20 May 2022
EMA/PDCO/247621/2022
Human Medicines Division

Paediatric Committee (PDCO)

Minutes for the meeting on 19-22 April 2022

Chair: Koenraad Norga – Vice-Chair: Sabine Scherer

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.

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

The Chairperson opened the meeting by welcoming all participants. Due to the current coronavirus (COVID-19) outbreak, and the associated EMA Business Continuity Plan (BCP), the meeting was held remotely.

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. 17 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 for 19-22 April 2022 meeting was adopted.

1.3. Adoption of the minutes

The minutes for 22-25 March 2022 meeting were adopted and will be published on the EMA website.

2. Opinions

Some information related to this section cannot be disclosed at the present time as it is deemed to contain commercially confidential information.

2.1. Opinions on Products

2.1.1. Dersimelagon - EMEA-002850-PIP02-21

Mitsubishi Tanabe Pharma GmbH; Treatment of X-linked protoporphyria / Treatment of

erythropoietic protoporphyria

Day 120 opinion

Dermatology

Summary of Committee discussion:

In the written response, the applicant addressed the remaining issues raised by the Committee. Based on the assessment of this application and the additional information provided by the applicant and additional changes implemented in the opinion, a positive opinion for the PIP for the proposed medicine for the age subset from 1 year to less than 18 years of age in the conditions of treatment of erythropoietic protoporphyria and treatment of X-linked protoporphyria was adopted. The PDCO agreed on a waiver in a subset of children on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2.1.2. Humanised KLB/FGFR1c monoclonal antibody (MK-3655) - EMEA-003058-PIP01-21

Merck Sharp & Dohme (Europe), Inc.; Treatment of non-alcoholic steatohepatitis

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion was adopted for the PIP for the proposed medicine for adolescents from age at attaining 98% of growth based on bone age to less than 18 years of age, in the condition treatment non-alcoholic steatohepatitis. The PDCO agreed on a waiver in a subset of children from birth to age prior to attaining 98% of growth based on bone age on the grounds that the specific medicinal product is likely to be unsafe. The PDCO granted a deferral for the completion of this PIP.

2.1.3. Apraglutide - Orphan - EMEA-003016-PIP01-21

VectivBio AG; Treatment of short bowel syndrome

Day 120 opinion

Gastroenterology-Hepatology

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion was adopted for the PIP for the proposed medicine for children and adolescents from 4 months to less than 18 years of age, in the condition treatment of short bowel syndrome. The PDCO agreed on a waiver in a subset of children from birth to less than 4 months of age on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients. The PDCO granted a deferral for the completion of this PIP.

2.1.4. Recombinant adeno-associated viral (rAAV) vector expressing the human ornithine transcarbamylase (hOTC) gene - EMEA-002983-PIP01-21

Selecta Biosciences, Inc.; Treatment of ornithine transcarbamylase deficiency

Day 120 opinion

Gastroenterology-Hepatology

Summary of Committee discussion:

In the written response, the applicant addressed the remaining issues raised by the Committee. Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the PIP for the proposed medicine for the age subset from 6 months to less than 18 years of age in the condition of treatment of ornithine transcarbamylase deficiency was adopted. The PDCO agreed on a waiver in a subset of children on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2.1.5. Sirolimus - EMEA-002982-PIP01-21

Selecta Biosciences, Inc.; Treatment of ornithine transcarbamylase deficiency

Day 120 opinion

Gastroenterology-Hepatology

Summary of Committee discussion:

In the written response, the applicant addressed the remaining issues raised by the Committee. Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the PIP for the proposed medicine for the age subset from 6 months to less than 18 years of age in the condition of treatment of ornithine transcarbamylase deficiency was adopted. The PDCO agreed on a waiver in a subset of children on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2.1.6. Haematopoietic stem cells and blood progenitors umbilical cord-derived expanded with (1R,4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexane-1,4-diamine dihydrobromide dihydrate (ECT-001-CB) - Orphan - EMEA-003025-PIP02-21

ExCellThera; Allogeneic haematopoietic stem cell transplantation

Day 120 opinion

Immunology-Rheumatology-Transplantation / Oncology / Haematology-Hemostaseology

Note: Withdrawal request received on 2 April 2022

2.1.7. Reparixin - Orphan - EMEA-001693-PIP03-21

Dompé farmaceutici S.p.A.; Treatment of coronavirus disease 2019 (COVID-19)

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 agreed a PIP for reparixin in treatment of coronavirus disease 2019 (COVID-19) with a deferral.
The PIP includes two quality studies a single arm-clinical study, two modelling and simulation studies and an extrapolation study. The clinical study initiation is to be agreed with PDCO after completion of safety and efficacy studies in adults.

