with obesity and a body mass index (BMI) of at least 30 for adults and above the 97th percentile for children who failed to achieve adequate therapeutic response with comprehensive weight loss measures alone.

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.2. Elafibranor - EMEA-001857-PIP01-15

Treatment of non-alcoholic fatty liver disease (NAFLD), Treatment of non-alcoholic steatohepatitis (NASH), Treatment of non-alcoholic fatty liver disease (NAFLD)

Day 90 discussion

Gastroenterology-Hepatology

3.1.3. Eculizumab - Orphan - EMEA-000876-PIP07-15

Alexion Europe SAS; Prevention of delayed graft function after solid organ transplantation / Prevention of delayed graft function after kidney transplantation in patients at increased risk of delayed graft function

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.4. Angiotensin II - EMEA-001912-PIP01-15

Treatment of Catecholamine-resistant hypotension associated with distributive shock

Day 90 discussion

Other

3.1.5. Autologous cartilage derived cultured chondrocytes - EMEA-001823-PIP01-15

Treatment of cartilage disorders

Day 90 discussion

Other

3.1.6. derivative of 4H-pyrazolo[3,4-d]pyrimidin-4-one - EMEA-001742-PIP01-14

Treatment of schizophrenia / Cognitive Impairment Associated with Schizophrenia

Day 90 discussion

Psychiatry

3.1.7. pegvaliase - Orphan - EMEA-001951-PIP01-16

BioMarin International Limited; For the treatment of hyperphenylalaninaemia / For the treatment of hyperphenylalaninaemia in paediatric patients of all ages with phenylketonuria

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.8. EMEA-001929-PIP01-16

Crohn's disease, Ulcerative colitis / Treatment of children 4 to 17 years of age with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to treatment with a tumour necrosis factor-alpha inhibitor;or immunomodulator, or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids., Treatment of children 4 to 17 years of age with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to treatment with a tumour necrosis factor-alpha inhibitor;or immunomodulator, or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids.

Day 60 discussion

Gastroenterology-Hepatology

3.1.9. EMEA-001944-PIP01-16

Anaemia secondary to chronic kidney disease / Treatment of anaemia secondary to chronic kidney disease

Day 60 discussion

Haematology-Hemostaseology

3.1.10. Autologous CD34+ cells transduced with lentiviral vector encoding the human beta-globin gene - EMEA-001933-PIP01-16

Beta-thalassemia major and intermedia / Treatment of Beta thalassemia major and intermedia

Day 60 discussion

Haematology-Hemostaseology

3.1.11. EMEA-001923-PIP01-15

Chronic idiopathic arthritis, including rheumatoid arthritis, axial spondyloarthritis, psoriatic arthritis and juvenile idiopathic arthritis (pJIA indication), Chronic idiopathic arthritis, including rheumatoid arthritis, axial spondyloarthritis, psoriatic arthritis and juvenile idiopathic arthritis (sJIA indication) / Treatment of systemic Juvenile Idiopathic Arthritis (sJIA), Treatment of polyarticular-course Juvenile Idiopathic Arthritis (pJIA).

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.12. Dolutegravir (DTG) / Lamivudine (3TC) - EMEA-001940-PIP01-16

Treatment of human immunodeficiency virus (HIV-1) infection / Treatment of human immunodeficiency virus (HIV-1) infection

Day 60 discussion

Infectious Diseases

3.1.13. Anti-(human calcitonin gene-related peptide receptor) human monoclonal antibody - EMEA-001664-PIP02-15

Migraine headaches / Prophylaxis of migraine

Day 60 discussion

Neurology

3.1.14. Humanized monoclonal calcitonin gene-related peptide neutralizing antibody - EMEA-001860-PIP04-16

Prophylactic treatment of cluster headache

Day 60 discussion

Neurology

3.1.15. Pembrolizumab - EMEA-001474-PIP02-16

Treatment of all conditions included in the category of malignant neoplasms (except

nervous system, haematopoietic and lymphoid tissue)., Treatment of Hodgkin Lymphoma / Treatment of relapsed or refractory classical Hodgkin Lymphoma in children from 5 years to less than 18 years of age., Treatment of advanced, untreated or previously treated, malignant melanoma in children from 12 year old to less than 18 years of age. Treatment as monotherapy of a PD-L1 positive paediatric malignant solid tumor in children from 6 months to less than 18 years of age

