21 February 2017
EMA/PDCO/50789/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes for the meeting on 24-27 January 2017

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

24 January 2017, 14:00- 19:00, room 3A

25 January 2017, 08:30- 19:00, room 3A

26 January 2017, 08:30- 19:00, room 3A

27 January 2017, 08:30- 13:00, room 3A

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 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).

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. 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. Gadolinium, [α3,α6,α9-tris[3-[(2,3-dihydroxypropyl)amino]-3-oxopropyl]-3,6,9,15-tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene-3,6,9-triacetato(3-)-κN3,κN6,κN9,κN15,κO3,κO6,κO9]-(P03277) - EMEA-001949-PIP01-16

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

Day 120 opinion

Diagnostic

Summary of committee discussion:

As there is no outstanding issue left, a positive opinion endorsing the PIP has been adopted accordingly.

2.1.2. 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 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the applicant's PIP proposal and adopted a positive opinion.

2.1.3. Somapacitan - EMEA-001469-PIP01-13

Novo Nordisk A/S; Growth Hormone Deficiency

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

A positive opinion was adopted.

2.1.4. Testosterone - EMEA-001529-PIP02-14

Acerus Pharmaceuticals SRL; Male hypogonadism

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The Committee therefore adopted a positive opinion.

2.1.5. Autologous CD34+ hematopoietic stem cells transduced ex vivo with EFS lentiviral vector encoding for the human ADA gene - Orphan - EMEA-001974-PIP01-16

Pr Bobby Gaspar; Severe combined immunodeficiency disorder due to adenosine deaminase deficiency [ADA-SCID] / Treatment of severe combined immunodeficiency disorder due to adenosine deaminase deficiency [ADA-SCID]

Day 120 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO re-discussed this product on the 27th of January 2017.
The Committee assessed the answers and clarifications the applicant provided to the requests the PDCO made at day 90 and noted that all outstanding issues have now been resolved.
Taking into account the previous discussions and the above considerations, the PDCO adopted a positive Opinion at Day 120.

2.1.6. T-lymphocytes enriched leukocyte preparation depleted ex vivo of host host-alloreactive T cells using photodynamic treatment - Orphan - EMEA-001980-PIP01-16

Kiadis Pharma Netherlands B.V.; Adjunctive treatment in haematopoietic stem cell transplantation for a malignant disease / Adjunctive treatment to a haploidentical haematopoietic stem cell transplantation with CD34+ selected cells, in patients with a haematological malignancy, for the reduction of morbidity (i.e. incidences and severity of graft versus host disease) and mortality due to infection and relapse.

Day 120 opinion

Immunology-Rheumatology-Transplantation / Oncology

Summary of committee discussion:

The Committee discussed on 26 January 2017 the application for agreement of a PIP for ATIR101 (T-lymphocytes enriched leukocyte preparation depleted ex vivo of host-alloreactive T cells using photodynamic treatment), taking into account the supplementary information recently received.

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

ViiV Healthcare UK Limited; Treatment of human immunodeficiency virus (HIV-1) infection / Treatment of human immunodeficiency virus (HIV-1) infection

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 at their January 2017 meeting agreed a positive opinion on the PIP for Lamivudine (3TC) / Dolutegravir (DTG) in the condition of Treatment of human immunodeficiency virus (HIV-1) infection including a deferral.

2.1.8. 8-chloro-5-methyl-1-[trans-4-(pyridin-2-yloxy)cyclohexyl]-5,6-dihydro-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine - EMEA-001918-PIP01-15

Roche Registration Ltd; ICD10 F84: Treatment of autism spectrum disorder

Day 120 opinion

Neurology

Summary of committee discussion:

The PDCO confirmed the conclusion of the discussion at D90, and adopted a positive opinion by consensus on the agreement of a PIP, including a deferral.

2.1.9. Avelumab - Orphan - EMEA-001849-PIP02-15

Merck KGaA; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms)

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the application for avelumab considering the responses provided by the applicant after the D90 discussion, the feedback from the Modelling and Simulation Working Group and applicant's comments on the draft opinion.
All pending issues were considered solved.
In conclusion the PDCO recommended granting a paediatric investigation plan for the entire paediatric population from birth to less than 18 years of age for avelumab and a deferral.

2.1.10. atorvastatin (calcium) / ezetimibe - EMEA-002047-PIP01-16

Midas Pharma GmbH; Dyslipidaemia

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

Based on the assessment of this application the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for atorvastatin (calcium) / ezetimibe for all subsets of the paediatric population (0 to 18 years of age) in the condition 'Treatment of elevated cholesterol'.

2.1.11. 5-(4-cyclopropyl-1H-imidazol-1-yl)-2-fluoro-N-(6-(4-isopropyl-4H-1,2,4- triazol-3-yl)pyridi-2-yl)-4-methylbenzamide - EMEA-001868-PIP02-16

Gilead Sciences International Ltd.; K70.1 Alcoholic hepatitis

Day 60 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee including contributions of external expert(s), the PDCO agrees with the

applicant's request for a waiver. The PDCO recommends granting a waiver for 5-(4-cyclopropyl-1H-imidazol-1-yl)-2-fluoro-N-(6-(4-isopropyl-4H-1,2,4- triazol-3-yl)pyridi-2-yl)-4-methylbenzamide for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of Alcoholic hepatitis.

2.1.12. alpelisib - EMEA-002016-PIP02-16

Novartis Europharm Ltd; Treatment of breast cancer

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO discussed on 25 January the application for the granting of a waiver for the totality of the paediatric population in the scope of the condition treatment of breast cancer, taking into account the supplementary information that addressed the questions raised during the discussion at day 30 of the procedure (above).
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 such as discussed above. 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. rivaroxaban - EMEA-C3-000430-PIP01-08-M09

Bayer Pharma AG; Treatment of thromboembolic events

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The PDCO finalised on 27-January 2017 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.

2.2.2. Pneumococcal polysaccharide serotype 6B conjugated to Protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 23F 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 18C conjugated to tetanus toxoid / Pneumococcal polysaccharide serotype 19F conjugated to diphtheria toxoid /

Pneumococcal polysaccharide serotype 7F 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 14 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 / Pneumococcal polysaccharide serotype 5 conjugated to Protein D (derived from non-typeable Haemophilus influenzae) carrier protein - EMEA-C-000673-PIP01-09-M09

GlaxoSmithKline Biologicals S.A.; Prevention of acute otitis media caused by non-typeable Haemophilus influenzae

Day 60 opinion

Vaccines

Summary of committee discussion:

The completed study was checked for compliance. The PDCO took note of preceding procedures and reports on partially completed compliance (EMEA-C1-000673-PIP01-09; EMEA-C2-000673-PIP01-09-M03; EMEA-C3-000673-PIP01-09-M05; EMEA-C4-000673-PIP01-09-M08; EMEA-C5-000673-PIP01-09-M08). The PDCO adopted on 24 June 2016 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0209/2016) of 12 August 2016.