2.1.8. Omaveloxolone - Orphan - EMEA-002487-PIP01-18

Reata Ireland Limited; Treatment of Friedreich's ataxia

Day 120 opinion

Neurology

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the PIP for the proposed medicine for patients from 2 to less than 18 years of age in the condition of treatment of Friedreich's ataxia was adopted. The PDCO agreed on a waiver in a subset of children from birth to less than 2 years of age on the ground that the product cannot be expected to be of significant therapeutic benefit. The PDCO granted a deferral for the completion of this PIP.

2.1.9. Cedazuridine / decitabine / decitabine: 4-amino-1-[(2R,4S,5R)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,3,5-triazin-2(1H)-one - Orphan - EMEA-003071-PIP01-21

Otsuka Pharmaceutical Netherlands B.V.; Treatment of acute myeloid leukaemia

Day 120 opinion

Oncology / Haematology-Hemostaseology

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the PIP for the proposed medicine for reduction of measurable residual disease (MRD) in patients with high-risk de novo acute myeloid leukaemia (AML), therapy-related AML, or relapsed or refractory AML who have minimal residual disease (MRD) positivity after standard induction therapy and who will receive a myeloablative, allogeneic hematopoietic stem cell transplant (HSCT), in the condition of treatment of acute myeloid leukaemia was adopted. The PDCO agreed on a waiver in a subset of children from birth to less than 3 months of age on the grounds of lack of significant therapeutic benefit. The PDCO granted a deferral for the completion of this PIP.

2.1.10. Whole-cell heat-inactivated bacterial strains of *Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris* and *Enterococcus faecalis* - EMEA-003026-PIP02-21

Inmunotek S.L.; Prevention of urinary tract infections

Day 120 opinion

Vaccines / Infectious Diseases / Uro-nephrology

Summary of Committee discussion:

Based on the assessment of this application, the PDCO agreed with the applicant's request of a PIP for whole-cell heat-inactivated bacterial strains of *Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris* and *Enterococcus faecalis* with a deferral and a waiver for the paediatric population from birth to less than 4 years of age in the condition of prevention of urinary tract infections on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2.1.11. Indapamide / perindopril arginine - EMEA-003186-PIP01-22

Les Laboratoires Servier; Treatment of hypertension

Day 60 opinion

Cardiovascular Diseases

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for perindopril arginine and indapamide for all subsets of the paediatric population (0 to 18 years of age) for the condition of treatment of hypertension on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.
The PDCO emphasised 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.

2.1.12. Flortaucipir F18 - EMEA-003187-PIP01-22

Eli Lilly and Co. Ltd.; Diagnosis of Alzheimer's disease

Day 60 opinion

Neurology

Summary of Committee discussion:

At the April 2022 plenary the PDCO discussed the application for a product-specific full waiver for Flortaucipir (18F) in the diagnosis of Alzheimer’s disease.
The PDCO took into consideration the clarifications provided by the applicant between D30 and D60. Based on the assessment of this application, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for Flortaucipir F18 for all subsets of the paediatric population (from birth to 18 years of age) in the condition of

diagnosis of Alzheimer's disease. The PDCO recommended to extend the waiver to all pharmaceutical forms and all routes of administration to which the applicant agreed.
The PDCO emphasised 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.

2.1.13. Anti-TGFbeta fully human monoclonal antibody - EMEA-003178-PIP01-21

Novartis Europharm Limited; Treatment of pancreatic cancer

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed at Day 60, during the April 2022 plenary meeting, an application for a product specific waiver for anti-TGFbeta fully human monoclonal antibody (NIS793), for the "treatment of metastatic pancreatic ductal adenocarcinoma" on the grounds that the disease does not occur in the paediatric population.
The PDCO took into consideration the information the applicant provided between Day 30 and Day 60 on the availability of paediatric patients with pancreatic cancer and confirmed all conclusions reached at Day 30.
The Committee adopted a positive opinion at Day 60 on a product specific waiver for this product for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of "treatment of pancreatic cancer" on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adult populations.
The applicant agreed for the waiver to be extended to all pharmaceutical forms and all routes of administration.