Day 60 discussion

Oncology

3.1.16. Recombinant human monoclonal IgG1 antibody directed against Programmed Death Ligand-1 (anti-PD-L1) - Orphan - EMEA-001849-PIP02-15

Merck KGaA; The treatment of solid malignant neoplasms

Day 60 discussion

Oncology

3.1.17. Dexamethasone / Povidone-Iodine - EMEA-001936-PIP01-16

Treatment of Infectious conjunctivitis (adenoviral and bacterial)

Day 60 discussion

Ophthalmology

3.1.18. EMEA-001947-PIP01-16

Grass pollen-induced allergic rhinitis/rhinoconjunctivitis / Treatment of grass pollen-induced allergic rhinitis, with or without conjunctivitis (AR/C)

Day 60 discussion

Pneumology - Allergology / Oto-rhino-laryngology

3.1.19. Ezetimibe / Rosuvastatin (calcium) - EMEA-001941-PIP01-16

Treatment of hypercholesterolaemia

Day 30 discussion

Cardiovascular Diseases

3.1.20. Indapamid / Amlodipine besylate / Perindopril erbumine - EMEA-001948-PIP01-16

Treatment of essential hypertension

Day 30 discussion

Cardiovascular Diseases

3.1.21. Lauromacrogol 400 - EMEA-001704-PIP03-16

Venous therapeutic procedures

Day 30 discussion

Cardiovascular Diseases

3.1.22. tadalafil / macitentan - EMEA-001961-PIP01-16

I27.0: Primary pulmonary hypertension / Treatment of Pulmonary Arterial Hypertension

Day 30 discussion

Cardiovascular Diseases

3.1.23. Humanized IgG1, kappa anti-serum amyloid A and anti-AL amyloid antibody - Orphan - EMEA-001962-PIP01-16

Prothena Therapeutics Limited; Treatment of Light Chain (AL) Amyloidosis

Day 30 discussion

Cardiovascular Diseases / Haematology-Hemostaseology

3.1.24. Birch bark extract - Orphan - EMEA-001299-PIP02-16

Birken AG; Treatment of epidermolysis bullosa / Treatment of epidermolysis bullosa

Day 30 discussion

Dermatology

3.1.25. EMEA-001949-PIP01-16

Detection and visualisation of areas with disruption of the blood brain barrier and/or abnormal vascularity for diagnostic purposes

Day 30 discussion

Diagnostic

3.1.26. (S)-lactic acid - EMEA-001953-PIP01-16

Pregnancy / Prevention of pregnancy

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.27. Recombinant human alpha-glucosidase conjugated with multiple copies of synthetic bismannose-6-phosphate-tetra-mannose glycan - Orphan - EMEA-001945-PIP01-16

Genzyme Europe B.V.; ICD-10: E74.0; Glycogen storage disease (Pompe disease) / Long-term use as an ERT for the treatment of patients with a confirmed diagnosis of Pompe disease (acid α-glucosidase deficiency)

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.28. allopurinol / lesinurad - EMEA-001952-PIP01-16

hyperuricaemia associated with gout

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.29. Seletalisib - EMEA-001938-PIP01-16

Primary Immunodeficiency syndrome

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.30. EMEA-001981-PIP01-16

Treatment of Chronic Hepatitis C Virus Infection / Treatment of chronic hepatitis C infection of genotypes 1 to 6 with the combination regimen of MK-3682, MK 5172 and MK-8408 in children and adolescents from 3 years to < 18 years of age.