2.2.3. Purified Pertussis Toxoid (PT) / Hepatitis B Surface Antigen, recombinant (HBsAg) / Purified Filamentous Haemagglutinin (FHA) / Inactivated Type 2 Poliovirus (MEF-1) / Haemophilus influenzae type b polysaccharide conjugated to tetanus protein / Inactivated Type 3 Poliovirus (Saukett) / Purified Diphtheria Toxoid / Inactivated Type 1 Poliovirus (Mahoney) / Purified Tetanus Toxoid - EMEA-C-001201-PIP01-11-M02

Sanofi Pasteur; Prevention of infections caused by Corynebacterium diphtheriae, Clostridium tetani, Bordetella pertussis, poliovirus types 1, 2 and 3, prevention against invasive infections caused by Haemophilus influenzae type b and infection caused by hepatitis B virus

Day 60 opinion

Vaccines

Summary of committee discussion:

The completed studies were checked for compliance.
The PDCO took note of preceding procedures and reports on partially completed compliance (EMEA-C1-001201-PIP01-11-M01) for completed studies.
The PDCO adopted on 27 January 2017 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0229/2013) of 23 September 2013.

2.2.4. Tocilizumab - EMEA-C3-000309-PIP01-08-M07 – Adopted at D30

Roche Registration Limited; Chronic Idiopathic Arthritis

Day 30 discussion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO discussed the completed study and considered that it is compliant with the latest Agency's Decision (P/0266/2015) of 27 November 2015.
The PDCO finalised on 27/01/2017 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. Vericiguat - EMEA-001636-PIP01-14-M01

Bayer Pharma AG; Treatment of left ventricular failure / Treatment of chronic left ventricular failure with reduced ejection fraction in paediatric patients with dilated cardiomyopathies

Day 60 opinion

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

2.3.2. dupilumab - EMEA-001501-PIP01-13-M04

Regeneron Pharmaceuticals, Inc; Atopic Dermatitis / Atopic Dermatitis

Day 60 opinion

Dermatology

Summary of committee discussion:

The PDCO considers that the applicant has not provided convincing argument. The applicant’s proposal is not considered appropriate.

2.3.3. tofacitinib - EMEA-000576-PIP02-11-M04

Pfizer Limited; Treatment of psoriasis / Treatment of severe plaque psoriasis

Day 60 opinion

Dermatology

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/0216/2014 of 3 September 2014). The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.4. saxagliptin - EMEA-000200-PIP01-08-M07

AstraZeneca AB; E11 Type 2 Diabetes / Treatment of Type 2 Diabetes

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

A positive opinion has been adopted.

2.3.5. Tofacitinib - EMEA-000576-PIP01-09-M06

Pfizer Limited; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis) / Juvenile idiopathic arthritis

Day 60 opinion

Immunology-Rheumatology-Transplantation

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/0013/2015 of 30 January 2016). The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.6. Treosulfan - Orphan - EMEA-000883-PIP01-10-M03

medac Gesellschaft für klinische Spezialpräparate mbH; Conditioning treatment prior to haematopoietic progenitor cell transplantation / Conditioning treatment prior to haematopoietic progenitor cell transplantation

Day 60 opinion

Immunology-Rheumatology-Transplantation / Oncology

Summary of committee discussion:

The PDCO discussed the request for modification on 25 January 2017 taking into account the supplementary information and the exchange of the applicant with the PDCO Rapporteur and EMA; the applicant did not have comments on a draft Opinion.
Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that some of 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. The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.7. Anidulafungin - EMEA-000469-PIP01-08-M07

Pfizer Limited; Treatment of invasive candidiasis

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO's views expressed at day 30 were re-discussed and endorsed.
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/0208/2016 of 12 August 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.8. avibactam / ceftazidime - EMEA-001313-PIP01-12-M05

AstraZeneca AB; Treatment of bacterial infections / For the treatment of complicated urinary tract infections, For the treatment hospital acquired pneumonia, For the treatment of complicated intra-abdominal infections, For the treatment of Gram-negative bacterial infections

Day 60 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/0251/2015 of 30 October 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.9. Cobicistat - EMEA-000969-PIP01-10-M04

Gilead Sciences International Ltd.; Treatment of human immunodeficiency virus type-1 (HIV-1) infection / Treatment of human immunodeficiency virus type-1 (HIV-1) infection - pharmacoenhancer for use in combination with antiretroviral agents.

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The applicant provided additional information on 9 January 2017.

In conclusion, based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO therefore considered that some but not all of 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/0212/2014 of 01 September 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.10. dasabuvir sodium monohydrate - EMEA-001439-PIP01-13-M01

Abbvie Ltd; Treatment of chronic hepatitis C / Treatment of children and adolescents from >= 3 years to less than 18 years of age with chronic HCV infection with compensated cirrhosis or without compensated cirrhosis in combination with ombitasvir, paritaprevir and ritonavir

Day 60 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 therefore 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/0314/2013 of 19 December 2013).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.11. Fidaxomicin - EMEA-000636-PIP01-09-M05

Astellas Pharma Europe B.V.; Treatment of enterocolitis caused by clostridium difficile / Treatment of Clostridium difficile infections (CDI) also known as C. difficile-associated diarrhoea (CDAD).

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO confirmed the outcome of the Day 30 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/0098/2016 of 15 April 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.12. ledipasvir / sofosbuvir - EMEA-001411-PIP01-12-M04

Gilead Sciences International Ltd.; Treatment of chronic hepatitis C / Treatment of chronic hepatitis C

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

After the Day 30 discussion the applicant provided the requested additional information on Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan the PDCO thus 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/0174/2016 of 30 June 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.13. ritonavir / paritaprevir / ombitasvir - EMEA-001440-PIP01-13-M01

Abbvie Ltd; Treatment of chronic hepatitis C / Treatment of children and adolescents from >= 3 years to < 18 years of age with chronic HCV infection with compensated cirrhosis or without compensated cirrhosis in combination with other medicinal products

Day 60 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 therefore 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/0315/2013 of 19 December 2013).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.14. tazobactam / ceftolozane - EMEA-001142-PIP01-11-M02

Merck Sharp & Dohme (Europe), Inc.; treatment of abdominal and gastrointestinal infections, treatment of urinary tract infections / Treatment of complicated urinary tract infections (cUTI), Treatment of complicated intra-abdominal infections (cIAI)

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO confirmed the outcome of the discussion at Day 30. 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.
In addition, the wording of the pharmaceutical form was corrected from "powder for solution for infusion" to "powder for concentrate for solution for infusion".
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0126/2014 of 16 May 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.15. Brivaracetam - Orphan - EMEA-000332-PIP01-08-M11