2.1.14. Sugemalimab - EMEA-003179-PIP01-22

EQRx Inc.; Treatment of lung cancer

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed this application in line with the outcome conclusion from D30. Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for sugemalimab for all subsets of the paediatric population (birth to less than 18 years of age) in the condition of treatment of lung cancer. Since the agreed waiver ground is that the disease does not occur in the paediatric population, the possibility to apply this to all pharmaceutical forms and all routes of administrations was agreed to by the applicant.
The PDCO emphasised 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

2.2.1. Alirocumab - EMEA-C1-001169-PIP01-11-M05

sanofi-aventis recherche & développement; Treatment of elevated cholesterol

Day 60 letter

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/0550/2021) of 31 December 2021.

The PDCO finalised this partially completed compliance procedure on D60.

2.2.2. Elosulfase alfa - EMEA-C2-000973-PIP01-10-M03

BioMarin International Limited; Treatment of mucopolysaccharidosis, type IVA (Morquio A syndrome)

Day 60 letter

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

The PDCO re-discussed at Day 60, during the April 2022 plenary meeting, an application for a partial compliance check for elosulfase alfa, for the treatment of mucopolysaccharidosis, type IVA (Morquio A syndrome).
The PDCO discussed the completed studies of this partial compliance check and considered that they are compliant with the latest Agency's Decision (P/0055/2015) of 30 March 2015.

2.2.3. Lumacaftor / ivacaftor - EMEA-C6-001582-PIP01-13-M10

Vertex Pharmaceuticals (Ireland) Limited; Treatment of cystic fibrosis

Day 60 letter

Other

Summary of Committee discussion:

The PDCO discussed the completed Studies 16 and 2 (for the population from 1 year to less than 2 years of age) and considered that these are compliant with the latest Agency's Decision (P/0506/2020) of 22 December 2020.
The PDCO finalised this partially completed compliance procedure on Day 60.

2.2.4. Crisantapase - EMEA-C1-002934-PIP01-20

Jazz Pharmaceuticals Ireland Limited; Treatment of lymphoblastic lymphoma

Day 30 letter

Oncology

Summary of Committee discussion:

The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0453/2021) of 29 October 2021.
The PDCO finalised this partially completed compliance procedure on 22 April 2022.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Nemolizumab - EMEA-001624-PIP01-14-M05

Galderma International S.A.S; Treatment of atopic dermatitis

Day 60 opinion

Dermatology

Summary of Committee discussion:

Based on the responses submitted by the applicant 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/0545/2021 of 4 January 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.2. Canagliflozin (1s)-1,5-anhydro-1-[3-[[5-(4-fluorophenyl)-2-thienyl]methyl]-4-methylphenyl]-D-glucitol hemihydrate - EMEA-001030-PIP01-10-M10

Janssen-Cilag International NV; Treatment of type 2 diabetes mellitus

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, the PDCO considered that the proposed one of two 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/0268/2021 of 9 July 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.3. Aztreonam / avibactam - EMEA-002283-PIP01-17-M03

Pfizer Europe MA EEIG; Treatment of infections caused by aerobic gram-negative bacteria

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/0350/2021 of 8 September 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.4. Posaconazole - EMEA-000468-PIP02-12-M07

Merck Sharp & Dohme (Europe), Inc.; Treatment of invasive fungal infections / Prevention of invasive fungal 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, including the additional information provided after Day 30, 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/0101/2020 of 18 March 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.5. Efinaconazole - EMEA-001627-PIP01-14-M02

Almirall, S.A.; Treatment of onychomycosis

Day 60 opinion

Infectious Diseases / 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/0047/2015 of 6 March 2015).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.6. Dopamine hydrochloride - EMEA-001105-PIP01-10-M06

Brepco Biopharma Limited; Treatment of vascular hypotensive disorders

Day 60 opinion

Neonatology - Paediatric Intensive Care / 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. An unmet need was also acknowledged by the PDCO, specifically the need for a lower strength dopamine formulation suitable for the use in neonates.

The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0108/2018 of 11 April 2018).