Day 30 discussion

Infectious Diseases

3.1.31. Allogeneic human neural stem cells genetically modified to express c-MycERTAM, a c-Myc and modified oestrogen receptor fusion protein (CTX0E03) - EMEA-001969-PIP01-16

Sequelae of cerebral infarction

Day 30 discussion

Neurology

3.1.32. Cannabidiol - Orphan - EMEA-001964-PIP01-16

GW Research Ltd; Treatment of Seizures

Day 30 discussion

Neurology

3.2. Discussions on Compliance Check

The following compliance checks have been put up for discussion and the members of the PDCO have been invited to comment on issues of possible non-compliance

3.2.1. Aripiprazole - EMEA-C-000235-PIP02-10-M02

Otsuka Pharmaceutical Europe Ltd.; Treatment of Schizophrenia

Day 30 opinion

Psychiatry

Summary of committee discussion:

The PDCO adopted an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0256/2012) of 26 October 2012.Discussions on Modification of an Agreed Paediatric Investigation Plan.

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Evolocumab - EMEA-001268-PIP01-12-M03

Amgen Europe B.V.; Treatment of mixed dyslipidaemia, Treatment of elevated cholesterol / , Heterozygous Familial Hypercholesterolaemia (HeFH) and Homozygous Familial Hypercholesterolaemia (HoFH) after Prior Lipid-Lowering Therapy in paediatric subjects aged 10 years and above.

Day 30 discussion

Cardiovascular Diseases

3.3.2. dupilumab - EMEA-001501-PIP01-13-M03

Regeneron Pharmaceuticals, Inc; Atopic Dermatitis / Atopic Dermatitis

Day 30 discussion

Dermatology

3.3.3. Linaclotide - EMEA-000927-PIP01-10-M03

Allergan Pharmaceuticals International Limited; Functional Constipation / in children

Day 30 discussion

Gastroenterology-Hepatology

3.3.4. Lubiprostone - EMEA-000245-PIP01-08-M03

Sucampo Pharma Europe Ltd.; chronic idiopathic constipation / chronic idiopathic constipation

Day 30 discussion

Gastroenterology-Hepatology

3.3.5. vedolizumab - EMEA-000645-PIP01-09-M04

Takeda Pharma A/S; ulcerative colitis, Crohn's disease

Day 30 discussion

Gastroenterology-Hepatology

3.3.6. ixekizumab - EMEA-001050-PIP01-10-M02

Eli Lilly & Company Limited; Treatment of psoriasis vulgaris, Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis) / Treatment of moderate to severe chronic plaque psoriasis in paediatric patients from the age of 6 years who are not adequately controlled by topical therapies., Treatment of JIA (including polyarticular arthritis, extended oligoarticular arthritis, sJIA without active systemic features, and ERA including JoAS and JPsA) in paediatric patients from the age of 2 years and for the treatment of sJIA with active systemic features in paediatric patients from the age of 1 year.

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.7. piperaquine tetraphosphate / dihydroartemisinin - EMEA-000153-PIP01-07-M04

Sigma-Tau SpA; Uncomplicated malaria caused by Plasmodium falciparum (ICD-10 code B50) / Treatment of uncomplicated malaria caused by Plasmodium falciparum

Day 30 discussion

Infectious Diseases

3.3.8. solithromycin - EMEA-001581-PIP01-13-M03

Triskel EU Services, Ltd; Treatment of community acquired pneumoniae, Treatment of infection by Francisella tularaensis (tularaemia), Treatment of infection by Bacillus anthracis (anthrax) / Treatment of community acquired pneumoniae, Treatment of inhalation tularaemia following exposure to Francisella tularaensis, Treatment of inhalation anthrax following exposure to Bacillus anthracis

Day 30 opinion

Infectious Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted. The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0119/2016 of 28 April 2016). The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

3.3.9. Fingolimod hydrochloride - EMEA-000087-PIP01-07-M04

Novartis Europharm Limited; Multiple Sclerosis / Multiple Sclerosis

Day 30 discussion

Neurology

3.3.10. Brexpiprazole - EMEA-001185-PIP01-11-M03

Otsuka Europe Development and Commercialisation Ltd, Zweigniederlassung Frankfurt am Main; Schizophrenia / Treatment of schizophrenia in adolescents 13 to 17 years of age