UCB Pharma S.A.; treatment of paediatric epilepsy syndromes, Treatment of epilepsy with partial onset seizures, Treatment of neonatal seizures / Treatment of neonatal seizures with adjunctive administration of brivaracetam, Treatment of paediatric patients with partial onset seizures, treatment of refractory paediatric epilepsy syndromes with adjunctive administration of brivaracetam

Day 60 opinion

Neurology

Summary of committee discussion:

Based on the review of the rationale submitted by the application including further clarification after D30 for modifying the agreed paediatric investigation plan, the PDCO considered that most of 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/0182/2016 of 15 July 2016)
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.16. Fingolimod hydrochloride - EMEA-000087-PIP01-07-M05

Novartis Europharm Limited; Multiple Sclerosis / Multiple Sclerosis

Day 60 opinion

Neurology

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 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/0230/2016 of 9 September 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.17. Iacosamide - EMEA-000402-PIP02-11-M03

UCB Pharma S.A.; Treatment of Epilepsy - Partial-onset seizures [G40.0 - G40.1 - G40.2], Treatment of Generalized Epilepsy and Epilepsy Syndromes: Epilepsy - generalized idiopathic epilepsy and epilepsy syndromes [G40.3] Epilepsy - Other generalized epilepsy and epileptic syndromes [G40.4] / Adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in pediatric patients with epilepsy (birth to <16 years), Monotherapy in the treatment of partial-onset seizures with or without secondary generalization in pediatric patients (1 month to <18 years), Adjunctive therapy in the treatment of primary generalized tonic-clonic seizures (PGTCS) in pediatric patients with idiopathic generalized epilepsy (IGE)(4 years to <18 years), Adjunctive therapy in the treatment of epileptic syndromes associated with generalized seizures in pediatric patients with epilepsy birth to <18 years (specific epileptic syndrome(s) to be based on future clinical development further to exploratory study results)

Day 60 opinion

Neurology

Summary of committee discussion:

Based on the review of the rationale submitted by the application including further clarification after D30 for modifying the agreed paediatric investigation plan, the PDCO considered that most 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/0183/2015 of 17 August 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.18. cobimetinib - EMEA-001425-PIP01-13-M02

Roche Registration Limited; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue) with Ras, Raf or MEK pathway activation / Treatment of children with a paediatric solid malignant tumour with known or expected Ras, Raf or MEK pathway activation, at first relapse or refractory to initial treatment.

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO discussed on 26 January 2017 the modification request concerning the PIP agreed for cobimetinib, an oral MEK1/2 inhibitor, to target the treatment of paediatric a solid malignant tumour with known or expected Ras, Raf or MEK pathway activation, at first relapse or refractory to initial treatment. The Committee took into account supplementary information and comments on a draft of the Opinion by the applicant.
Based on the information provided, the Committee finalised the discussion and agreed to modify the PIP.
Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that some of 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. The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.19. Sirolimus - Orphan - EMEA-001416-PIP01-12-M01

Santen Incorporated; Treatment of chronic non-infectious uveitis

Day 60 opinion

Ophthalmology

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/0079/2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.20. tafluprost - EMEA-001187-PIP01-11-M04

Santen Oy; Glaucoma (ICD: H40) / Tafluprost preservative-free is indicated for the treatment of elevated intraocular pressure in paediatric patients 1 month post-natal to less than 18 years of age.

Day 60 opinion

Ophthalmology

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, and the fact the applicant addressed the concerns raised by the PDCO at D30
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0190/2016 of 15 July 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.21. Conestat Alfa - EMEA-000367-PIP01-08-M06

Pharming Group N.V.; D84.1 Defects in the complement system C1 esterase inhibitor (C1-INH) deficiency / treatment of acute attacks of angioedema associated with hereditary C1 esterase inhibitor deficiency

Day 60 opinion

Other

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/0004/2016 of 22 January 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.22. mepolizumab - Orphan - EMEA-000069-PIP02-10-M07

GSK Trading Services Limited; treatment of asthma / add-on treatment for severe refractory eosinophilic asthma

Day 60 opinion

Pneumology - Allergology

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/0139/2015 of 10 July 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.23. mirabegron - EMEA-000597-PIP03-15-M03

Astellas Pharma Europe B.V.; Treatment of neurogenic detrusor overactivity / Treatment of detrusor overactivity in children and adolescents with neurogenic bladder dysfunction

Day 60 opinion

Uro-nephrology

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/0288/2016 of 04/11/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.24. Influenza virus surface antigens - A/turkey/Turkey/1/05 (H5N1)-like strain (NIBRG-23) - EMEA-000599-PIP01-09-M05

Seqirus S.r.l.; Prevention of influenza / Active immunization against H5N1 subtype of Influenza A virus

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/0230/2014 of 5 September 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.25. Naldemedine - EMEA-001893-PIP01-15-M01 – adopted at D30

Shionogi Limited; Opioid-induced Constipation (OIC)

Day 30 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The PDCO discussed at their January meeting a modification request for the recently adopted PIP for naldemedine. The Modification was supported and agreed at D30.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0312/2016 of 11/11/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.26. Vigabatrin - EMEA-000717-PIP02-13-M02 – adopted at D30

ORPHELIA Pharma SA; Infantile spasms (West syndrome; ICD10: G40.82), Refractory partial epilepsy (ICD10: G40.01, G40.11, G40.21) / Treatment of infantile spasms, Treatment of refractory partial epilepsy

Day 30 opinion

Neurology

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/0271/2015 of 27 November 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. Macimorelin - EMEA-001988-PIP01-16

Growth hormone deficiency / Diagnosis of growth hormone deficiency

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Diagnostic

3.1.2. Allogeneic, non-expanded, umbilical cord blood-derived, hematopoietic mature myeloid and lymphoid cells (NF) / Allogeneic, ex vivo expanded, umbilical cord

blood-derived, hematopoietic CD34+ progenitor cells (CF) - Orphan - EMEA-001913-PIP01-15

Gamida Cell Limited; acute lymphoblastic leukaemia, myelodysplastic syndrome, acute myeloid leukaemia, chronic myeloid leukaemia / treatment of patients with hematological malignancies who are medically indicated for allogeneic haematopoietic stem cell transplantation

Day 90 discussion

Haematology-Hemostaseology

3.1.3. Human fibrinogen concentrate - EMEA-001931-PIP01-16

Treatment of congenital fibrinogen deficiency

Day 90 discussion

Haematology-Hemostaseology

3.1.4. 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 90 discussion

Immunology-Rheumatology-Transplantation

3.1.5. Entolimod - Orphan - EMEA-002020-PIP01-16

Cleveland BioLabs Inc; Treatment of acute Radiation Syndrome / Entolimod is indicated for reducing the risk of death following exposure to potentially lethal irradiation occurring as the results of a radiation disaster