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

2.3.7. Inebilizumab - Orphan - EMEA-001911-PIP01-15-M04

Horizon Therapeutics Ireland DAC; Treatment of neuromyelitis optica spectrum disorders

Day 60 opinion

Neurology

Summary of Committee discussion:

Based on the review of the rationale submitted by the applicant 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/0428/2020 of 28 October 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.8. Erdafitinib - EMEA-002042-PIP02-20-M01

Janssen-Cilag International N.V.; Treatment of all conditions included in the category of malignant neoplasms (except urothelial carcinoma, haematopoietic and lymphoid tissue neoplasms)

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, 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/0223/2021 of 8 June 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.9. Tisagenlecleucel - Orphan - EMEA-001654-PIP01-14-M04

Novartis Europharm Limited; Treatment of B cell acute lymphoblastic leukaemia/lymphoblastic lymphoma

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed at Day 60 during the April 2022 plenary meeting this request for modification for tisagenlecleucel for the treatment of B cell acute lymphoblastic leukaemia / lymphoblastic lymphoma.
Based on the review of the documentation submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be acceptable. Therefore, the PDCO adopted a positive opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0008/2019 of 3 January 2019).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.10. Zanubrutinib - EMEA-002354-PIP02-18-M01

BeiGene Ireland Ltd.; Treatment of mature B cell neoplasms (excluding lymphoplasmacytic lymphoma) / Treatment of lymphoplasmacytic lymphoma

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, 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/0398/2019 of 4 December 2019).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.11. Lanadelumab - Orphan - EMEA-001864-PIP01-15-M07

Takeda Pharmaceuticals International AG Ireland Branch; Prevention of hereditary angioedema attacks

Day 60 opinion

Other

Summary of Committee discussion:

Based on the review of the rationale submitted by the applicant 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/0264/2021 of 7 July 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.12. Sodium chloride solution 4.2% (w/v) / 3,5-diamino-6-chloro-N-(N-(4-(4-(2-(hexyl((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl)amino)ethoxy)phenyl)butyl)-carbamimidoyl)pyrazine-2-carboxamide - Orphan - EMEA-002935-PIP01-20-M01

Parion Sciences, Inc.; Treatment of primary ciliary dyskinesia (PCD)

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, and the clarification 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/0377/2021 of 2 September 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.13. Loxapine - EMEA-001115-PIP01-10-M08

Ferrer Internacional, S.A.; Treatment of schizophrenia / Treatment of bipolar disorder

Day 60 opinion

Psychiatry

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, including the new information submitted after Day 30, the PDCO considered that the proposed changes could be accepted. The Committee decided though to establish a deadline for the initiation date as well, in line with the applicant's plan.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0385/2019 of 4 December 2019).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.14. Mirabegron - EMEA-000597-PIP03-15-M05

Astellas Pharma Europe B.V.; Treatment of neurogenic detrusor overactivity

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, and additional information submitted by the applicant prior to Day 60, 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/0402/2021 of 1 October 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.15. Ravulizumab (ALXN1210) - Orphan - EMEA-001943-PIP01-16-M07

Alexion Europe SAS; Treatment of atypical haemolytic uremic syndrome

Day 60 opinion

Uro-nephrology

Summary of Committee discussion:

In the written response the applicant addressed the remaining issues raised by the Committee. 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/0474/2021 of 21 December 2021). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.16. Ravulizumab (ALXN1210) - Orphan - EMEA-002077-PIP01-16-M05

Alexion Europe SAS; Treatment of paroxysmal nocturnal haemoglobinuria

Day 60 opinion

Uro-nephrology

Summary of Committee discussion:

In the written response the applicant addressed the remaining issues raised by the Committee. 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/0239/2021 of 17 June 2021). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.17. Ravulizumab (ALXN1210) - EMEA-001943-PIP02-20-M01

Alexion Europe SAS; Treatment of patients with haematopoietic stem cell transplant associated thrombotic microangiopathy (HSCT-TMA)

Day 60 opinion

Uro-nephrology / Haematology-Hemostaseology

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/0474/2021 of 21 December 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.4. Opinions on Re-examinations

No item

2.5. Opinions on Review of Granted Waivers

No item

2.6. Finalisation and adoption of Opinions

No item

2.7. Partial Compliance Checks completed by EMA

The following partial compliance checks have been identified by the PME coordinator and PDCO rapporteur as not needing to be referred to the PDCO for discussion. The PDCO has been informed in writing.