Day 30 discussion

Psychiatry

3.3.11. Lanthanum carbonate hydrate - EMEA-000637-PIP02-10-M05

Shire Pharmaceutical Contracts Ltd; Hyperphosphataemia / No indication in the paediatric population is proposed

Day 30 discussion

Uro-nephrology

3.3.12. Levamisole (hydrochloride) - Orphan - EMEA-001885-PIP01-15-M01

ACE Pharmaceuticals BV; Glomerulonephritis and Nephrotic syndrome / Treatment of steroid sensitive nephrotic syndrome

Day 30 discussion

Uro-nephrology

3.3.13. Recombinant Human TriPeptidyl Peptidase 1 (rhTPP1) - EMEA-001362-PIP01-12-M03

BioMarin International Limited; Treatment of Neuronal Ceroid Lipofuscinosis Type 2 (CLN2)

Day 0 discussion

Neurology

4. Nominations

Disclosure of information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

4.1. List of letters of intent received for submission of applications with start of procedure 16 August 2016 for Nomination of Rapporteur and Peer reviewer

Summary of committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

4.2. Nomination of Rapporteur for requests of confirmation on the applicability of the EMA decision on class waiver.

Summary of committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

4.3. Nominations for other activities

4.3.1. Call for expression of interest to become PDCO representative in Enpr-EMA Coordinating Group

Scope: Replacement of Christoph Male

Summary of committee discussion:

Marek Migdal was nominated as PDCO representative to the Enpr-EMA Coordinating group.

4.3.2. Appointment of PDCO representative at the SAWP

Scope: Re-appointment of Karl-Heinz Huemer/appointment of another PDCO member

Summary of committee discussion:

Karl-Heinz Huemer was re-appointed as PDCO representative at the SAWP.

4.3.3. Appointment of alternate at Formulation Working Group

Scope: Appointment of Daniela Reins as alternate to member Andreas Grummel at PDCO Formulation Working Group

Summary of committee discussion:

Daniela Reins was appointed as alternate to member Andreas Grummel at the PDCO Formulation Working Group.

5. Scientific Advice Working Party (SAWP) and Paediatric Committee (PDCO) Interaction

Disclosure of information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

6. Discussion on the applicability of class waivers

Disclosure of some information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

6.1. Discussions on the applicability of class waiver for products

6.1.1. {2-amino-8-[4-(pyrrolidinylcarbonyl)phenyl]-(3H-benzo[f]azepin-4-yl)}-N,N-dipropylcarboxamide –Orphan – EMEA-18-2016

VentiRx Pharmaceuticals, Inc.; Treatment of ovarian carcinoma (excluding rhabdomyosarcoma and germ cell tumours), Treatment of Fallopian tube carcinoma (excluding rhabdomyosarcoma and germ cell tumours), Treatment of peritoneal carcinoma (excluding blastomas and sarcomas) / Treatment in combination with pegylated liposomal doxorubicin of adult patients with platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer

Summary of committee discussion:

The applicability of the class waiver as referred to in the Agency's Decision CW/1/2011 to the planned therapeutic indications was confirmed.

Other potential paediatric interest of this medicine suggested by PDCO: treatment of paediatric solid tumours (e.g. glioblastoma multiforme).

Note: in case of removal from the list of class waivers listed in the Agency's Decision CW/1/2011, the requirements set out in Article 7 and 8 of Regulation (EC) No 1901/2006 of the Agency's Decision CW/0001/2015 shall apply after 36 months from the date of the removal from the list of class waivers.

6.1.2. Glycopyrronium bromide/Formoterol fumarate dihydrate - EMEA-19-2016

Teva B.V.; Chronic Obstructive Pulmonary Disease (COPD) (excluding chronic lung diseases associated with long-term airflow limitation, such as asthma, bronchopulmonary dysplasia, primary cilia dyskinesia, obstructive lung disease related to graft-versus-host disease after (bone-marrow) transplantation)/ long-term, maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease, including chronic bronchitis and emphysema

Summary of committee discussion:

The applicability of the class waiver as referred to in the Agency's Decision CW/1/2011 to the planned therapeutic indications was confirmed.