Day 90 discussion

Other

3.1.6. bempedoic acid - EMEA-001872-PIP01-15

Primary Hypercholesterolemia / Treatment of heterozygous familial hypercholesterolaemia

Day 90 discussion

Other / Cardiovascular Diseases

3.1.7. olodaterol hydrochloride - EMEA-001965-PIP01-16

Treatment of cystic fibrosis

Day 90 discussion

Pneumology - Allergology

3.1.8. Baclofen - EMEA-001549-PIP02-14

Alcohol use disorders (DSM-5) / Reduction of alcohol consumption as a second line treatment after psychosocial intervention, in 15-17 years adolescents with alcohol use disorders according to DSM 5

Day 90 discussion

Psychiatry

3.1.9. rVSVΔG-ZEBOV-GP - EMEA-001786-PIP01-15

Prevention of Ebola disease

Day 90 discussion

Vaccines

3.1.10. Crisaborole - EMEA-002065-PIP01-16

Mild to moderate atopic dermatitis

Day 60 discussion

Dermatology

3.1.11. lebrikizumab - EMEA-001053-PIP03-16

Treatment of atopic dermatitis

Day 60 discussion

Dermatology

3.1.12. (2S)-2-{[(2R)-2-[({[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-l]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino}butanoic acid - Orphan - EMEA-002054-PIP01-16

Albireo AB; Treatment of Progressive Familial Intrahepatic Cholestasis

Day 60 discussion

Gastroenterology-Hepatology

3.1.13. Fc- and CDR-modified humanised monoclonal antibody against C5 - Orphan - EMEA-002077-PIP01-16

Alexion Europe SAS; Paroxysmal Nocturnal Haemoglobinuria / Treatment of Paroxysmal Nocturnal Haemoglobinuria

Day 60 discussion

Haematology-Hemostaseology

3.1.14. EMEA-001741-PIP03-16

Treatment of Crohn's Disease

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.15. EMEA-002057-PIP01-16

Post ischemic stroke recovery / Treatment of ischemic stroke to improve recovery

Day 60 discussion

Neurology

3.1.16. Deutetrabenazine - EMEA-002052-PIP01-16

Treatment of tics associated with Tourette syndrome

Day 60 discussion

Neurology

3.1.17. Recombinant human arylsulfatase A (rhASA) - Orphan - EMEA-002050-PIP01-16

Shire Pharmaceuticals Ireland Limited; Treatment of metachromatic leukodystrophy (MLD) / Treatment of metachromatic leukodystrophy (MLD)

Day 60 discussion

Neurology

3.1.18. (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide hydrogen sulfate - Orphan - EMEA-001971-PIP02-16

Loxo Oncology, Inc.; Treatment of solid tumours / The treatment of adults, adolescents and children (> 1 month of age) with advanced solid tumours harbouring an NTRK fusion, as established prior to initiation of LOXO-101 therapy.

Day 60 discussion

Oncology

3.1.19. Allogeneic Epstein-Barr virus specific cytotoxic T lymphocytes - Orphan - EMEA-002025-PIP02-16

Atara Biotherapeutics, Inc.; Treatment of Epstein-Barr virus associated post-transplant lymphoproliferative disorder / Treatment of allogeneic haematopoietic cell transplant (alloHCT) patients with Epstein-Barr virus associated Post Transplant Lymphoproliferative Disease (EBV-PTLD) who have failed prior therapy with rituximab

Day 60 discussion

Oncology

3.1.20. gilteritinib (as fumarate) - EMEA-002064-PIP01-16

Treatment of acute myeloid leukemia / Treatment of FLT3/ITD positive acute myeloid leukemia

Day 60 discussion

Oncology / Haematology-Hemostaseology

3.1.21. Venetoclax - Orphan - EMEA-002018-PIP02-16

AbbVie Ltd; Treatment of haematopoietic and lymphoid malignant neoplasms, Treatment of solid tumour malignant neoplasms / As monotherapy, or in combination with chemotherapy, for the treatment of relapsed or refractory NHL patients < 18 years of age, who have progressed following autologous stem cell transplantation or who are ineligible for transplantation, As monotherapy or in combination for the treatment of patients with relapsed or refractory neuroblastoma < 18 years of age, As monotherapy, or in combination with chemotherapy, for the treatment of relapsed or refractory ALL in the third line setting in patients < 18 years of age, As monotherapy, or in combination with chemotherapy, for the treatment of relapsed or refractory AML in patients < 18 years of age

Day 60 discussion

Oncology / Haematology-Hemostaseology

3.1.22. Fluocinolone Acetonide - Orphan - EMEA-000801-PIP03-16

CAMPHARM Limited; Chronic non-infectious uveitis affecting the posterior segment of the eye

Day 60 discussion

Ophthalmology

3.1.23. EMEA-002082-PIP01-16

Treatment of cystic fibrosis /is indicated to improve lung function and reduce pulmonary

exacerbations for patients in all age groups with cystic fibrosis in conjunction with standard therapies.

Day 60 discussion

Pneumology - Allergology

3.1.24. Acetylsalicylic acid / Prasugrel HCl - EMEA-002071-PIP01-16

Prevention of atherosclerosis, thrombosis and thromboembolic events

Day 30 discussion

Cardiovascular Diseases

3.1.25. Amlodipine / Candesartan - EMEA-002090-PIP01-16

Hypertension

Day 30 discussion

Cardiovascular Diseases

3.1.26. Amlodipine / Perindopril - EMEA-002091-PIP01-16

Hypertension

Day 30 discussion

Cardiovascular Diseases

3.1.27. Tetrofosmin - Orphan - EMEA-002019-PIP02-16

proACTINA SA; Diagnosis of malignant Glioma

Day 30 discussion

Diagnostic

3.1.28. Alicaforsen - Orphan - EMEA-002060-PIP01-16

Atlantic Pharmaceuticals Ltd; Treatment of gastrointestinal procedural complications / Treatment of active episodes of antibiotic refractory pouchitis

Day 30 discussion

Gastroenterology-Hepatology

3.1.29. Levoglutamide - Orphan - EMEA-001996-PIP02-16

Emmaus Medical Europe Ltd.; Sickle cell disease / Levoglutamide is indicated for the prevention of sickle cell crises in adults, adolescents and children older than 5 years suffering from Sickle Cell Disease.