2.7.1. Sparsentan - EMEA-C2-001984-PIP02-20

Travere Therapeutics Ireland Limited; Treatment of focal segmental glomerular sclerosis (FSGS)

Day 30 letter

Uro-nephrology

2.7.2. Avacopan - EMEA-C3-002023-PIP01-16-M05

ChemoCentryx Ireland Ltd.; Treatment of ANCA-associated vasculitis

Day 30 letter

Immunology-Rheumatology-Transplantation

2.7.3. Sparsentan - EMEA-C1-001984-PIP03-20

Travere Therapeutics Ireland Limited; Treatment of IgA nephropathy (IgAN)

Day 30 letter

Uro-nephrology

3. Discussion of applications

Some information related to this section cannot be disclosed at the present time as it is deemed to contain commercially confidential information.

3.1. Discussions on Products D90-D60-D30

3.1.1. Semaglutide / cagrilintide - EMEA-003059-PIP01-21

Treatment of obesity

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.2. EMEA-003090-PIP01-21

Treatment of hereditary angioedema

Day 90 discussion

Haematology-Hemostaseology

3.1.3. Bepirovirsen - EMEA-003082-PIP01-21

Treatment of chronic hepatitis B infection

Day 90 discussion

Infectious Diseases

3.1.4. Lonafarnib - Orphan - EMEA-002516-PIP02-21

EigerBio Europe Limited; Treatment of hepatitis D virus infection

Day 90 discussion

Infectious Diseases

3.1.5. Mixture of 2 synthetic double-stranded N-acetyl-galactosamine conjugated siRNA oligonucleotides that are directed against hepatitis B virus - EMEA-002694-PIP02-21

Treatment of chronic hepatitis D infection

Day 90 discussion

Infectious Diseases

3.1.6. Alprazolam - EMEA-003043-PIP01-21

Treatment of epileptic seizures

Day 90 discussion

Neurology

3.1.7. Cannabidiol - EMEA-001964-PIP03-21

Treatment of epilepsy with myoclonic atonic seizures

Day 90 discussion

Neurology

3.1.8. Autologous tumour-infiltrating lymphocytes (TILs) isolated from a patient's cancer tissue and expanded ex vivo - EMEA-003072-PIP01-21

Treatment of advanced melanoma

Day 90 discussion

Oncology

3.1.9. Rituximab / CD3+CD4+CD25+CD127-FoxP3+ regulatory T cells - EMEA-002737-PIP01-19

Treatment of type 1 diabetes mellitus (T1DM)

Day 90 discussion

Other / Endocrinology-Gynaecology-Fertility-Metabolism

3.1.10. Benralizumab - EMEA-001214-PIP09-21

Treatment of eosinophilic granulomatosis with polyangiitis (EGPA)

Day 90 discussion

Pneumology - Allergology

3.1.11. Sibeprenlimab - Orphan - EMEA-003085-PIP01-21

Otsuka Pharmaceutical Netherlands B.V.; Treatment of primary IgA nephropathy

Day 90 discussion

Uro-nephrology

3.1.12. Respiratory syncytial virus stabilised prefusion F subunit vaccine (RSVpreF) - EMEA-002795-PIP02-21

Prevention of RSV-associated lower respiratory tract illness / Prevention of lower respiratory tract disease caused by respiratory syncytial virus

Day 90 discussion

Vaccines

3.1.13. A 2'-MOE antisense oligonucleotide targeting apoC-III - EMEA-003177-PIP01-21

Treatment of familial chylomicronaemia syndrome / Treatment of severe and extreme hypertriglyceridaemia

Day 60 discussion

Cardiovascular Diseases

3.1.14. Treprostinil - EMEA-003182-PIP01-22

Treatment of pulmonary arterial hypertension

Day 60 discussion

Cardiovascular Diseases

3.1.15. Beremagene geperpavec - Orphan - EMEA-002472-PIP03-22

Krystal Biotech, Inc.; Treatment of dystrophic epidermolysis bullosa

Day 60 discussion

Dermatology

3.1.16. Lenzilumab - EMEA-003188-PIP01-22

Treatment of coronavirus disease 2019 (COVID-19)

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.17. Methylphenidate hydrochloride - EMEA-003189-PIP01-22