Other potential paediatric interest of this medicine suggested by PDCO: treatment of asthma

Note: in case of removal from the list of class waivers listed in the Agency's Decision CW/1/2011, the requirements set out in Article 7 and 8 of Regulation (EC) No 1901/2006 of the Agency's Decision CW/0001/2015 shall apply after 36 months from the date of the removal from the list of class waivers.

7. Discussion on the inclusion of an indication within a condition in an agreed PIP/waiver

7.1. Discussion on the possibility to include an indication within a condition in an agreed PIP/waiver

None

8. Annual reports on deferrals

The members of the PDCO took note of the products listed in the Annex B.

9. Organisational, regulatory and methodological matters

9.1. Mandate and organisation of the PDCO

9.1.1. PDCO meeting dates 2016, 2017 and 2018

PDCO Chair: Dirk Mentzer

Summary of committee discussion:

The committee adopted the new meeting dates for 2016 - 2018. From November 2016 onwards the PDCO will start at 15:00hrs on Tuesday afternoon and will finish on Friday at 13:00hrs. The extension of the PDCO will be subject to amendment depending on the workload of the committee.

9.2. Coordination with EMA Scientific Committees or CMDh-v

9.2.1. Committee for Medicinal Products for Human Use (CHMP)

Summary of committee discussion:

The PDCO members were informed about 1 product, Revestive, for which the CHMP adopted positive opinions recommending a paediatric indication during their meeting in May 2016.

9.2.2. Recommendations on eligibility to PRIME – report from CHMP

Summary of committee discussion:

The members of the PDCO took note of the products for which the CHMP adopted the recommendation for PRIME eligibility during their meeting in May 2016. The individual outcomes are listed in PRIME Monthly Report on EMA website.

9.2.3. Report from the Strategic Review and Learning Meeting held on 1-3 June 2016, Utrecht

PDCO Chair: Dirk Mentzer

Summary of committee discussion:

The PDCO Chair reported from the Strategic Review and Learning Meeting discussion held in in Utrecht on 1-3 June 2016 highlighting the discussions regarding the optimisation of PDCO plenary meetings.

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

9.3.1. Non-clinical Working Group: D30 Products identified

PDCO member: Jacqueline Carleer

Summary of committee discussion:

The chair of the NcWG identified the products which will require NcWG evaluation and discussion.

9.3.2. Formulation Working Group

PDCO member: Brian Aylward

Summary of committee discussion:

Relevant products for FWG discussion were identified.

9.3.3. Paediatric Addendum to the Guideline on clinical investigation of medicinal products for the treatment of acute heart failure | Updated draft following public consultation and discussion at CVS WP May 2016 meeting

PDCO member: Christoph Male

Summary of committee discussion:

The Paediatric Addendum to the Guideline on clinical investigation of medicinal products for the treatment of acute heart failure was adopted by the PDCO.

9.3.4. Revision of the Guideline on the clinical investigation of human normal immunoglobulin for intravenous administration (IVIg)

Summary of committee discussion:

Jacqueline Kerr presented to the PDCO the changes made to the guideline and to the core SmPC, focusing on the wording of secondary immunodeficiencies (SID). The Kreuth group wished to broaden the wording but, at the same time, to narrow it to specific patients. The BPWP considered that the clinical manifestations of patients with high-level impairment due to SID are similar as those of primary immunodeficiencies and that patients who could receive IVIg could be narrowed to these with proven specific antibody failure (PSAF). PSAF was agreed by the BPWP to be defined as the failure to mount at least a 2-fold rise in IgG antibody titre to pneumococcal polysaccharide and polypeptide antigen vaccines.

It is noted that PSAF testing requires 2-3 weeks and that patients in a life-threatening situation should be treated immediately based on hypogammaglobulinaemia.

Considering the above, the BPWP amended the wording for SID including patients with severe, recurrent bacterial infections, ineffective antibiotic treatment and PSAF; or with life-threatening bacterial infections, ineffective antibiotic treatment and hypogammaglobulinaemia; or patients with paediatric HIV infection with severe recurrent bacterial infections, ineffective antibiotic treatment and PSAF.