Day 30 discussion

Haematology-Hemostaseology

3.1.30. Recombinant human monoclonal antibody to GM-CSF . - EMEA-001882-PIP02-16

Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis) / Treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 1 year of age and older, Treatment of active polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years of age and older

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.31. Iclaprim mesylate - EMEA-000345-PIP02-16

Infection with resistant Gram-positive bacteria. / Treatment of acute bacterial skin and skin structure infections caused by susceptible strains of Gram-positive bacteria.

Day 30 discussion

Infectious Diseases

3.1.32. Lefamulin - EMEA-002075-PIP01-16

Treatment of community-acquired pneumonia

Day 30 discussion

Infectious Diseases

3.1.33. Tobramycin - Orphan - EMEA-000184-PIP03-16

Novartis Europharm Limited; Treatment of Pseudomonas aeruginosa pulmonary colonisation in patients with bronchiectasis.

Day 30 discussion

Infectious Diseases

3.1.34. EMEA-002070-PIP01-16

Treatment of spinal muscular atrophy

Day 30 discussion

Neurology

3.1.35. fenfluramine hydrochloride - Orphan - EMEA-001990-PIP01-16

Zogenix International Ltd; Dravet Syndrome / The adjunctive treatment of seizures in

paediatric patients at least 2 years of age with Dravet Syndrome

Day 30 discussion

Neurology

3.1.36. Methylphenidate (hydrochloride) - EMEA-002034-PIP01-16 – adopted at D30

Mundipharma Research Limited; Attention-Deficit/Hyperactivity Disorder (ADHD)

Day 30 opinion

Neurology

Summary of committee discussion:

The PDCO reviewed the application along with the assessors' comments.
The PDCO has adopted a product-specific waiver for all paediatric subsets on its own motion for methylphenidate for the treatment of ADHD.

3.1.37. Autologous CD3+ T Cells Expressing CD19 Chimeric Antigen Receptor - EMEA-001994-PIP01-16

Treatment of B-cell non-Hodgkin's lymphoma, Treatment of B-cell acute lymphoblastic leukemia / Treatment of pediatric patients with relapsed or refractory B-cell acute lymphoblastic leukemia, Treatment of pediatric patients with relapsed or refractory diffuse large B-cell lymphoma, Burkitt lymphoma, and primary mediastinal large B-cell lymphoma

Day 30 discussion

Oncology

3.1.38. Autologous CD4+ and CD8+ T cells Expressing a CD19-Specific Chimeric Antigen Receptor - EMEA-001995-PIP01-16

Treatment of B-cell non-Hodgkin's lymphoma, Treatment of B-cell acute lymphoblastic leukemia / Treatment of pediatric patients with relapsed or refractory B-cell acute lymphoblastic leukemia, Treatment of pediatric patients with relapsed or refractory diffuse large B-cell lymphoma, Burkitt lymphoma, and primary mediastinal large B-cell lymphoma

Day 30 discussion

Oncology

3.1.39. Enasidenib - Orphan - EMEA-001798-PIP02-16

Celgene Europe Ltd; Treatment of Acute Myeloid Leukaemia / Treatment of patients aged 2 to 21 years old with relapsed or refractory IDH2- mutated AML after at least 2 prior induction attempts.

Day 30 discussion

Oncology

3.1.40. Entospletinib - EMEA-002058-PIP01-16

Treatment of Acute myeloid leukemia / Treatment of Acute myeloid leukemia

Day 30 discussion

Oncology

3.1.41. EMEA-002072-PIP01-16

Treatment of melanoma / Melanoma >12years - <18 years

Day 30 discussion

Oncology

3.1.42. Ramucirumab - EMEA-002074-PIP01-16

Treatment of soft tissue sarcoma, Treatment of intestinal malignant neoplasm, Treatment of gastric cancer and gastro-oesophageal junction adenocarcinoma, Treatment of liver cancer, Treatment of urinary tract malignant neoplasm, Treatment of lung malignant neoplasm / , Treatment of synovial sarcoma and / or desmoplastic small round cell tumour

Day 30 discussion

Oncology

3.1.43. ruxolitinib phosphate - EMEA-002056-PIP01-16

acute graft versus host disease / Steroid refractory (SR) acute (a) Graft vs Host Disease (GvHD) after allogeneic hematopoietic stem cell transplantation (alloSCT)

Day 30 discussion

Oncology

3.1.44. Vadastuximab Talirine - Orphan - EMEA-002013-PIP01-16

Seattle Genetics UK, Limited; Treatment of Acute Myeloid Leukaemia / Treatment of relapsed or refractory AML

Day 30 discussion

Oncology

3.1.45. Angiotensin II - EMEA-001912-PIP02-16

Catecholamine-resistant hypotension associated with distributive shock

Day 30 discussion

Other

3.1.46. Ketamine hydrochloride / Sufentanil citrate - EMEA-001739-PIP02-16

ICD10: R52 Pain, unspecified

Day 30 discussion

Pain

3.1.47. Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1) - EMEA-002068-PIP01-16

Influenza / Prevention of influenza

Day 30 discussion

Vaccines

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. fluticasone furoate / triphenylacetic acid - 4-{(1R)-2-[(6-{2-[(2,6-dichlorobenzyl)oxy]ethoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol - EMEA-C3-000431-PIP01-08-M09

Glaxo Group Limited; Treatment of asthma

Day 30 opinion

Pneumology - Allergology

Summary of committee discussion:

Completed studies were checked for compliance.
The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0276/2016) of 10 October 2016.
The PDCO finalised on 27 January 2017 this partially completed compliance procedure.

3.2.2. Bictegravir / Tenofovir alafenamide / emtricitabine - EMEA-C1-001766-PIP01-15-M01 – adopted at D30

Gilead Sciences International Ltd.; Treatment of human immunodeficiency virus (HIV-1) infection

Day 30 opinion

Infectious Diseases

Summary of committee discussion:

The completed study was checked for compliance.

The PDCO discussed the completed study and considered that it is compliant with the latest Agency's Decision (P/0339/2016) of 02 December 2016.
The PDCO finalised on 27 January 2017 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.

3.2.3. recombinant human beta-glucuronidase - EMEA-C1-001540-PIP01-13-M01 – adopted at D30

Ultragenyx Germany GmbH; Treatment of Mucopolysaccharidosis type 7 (MPS 7)

Day 30 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0202/2016) of 28 July 2016. The PDCO also confirmed compliance for the initiation of studies.
The PDCO finalised on 27 January 2017 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.