Treatment of attention-deficit hyperactivity disorder

Day 60 discussion

Neurology

3.1.18. Tolebrutinib - EMEA-002566-PIP02-22

Treatment of myasthenia gravis

Day 60 discussion

Neurology

3.1.19. Enzastaurin hydrochloride - EMEA-003096-PIP02-22

Treatment of vascular Ehlers-Danlos syndrome

Day 60 discussion

Other

3.1.20. Autologous bone marrow-derived mononuclear cell enriched white blood cells - EMEA-003193-PIP01-22

Chronic limb-threatening ischemia

Day 30 discussion

Cardiovascular Diseases

3.1.21. Botulinum toxin type E - EMEA-003190-PIP01-22

Treatment of muscle-induced wrinkles

Day 30 discussion

Dermatology

3.1.22. EMEA-003196-PIP01-22

Treatment of ulcerative colitis / Treatment of Crohn’s disease

Day 30 discussion

Gastroenterology-Hepatology

3.1.23. Derivative of 6-[2-(pyridin-2-yl)phenoxy]methyl}-1,2,3,4-tetrahydroisoquinoline - EMEA-003002-PIP02-22

Treatment of clinically significant portal hypertension (CSPH)

Day 30 discussion

Gastroenterology-Hepatology

3.1.24. 6-[(3S,4S)-4-methyl-1-(pyrimidin-2-ylmethyl)pyrrolidin-3-yl]-3-tetrahydropyran-4-yl-7H-imidazo[1,5-a]pyrazin-8-one - Orphan - EMEA-002991-PIP02-22

Imara Inc.; Treatment of sickle cell disease

Day 30 discussion

Haematology-Hemostaseology

3.1.25. Depemokimab - EMEA-003051-PIP05-22

Treatment of hypereosinophilic syndrome (HES)

Day 30 discussion

Haematology-Hemostaseology

3.1.26. Vidofludimus - EMEA-003195-PIP01-22

Treatment of multiple sclerosis

Day 30 discussion

Immunology-Rheumatology-Transplantation / Neurology

3.1.27. Clonidine - EMEA-003198-PIP01-22

Treatment of attention deficit hyperactivity disorder

Day 30 discussion

Neurology

3.1.28. Exenatide (acetate) - Orphan - EMEA-003183-PIP02-22

Invex Therapeutics Ltd; Treatment of idiopathic intracranial hypertension

Day 30 discussion

Neurology

3.1.29. Troriluzole - Orphan - EMEA-003084-PIP03-22

Biohaven Pharmaceutical Ireland DAC; Treatment of hereditary spinocerebellar ataxia

Day 30 discussion

Neurology

3.1.30. Infigratinib - Orphan - EMEA-002594-PIP04-22

Helsinn Birex Pharmaceuticals Ltd.; Treatment of paediatric low-grade gliomas (LGG)

Day 30 discussion

Oncology

3.1.31. Lurbinectedin - Orphan - EMEA-002846-PIP02-22

Pharma Mar, S.A.; Treatment of malignant mesothelioma

Day 30 discussion

Oncology

3.1.32. Parsaclisib (as hydrochloride) - Orphan - EMEA-002696-PIP03-22

Incyte Biosciences Distribution B.V.; Treatment of primary myelofibrosis (ICD-11: XH7GG7), including primary myelofibrosis and secondary myelofibrosis from previous polycythaemia vera (PV) or essential thrombocythaemia (ET) (post-polycythaemia vera myelofibrosis (PPV-MF) or post-essential thrombocythaemia myelofibrosis (PET-MF))

Day 30 discussion

Oncology

3.1.33. Peptide KLBPVQLWV / Peptide SMPPPGTRV / Peptide YLQLVFGIEV / Peptide RLLQETELV / Peptide YLSGADLNL / Peptide LLTFWNPPV / Peptide IMIGHLVGV / Peptide KVAEIVHFL / Peptide KVFGSLAFV / Pan HLA DR-binding epitope D-Ala-Lys-Cha-Val-Ala-Ala-Trp-Thr-Leu-Lys-Ala-Ala-D-Ala - EMEA-003181-PIP01-22

Treatment of lung cancer

Day 30 discussion

Oncology

3.1.34. Radium-224 adsorbed in calcium carbonate microparticles - EMEA-003199-PIP01-22

Treatment of peritoneal carcinomatosis

Day 30 discussion

Oncology

3.1.35. Trabectedin - Orphan - EMEA-000610-PIP02-22

Pharma Mar, S.A.; Treatment of leiomyosarcoma

Day 30 discussion

Oncology

3.1.36. Botulinum toxin type A - EMEA-003202-PIP01-22

Treatment of upper facial wrinkles

Day 30 discussion

Other

3.1.37. Efavaleukin alfa - EMEA-003156-PIP02-22

Treatment of ulcerative colitis

Day 30 discussion

Other

3.1.38. Depemokimab - EMEA-003051-PIP04-22

Treatment of eosinophilic granulomatosis with polyangiitis (EGPA)