Other changes include the addition of Chronic inflammatory demyelinating polyneuropathy and Multifocal motor neuropathy as established indications, correction of the dosing for Kawasaki disease and the inclusion of neutropenia/leukopenia in section 4.4 of the SmPC.

Jacqueline Kerr confirmed that applicants will still get the SID indications without further studies if they perform a study in PID with 40 subjects, of which approximately half should be children.

The PDCO expressed agreement with the changes in the guideline and SmPC and had no further comments.

The PDCO was informed of the next steps:

- Receipt comments from Guideline Consistency Group (GCG) in August 2016;
- Written procedure for agreement at Blood Products Working Party (BPWP);
- Adoption at CHMP in October
- 3 months public consultation

9.4. Cooperation within the EU regulatory network

9.4.1. European Commission (EC) 10-year report on Paediatric Regulation: draft economic impact study

Summary of committee discussion:

The draft economic impact study was presented to the PDCO.

9.5. Cooperation with International Regulators

None

9.6. Contacts of the PDCO with external parties and interaction with the Interested Parties to the Committee

9.6.1. Recommendations for Pharmacological Clinical Trials in Children with Irritable Bowel Syndrome (IBS) from the Rome Foundation Paediatric Subcommittee on Clinical Trials

PDCO Member: Johannes Taminiau

Summary of committee discussion:

Topic postponed to the PDCO July 2016 meeting.

9.7. PDCO work plan

None

9.8. Planning and reporting

None

9.9. PDCO ORGAM

None

10. Any other business

10.1.1. Templates for the summaries of the PDCO opinions

Summary of committee discussion:

Topic postponed to the PDCO July 2016 meeting.

10.1.2. Requests for participation at scientific/regulatory meetings of EMA staff – PDCO members

Summary of committee discussion:

The PDCO was informed that whenever requests for presentation or participation in scientific or regulatory meetings are received by EMA staff and where the EMA and the PDCO do not agree with an official representation of the committee in this meeting, the requesters [i.e. organiser of the meeting] are advised that they can contact PDCO members directly, should they wish to invite a PDCO member in a personal capacity as an individual expert not formally representing the PDCO or the EMA.

In case a PDCO member is requested to represent the committee or the EMA, specific rules and policies for such representation apply, including a formal agreement by the EMA and the PDCO and the availability of funding.

Policy on scientific publication and representation can be found at:
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/10/WC500004627.pdf

10.1.3. Overview of PIPs for HIV

Summary of committee discussion:

The committee was informed of the findings of cross analysis of PIP applications in the area of HIV.

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

Extrapolation of efficacy in oncology was discussed. The kick-off meeting of the Enpr-EMA working group on paediatric oncology and haematology was prepared.

11.1.2. Neonatology

Summary of committee discussion:

This meeting was cancelled.

The Chair thanked the participants and closed the meeting.