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Evolocumab - EMEA-001268-PIP01-12-M04

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. Trifarotene - EMEA-001492-PIP01-13-M01

GALDERMA R&D; L70.0 Acne vulgaris / Treatment of acne vulgaris

Day 30 discussion

Dermatology

3.3.3. Recombinant human N-acetylglucosaminidase (rhNAGLU) - Orphan - EMEA-001653-PIP01-14-M02

Alexion Europe SAS; Mucopolysaccharidosis IIIB (Sanfilippo B) / Treatment of Mucopolysaccharidosis IIIB (Sanfilippo B)

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.4. ferric maltol - EMEA-001195-PIP01-11-M02

Shield TX (UK) Limited; Iron deficiency anaemia / Treatment for iron deficiency anaemia (IDA)

Day 30 discussion

Haematology-Hemostaseology

3.3.5. ustekinumab - EMEA-000311-PIP03-11-M02

Janssen-Cilag International NV; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, spondyloarthritis, PsA and juvenile idiopathic arthritis [JIA]) / Treatment of juvenile idiopathic arthritis (jPsA and ERA)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.6. rituximab - EMEA-000308-PIP01-08-M03

Roche Registration Limited; Treatment of diffuse large B-cell lymphoma, Treatment of autoimmune arthritis / Treatment of mature B-cell malignancies, that is, diffuse large B-cell lymphoma, Burkitt and Burkitt-like lymphoma/leukaemia., Agreed waiver for all subsets of the paediatric population from birth to less than 18 years of age.

Day 30 discussion

Immunology-Rheumatology-Transplantation / Oncology

3.3.7. letermovir - Orphan - EMEA-001631-PIP01-14-M02

Merck Sharp & Dohme (Europe), Inc.; Prevention of cytomegalovirus infection / Prevention of CMV viremia and/or disease in at-risk patients having undergone an allogeneic HSCT or SOT

Day 30 discussion

Infectious Diseases

3.3.8. Oseltamivir phosphate - EMEA-000365-PIP01-08-M08

Roche Registration Limited; Treatment and prevention of influenza / Treatment and prevention of influenza in healthy and immunocompromised patients from 0 to less than 18 years of age.

Day 30 discussion

Infectious Diseases

3.3.9. posaconazole - EMEA-000468-PIP02-12-M03

Merck Sharp & Dohme (Europe), Inc.; Prevention of invasive fungal infections, Treatment of invasive fungal infections / For treatment of invasive fungal infections in the following paediatric patients: -Invasive aspergillosis in patients with disease that is refractroy to amphotericin B or itraconazole or in patients who are intolerant of these medicinal products;, Treatment of invasive aspergillosis, -Patients receiving remission-induction chemotherapy for acute myelogenous leukemia (AML) or myelodysplastic syndromes (MDS) expected to result in prolonged neutropenia and who are at high risk of developing invasive fungal infections; - Hematopoietic stem cell transplant (HSCT) recipients who are undergoing high-dose immunosuppressive therapy for graft versus host disease and who are at high risk of developing invasive fungal infections.

Day 30 discussion

Infectious Diseases

3.3.10. telaprevir - EMEA-000196-PIP01-08-M04

Janssen-Cilag International NV; Chronic viral hepatitis C

Day 30 discussion

Infectious Diseases

3.3.11. Oritavancin diphosphate - EMEA-001270-PIP01-12-M01

The Medicines Company; Treatment of acute bacterial skin and skin structure infections

Day 30 discussion

Infectious Diseases / Dermatology

3.3.12. Bivalent anti-human myostatin adnectin recombinant human IgG1-Fc fusion protein - EMEA-001793-PIP01-15-M01

Bristol-Myers Squibb International Corporation; Treatment of Duchenne Muscular Dystrophy / Treatment of Duchenne Muscular Dystrophy in patients from 2 to less than 18 years of age

Day 30 discussion

Neurology

3.3.13. Siponimod hemifumarate - EMEA-000716-PIP01-09-M02

Novartis Europharm Limited; Multiple Sclerosis / Treatment of children/adolescent patients (10-18 years old) with relapsing forms of multiple sclerosis

Day 30 discussion

Neurology

3.3.14. HSV-1/ICP34.5-/ICP47-/hGM-CSF - EMEA-001251-PIP01-11-M03

Amgen Europe B.V.; Treatment of solid malignant non-CNS tumours

Day 30 discussion

Oncology

3.3.15. ibrutinib - Orphan - EMEA-001397-PIP03-14-M02

Janssen-Cilag International N.V.; Treatment of mature B-cell neoplasm / Treatment of children from 1 year to less than 18 years of age with newly-diagnosed and relapsed/refractory mature B-cell lymphoma, that is, diffuse large B-cell lymphoma or Burkitt and Burkitt-like lymphoma.

Day 30 discussion

Oncology

3.3.16. Lenvatinib - Orphan - EMEA-001119-PIP02-12-M03

Eisai Europe Ltd; Treatment of papillary thyroid carcinoma, Treatment of Osteosarcoma, Treatment of follicular thyroid carcinoma / Treatment of refractory or relapsed osteosarcoma in children and adolescents, Treatment of progressive, radioiodine-refractory differentiated thyroid cancer in children and adolescents

Day 30 discussion

Oncology

3.3.17. Regorafenib - EMEA-001178-PIP01-11-M03

Bayer Pharma; Treatment of all conditions contained in the category of malignant neoplasms (except haematopoietic and lymphoid tissue) / Treatment of paediatric patients with a solid malignant tumour(s) integrated with anti-cancer therapy

Day 30 discussion

Oncology

3.3.18. Eliglustat - Orphan - EMEA-000461-PIP02-11-M02

Genzyme Europe B.V.; Treatment of Gaucher disease Type 1 and Type 3 / Treatment of

Gaucher disease Type 3, Treatment of Gaucher disease Type 1

Day 30 discussion

Other

3.3.19. ivacaftor / lumacaftor - EMEA-001582-PIP01-13-M05

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

Day 30 discussion

Other

3.3.20. Dermatophagoides pteronyssinus/ Dermatophagoides farinae (50%/50%) - EMEA-001258-PIP01-11-M02

ALK-Abelló A/S; Treatment of allergic rhinitis, Treatment of asthma / allergic rhinitis, allergic asthma

Day 30 discussion

Pneumology - Allergology

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 21 March 2017 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. Nominations of external experts (paediatric neurologists) for ad hoc expert group meeting for Cerliponase Alfa

Summary of committee discussion:

The PDCO was asked for nomination of external experts (paediatric neurologists) to attend the ad-hoc expert group meeting, to provide clinical expertise.

4.3.2. Participation of PDCO member, Sylvie Benchetrit, at 'Research Roundtable for Epilepsy' to be held on March 2-3, 2017 in Washington

Summary of committee discussion:

The PDCO member Dr Benchetrit was mandated to represent PDCO at the meeting 'Research Roundtable for Epilepsy' to be held in March 2017 in Washington D.C. (USA).

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. Lorlatinib - EMEA-38-2016

Pfizer Limited; Treatment of lung carcinoma (small cell and non-small cell carcinoma)/

treatment of adult patients with advanced or metastatic ALK-positive NSCLC resistant or refractory to one or more prior ALK inhibitor therapies

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 indication was confirmed.