12. List of participants

List of participants including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 22-24 June 2016 meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Dirk Mentzer	Chair	Germany	No interests declared	
Karl-Heinz Huemer	Member	Austria	No interests declared	
Christoph Male	Alternate	Austria	No participation in final deliberations and voting on:	EMEA-000428-PIP01-08-M03
Koenraad Norga	Member (Vice-Chair)	Belgium	When chairing the meeting: To be replaced for discussions, final deliberations and voting on:	EMEA-000673-PIP01-09-M09 EMEA-001765-PIP02-15
Jacqueline Carleer	Alternate	Belgium		
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Suzana Mimica Matanovic	Alternate	Croatia	No participation in discussion, final deliberations and voting on:	EMEA-000978-PIP01-10-M01
Georgios Savva	Member	Cyprus	No interests declared	
Jaroslav Sterba	Member	Czech Republic	No interests declared	
Peter Szitanyi	Alternate	Czech Republic	No interests declared	
Marianne Orholm	Member	Denmark	No interests declared	
Marta Granström	Alternate	Denmark	No interests declared	
Jana Lass	Alternate	Estonia	No interests declared	
Ann Marie Kaukonen	Member	Finland	No interests declared	
Sylvie Benchetrit	Member	France	No interests declared	
Immanuel Barth	Member	Germany	No interests declared	
Sabine Scherer	Alternate	Germany	No interests declared	
Grigorios Melas	Member	Greece	No interests declared	
Ágnes Gyurasics	Member (CHMP member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	
Francesca Rocchi	Alternate	Italy	No restrictions applicable to this meeting	
Dina Apele-Freimane	Member	Latvia	No interests declared	
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No restrictions applicable to this meeting	
Herbert Lenicker	Alternate	Malta	No interests declared	
Siri Wang	Member	Norway	No interests declared	
Marek Migdal	Member	Poland		
Helena Fonseca	Member	Portugal	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Hugo Tavares	Alternate	Portugal	No interests declared	
Dana Gabriela Marin	Member (CHMP alternate)	Romania	No interests declared	
Stefan Grosek	Member	Slovenia	No interests declared	
Fernando de Andrés Trelles	Member	Spain	No interests declared	
Maria Jesús Fernández Cortizo	Alternate	Spain	No interests declared	
Ninna Gullberg	Member	Sweden	No interests declared	
Eva Agurell	Alternate	Sweden	No restrictions applicable to this meeting	
Angeliki Siapkara	Member	United Kingdom	No interests declared	
Martina Riegl	Alternate	United Kingdom	No interests declared	
Riccardo Riccardi	Member	Healthcare Professionals' Representative	No participation in discussion, final deliberations and voting on:	EMEA-001945-PIP01-16
Paolo Paolucci	Alternate	Healthcare Professionals' Representative	No interests declared	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Tsvetana Schyns-Liharska	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Jacqueline Kerr	Expert - via telephone*	Germany (Blood Products Working Party)	No interests declared	
Krishna Prasad	Expert - via telephone*	United Kingdom (Cardiovascular Working Party)	No restrictions applicable to this meeting	
Juliana Min	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Shiva Ramroop	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Frederike Lentz	Expert - via telephone*	Germany	No interests declared	
Uwe Muller	Expert - in person*	Germany	No interests declared	
A representative from the European Commission attended the meeting.				
Meeting run with support from relevant EMA staff				

* Experts were only evaluated against the agenda topics or activities they participated in.

13. Explanatory notes

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

Paediatric investigation plan (PIP) (section 2.1 Opinion on PIPs and section 3.1 Discussions on PIPs)
A paediatric investigation plan (PIP) is a development plan aimed at ensuring that the necessary data are obtained through studies in children, when it is safe to do so, to support the authorisation of a medicine for children. Pharmaceutical companies submit proposals for PIPs to the European Medicines Agency's Paediatric Committee (PDCO). This Committee is responsible for agreeing or refusing the plan.

Compliance checks (section 2.2 Opinions on Compliance check, section 3.2 Discussions on Compliance check)
A compliance check may be necessary before any application for marketing authorisation (even for an adult indication) can be considered valid, if there was no deferral for at least one of the studies agreed in the PIP, or after the due date of initiation or completion of a study/measure. The same applies to some regulatory applications for authorised products, as described above.

Modification of an Agreed Paediatric Investigation Plan (section 2.3 Opinions on Modification of an agreed PIP, section 3.3 Discussions on Modification of an agreed PIP)
The development plan for a medicine can be modified at a later stage as knowledge increases. Modifications can also be made if the applicant encounters such difficulties with the implementation of a PIP, which render it unworkable or no longer appropriate.
In some cases, studies can be deferred until after the studies in adults have been conducted. This ensures that research in children is done only when it is safe and ethical to do so. Even when studies are deferred, the PIP will include details of the paediatric studies and their timelines.

Class waiver (section 6 Discussion on the applicability of class waiver)
As some diseases do not affect children (for example Parkinson's disease), the development of medicines for these diseases should not be performed in children. In these cases, a PIP is not required and it will be waived**.** For more information on the classes of diseases subject to waivers, see class waivers.

Annual reports on deferrals (section 8)
If the medicinal product is approved in the EU, annual reports on the deferred measures in the PIP must be submitted to the Agency.

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