Other potential paediatric interests of this medicine suggested by PDCO: paediatric ALK-driven diseases such as anaplastic large cell lymphoma, neuroblastoma and inflammatory myofibroblastic tumour.

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. Beta-secretase inhibitor - EMEA-39-2016

All classes of medicinal products for treatment of Alzheimer's disease/ slowing of cognitive

decline in asymptomatic individuals at risk for Alzheimer's dementia

Summary of committee discussion:

The applicability of the class waiver as referred to in the Agency's Decision CW/0001/2015 to the planned therapeutic indication was confirmed.

Other potential paediatric interests of this medicine suggested by PDCO: none currently identified.

6.1.3. Pan- fibroblast growth factor receptor inhibitor - EMEA-40-2016

Treatment of ureter and bladder carcinoma/ treatment of FGFR positive locally advanced inoperable or metastatic urothelial bladder cancer patients following platinum based chemotherapy

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 indication was confirmed.

Other potential paediatric interests of this medicine suggested by PDCO: paediatric tumours whose cell growth, survival and migration is sustained by fibroblast growth factors and where patients can be identified by either FGFR-1, -2 -3 or -4 mRNA overexpression

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.

6.1.4. Phosphoinositide 3-kinase delta inhibitor - EMEA-41-2016

All classes of medicinal products for treatment of 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)/ Treatment of COPD exacerbations

Summary of committee discussion:

The applicability of the class waiver as referred to in the Agency's Decision CW/0001/2015 to the planned therapeutic indication was confirmed.

Other potential paediatric interests of this medicine suggested by PDCO: asthma and activated PI3 kinase delta syndrome.

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

7.1.1. baricitinib - EMEA-001220-PIP01-11-M01

Eli Lilly & Company Limited; Treatment of adult patients with psoriatic arthritis (PsA), Treatment of adult patients with ankylosing spondyloarthritis (AxSPA)/Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis)

Summary of committee discussion:

The PDCO agreed that the proposed indications are considered by the condition listed in the Agency Decision P/0192/2016.

8. Annual reports on deferrals

Note: The annual reports on deferrals to be noted by the members of the PDCO are flagged in the Annex B.

9. Organisational, regulatory and methodological matters

9.1. Mandate and organisation of the PDCO

None

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 presented the list of procedures with paediatric relevance starting at the CHMP in December 2016.

The members were also informed about 4 medicinal products, Cinryze, Ilaris, Tivicay, and Votubia for which the CHMP adopted a positive opinion recommending paediatric indication during their meeting in December 2016. For Tivicay two new strengths appropriate for paediatric use (10 mg and 25 mg tablets) were approved to support the extension of indication.

9.2.2. Report of the PDCO/PRAC joint Working Group

PDCO members: Dirk Mentzer; Sylvie Benchetrit

Summary of committee discussion:

EMA presented at the PDCO the outcome of the Joint meeting of the PDCO/PRAC working group held on 2 December 2016. Further strengthening of the co-operation between PRAC and PDCO was supported as a way to transfer important information of mutually assessed medicines. The outcome of the meeting will support some revisions of the draft GVP on special population V paediatric population that will be then finally discussed at the strategic review and learning meeting in Malta in April 2017. The PRAC will be presented with the report of the meeting too in February 2017.

9.2.3. Real world evidence data sources

Summary of committee discussion:

EMA presented an overview of a landscaping exercise being conducted by the EMA to fully characterise EU wide datasets and EU funded initiatives which may provide access to real world data or to methodologies by which to analyse it. The presentation highlighted the key importance of identifying sources of data relevant to paediatric prescribing but also highlighted the lack of data currently from secondary care. It also described some case studies illustrating examples where RWD had already contributed to medicines decision making and some of the key challenges in its use. The committee welcomed the presentation and commented of the value especially in the area of modelling and extrapolation. They looked forward to seeing further outputs of the work.

9.2.4. PDCO response to CHMP regarding the proposal for paediatric information for vancomycin medicinal products SmPC

PDCO member: Maria Fernandez Cortizo

Summary of committee discussion:

The PDCO discussed the drafted response including comments from PDCO members. A post-meeting update will be provided and the final version adopted via written procedure.

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 Non-clinical Working Group identified the products which will require Non-clinical Working Group evaluation and discussion.

9.3.2. Formulation Working Group

PDCO member: Brian Aylward

Summary of Committee discussion:

The chair of the Formulation Working Group identified the products which will require Formulation Working Group evaluation and discussion.

9.3.3. Minutes of the PCWP/HCPWP joint meeting – 20 September 2016

Summary of Committee discussion:

Document tabled for information

9.3.4. Extrapolation – Progress Update

PDCO member: Ine Rusten

Summary of committee discussion:

PDCO was informed that the extrapolation working group will review some products for learning and training purposes. The TCs will take place the week before PDCO and will be attended by experts from relevant disciplines and Committees. The first case was discussed in January 2017. The system to refer and handle cases is being set up. PDCO will be informed once the group is fully operational.

9.4. Cooperation within the EU regulatory network

9.4.1. European Network of Paediatric Research (Enpr) – at European Medicines Agency (Enpr-EMA): Presentation of PRINTO by Nicolino Ruperto

Summary of committee discussion:

The coordinator of the paediatric rheumatology network PRINTO was invited to present PRINTO's activities to PDCO and discuss the network's experience and involvement in paediatric studies agreed in a PIP. The need for early interaction of academia with applicants was stressed to provide input to the PIP preparation, study protocol and eventually identification of sites and conduct of the clinical studies. While PRINTO over the past decades since its establishment has succeeded in increasingly early interactions with industry, there is still a high need to improve and increase dialogue with regulators, in particular with PDCO to discuss important aspects of paediatric drug development, such as paediatric needs, study design, standard of care, etc. based on evolving knowledge and evidence. The committee supports increased interactions with academia and networks and suggested to use collaboration through Enpr-EMA.

9.4.2. Update on EDQM PaedForm project

PDCO Member: Siri Wang

Summary of committee discussion:

The Committee nominated Siri Wang as PDCO observer for the Paediatric Formulary project.

9.5. Cooperation with International Regulators

9.5.1. PDCO response to public consultation on ICH S9 Questions and answers

PDCO Members: Jacqueline Carleer, Jaroslav Sterba

Summary of committee discussion:

The PDCO adopted a comment to the draft ICH S9 Questions and answers.

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

None

9.7. PDCO work plan

9.7.1. PDCO Work-plan 2017

Summary of committee discussion:

The PDCO adopted the PDCO Work plan 2017.

9.8. Planning and reporting

9.8.1. Strategic Review and Learning Meeting (SRLM) to be held in Tallinn on 4-6 October 2017

PDCO member: Jana Lass

Summary of committee discussion:

PDCO members were informed of the next SRLM to be held in Tallinn on 4-6 October 2017. Agenda to follow.

10. Any other business

10.1.1. PEGylated products

PDCO member: Dirk Mentzer

Summary of committee discussion:

The polyethylene glycols (PEGs) have been increasingly used over the past decade as a chemical modifier of biopharmaceuticals to prolong their half-life (predominantly by

decreasing its renal clearance) and allow for reduced administration frequency.

Repeated parenteral administration of PEGylated proteins to animals has in some cases been associated with cellular vacuolation in macrophages and/or histiocytes in various organs and in renal tubular cells. Also, cases of cellular vacuolation of the choroid plexus epithelial cells have been observed in repeat-dose toxicity studies in animals (i.e. especially those conducted with proteins PEGylated with molecules $\geqslant$ 40 kDa). Many of the PEGylated medicinal products currently undergoing development are intended also for children (all ages) for repeated use where CNS development is still ongoing.

Considering the animal data, a preliminary attempt has been made by the regulators to estimate dose-based safety margins for choroid plexus epithelial cell vacuolation (i.e. considering the NOEL) for some pegylated products (incl authorized products as well as those still under development). For several of these products the safety margin appears to be below 10 fold. This raises concerns especially when considering the continuous increase in vacuole formation in these cells due to PEG accumulation over time and the fact that these products are intended for long term use in chronic diseases.

There are still several knowledge gaps as regards the mechanism and kinetics of PEG accumulation/elimination from choroid plexus epithelial cells, i.e. it is not clear when (or if at all) a steady state of PEG load can be achieved in these cells (turnover of these cells is about 2-3 years). Pre-clinical studies have only demonstrated partial reversibility of vacuolation associated with PEG accumulation (i.e. following a 1 year treatment free period in the juvenile monkey). Furthermore, a higher incidence/sensitivity of choroid plexus epithelial cell vacuolation in juvenile animals compared to adult animals cannot be excluded currently.

For the time being, uncertainty over potential long term sequelae of choroid plexus epithelial cell vacuolation remains with long term use of pegylated products in children. Furthermore, clinical safety monitoring of potential vacuole formation in the choroid plexus epithelial cells seems not to be possible.

Therefore, the PDCO questions the significant therapeutic benefit and long term safety in the paediatric population for several pegylated products; i.e. especially those with PEG moieties of at least 20-40kDa, intended for long term use, where authorised alternative therapies are available. The PDCO will have a further look into those Paediatric Investigation Plans (PIPs) that still have planned/ongoing paediatric developments agreed and then decide on next potential regulatory steps based on the available scientific evidence.

10.1.2. Possible actions and initiatives – lessons learned on the Paediatric Regulation

Summary of committee discussion:

The Committee discussed a draft list, elaborated by a PDCO panel together with EMA staff, of possible actions that could be considered for implementation, to address the lessons learned after 10 years of the Paediatric Regulation (as published in the EC website). Of these, some could be undertaken within the current legal and regulatory framework, while others would require amendment of existing EU legislation, or action at the level of the member states. The discussion will be continued at the next meeting.

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

The participants discussed the comment to S9 Questions and answers to be adopted, the forthcoming multistakeholder strategy forum meeting and the addendum on paediatric oncology.

11.1.2. Neonatology

Summary of committee discussion:

Participants discussed dosing recommendations for vancomycin for preterm and term neonates as well as organisational issues.

11.1.3. Inventory

Summary of committee discussion:

Participants discussed different sources of data to draft an inventory list in the area of ophthalmology. This would serve the purpose of a pilot phase using a new methodology to draft future inventories.

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 24 – 27 January 2017 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	
Koenraad Norga	Member (Vice-Chair)	Belgium	When chairing the meeting: To be replaced for discussions, final deliberations and voting on:	EMEA-C-000673-PIP01-09-M09 EMEA-000069-PIP02-10-M07 EMEA-001882-PIP02-16 EMEA-C3-000431-PIP01-08-M09 EMEA-41-2016
Jacqueline Carleer	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Adriana Andrić	Member	Croatia	No interests declared	
Suzana Mimica Matanovic	Alternate	Croatia	No participation in discussion, final deliberations and voting on:	EMEA-001918-PIP01-15 EMEA-C3-000309-PIP01-08-M07 EMEA-001425-PIP01-13-M02 EMEA-000365-PIP01-08-M08 EMEA-001053-PIP03-16 EMEA-002070-PIP01-16 EMEA-000308-PIP01-08-M03
Georgios Savva	Member	Cyprus	No interests declared	
Jaroslav Sterba	Member	Czech Republic	No interests declared	
Marianne Orholm	Member	Denmark	No interests declared	
Marta Granström	Alternate (via teleconference)	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	
Sabine Scherer	Member	Germany	No interests declared	
Immanuel Barth	Alternate	Germany	No interests declared	
Eleni Katsomiti	Member	Greece	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ágnes Gyurasics	Member (CHMP member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	
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	
Maaike van Dartel	Member	Netherlands	No interests declared	
Siri Wang	Member	Norway	No interests declared	
Ine Skottheim Rusten	Alternate	Norway	No interests declared	
Marek Migdal	Member	Poland	No interests declared	
Helena Fonseca	Member	Portugal	No interests declared	
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	
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 final deliberations and voting on: No participation in discussion, final deliberations and voting on:	EMEA-001425-PIP01-13-M02 EMEA-000461-PIP02-11-M02 EMEA-001945-PIP01-16
Jorrit Gerritsen	Alternate	Healthcare Professionals' Representative	No interests declared	
Antje Neubert	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Doina Plesca	Alternate	Healthcare Professionals' Representative	No participation in discussion, final deliberations and voting on:	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Paola Baiardi	Alternate	Patients' Organisation Representative	No participation in final deliberations and voting on:	EMEA-C-000673-PIP01-09-M09 EMEA-000069-PIP02-10-M07 EMEA-001882-PIP02-16 EMEA-C3-000431-PIP01-08-M09 EMEA-41-2016
Tsvetana Schyns-Liharska	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Shiva Ramroop	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Nicolino Ruperto	Expert Witness - in person*	EnprEMA	No restrictions applicable to this meeting	
Bart Van der Schueren	Expert - in person*	Belgium	No interests declared	
Pierre Demolis	Expert - via teleconference*	France	No interests declared	
Catriona Elizabeth Baker	Expert - in person*	United Kingdom	No interests declared	
Nele Berthels	Expert - via teleconference*	Belgium	No interests declared	
Gerard Pons	Expert - via teleconference*	France	No interests declared	
Juliana Min	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Meeting run with support from relevant EMA staff				

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

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/