Day 30 discussion

Pneumology - Allergology

3.1.39. Treprostinil palmitil - EMEA-003204-PIP01-22

Treatment of pulmonary hypertension associated with interstitial lung diseases (ILD-PH)

Day 30 discussion

Pneumology - Allergology

3.1.40. COVID-19 vaccine (recombinant, adjuvanted) - EMEA-003191-PIP01-22

Prevention of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Vaccines / Infectious Diseases

3.1.41. Stiripentol - Orphan - EMEA-003200-PIP01-22

Biocodex SA; Treatment of primary hyperoxaluria

Day 30 discussion

Uro-nephrology

3.2. Discussions on Compliance Check

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

3.2.1. Ritlecitinib - EMEA-C1-002451-PIP01-18

Pfizer Europe MA EEIG; Treatment of alopecia areata

Day 30 discussion

Dermatology

3.2.2. Pitolisant - EMEA-C-001176-PIP01-11-M06

BIOPROJET PHARMA; Treatment of narcolepsy

Day 30 discussion

Neurology

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Lebrikizumab - EMEA-002536-PIP01-18-M02

Eli Lilly and Company Limited; Treatment of atopic dermatitis

Day 30 discussion

Dermatology

3.3.2. Garadacimab - Orphan - EMEA-002726-PIP01-19-M02

CSL Behring GmbH; Treatment of hereditary angioedema attacks (HAE)

Day 30 discussion

Haematology-Hemostaseology

3.3.3. Vadadustat - EMEA-001944-PIP01-16-M04

Otsuka Pharmaceutical Development & Commercialisation Europe GmbH; Treatment of anaemia due to chronic disorders

Day 30 discussion

Haematology-Hemostaseology

3.3.4. Avacopan - Orphan - EMEA-002023-PIP01-16-M06

ChemoCentryx Ireland Ltd.; Treatment of anti-neutrophil cytoplasmic auto-antibody (ANCA)-associated vasculitis

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.5. Liposomal ciclosporin A (L-CsA) - Orphan - EMEA-002344-PIP02-18-M01

Zambon S.p.A.; Treatment of bronchiolitis obliterans syndrome (BOS)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.6. Oritavancin (diphosphate) - EMEA-001270-PIP01-12-M05

Menarini International Operations Luxembourg S.A.; Treatment of acute bacterial skin and skin structure infections

Day 30 discussion

Infectious Diseases

3.3.7. Remdesivir - EMEA-002826-PIP01-20-M03

Gilead Sciences International Ltd.; Treatment of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Infectious Diseases

3.3.8. Cannabidiol - Orphan - EMEA-001964-PIP01-16-M04

GW Pharma (International) B.V.; Treatment of infantile spasms / tuberous sclerosis complex / Dravet syndrome / Lennox Gastaut syndrome

Day 30 discussion

Neurology

3.3.9. Delandistrogene moxeparvovec - Orphan - EMEA-002677-PIP01-19-M02

Roche Registration GmbH; Treatment of Duchenne muscular dystrophy

Day 30 discussion

Neurology

3.3.10. Lacosamide - EMEA-000402-PIP03-17-M06

UCB Pharma S.A.; Treatment of generalized epilepsy and epilepsy syndromes

Day 30 discussion

Neurology

3.3.11. Daratumumab - Orphan - EMEA-002152-PIP01-17-M03

Janssen-Cilag International NV; Treatment of lymphoid malignancies (except mature B cell neoplasms)

Day 30 discussion

Oncology

3.3.12. Ixazomib - Orphan - EMEA-001410-PIP02-17-M04

Takeda Pharma A/S; Treatment of lymphoid malignancies (excluding multiple myeloma) / Treatment of multiple myeloma

Day 30 discussion

Oncology

3.3.13. Mometasone (furoate) / indacaterol (acetate) - EMEA-001217-PIP01-11-M08

Novartis Europharm Limited; Treatment of asthma

Day 30 discussion

Pneumology - Allergology

3.3.14. Dexmedetomidine (hydrochloride) - EMEA-002758-PIP01-19-M02

BioXcel Therapeutics, Inc.; Treatment of schizophrenia / Treatment of bipolar disorder

Day 30 discussion

Psychiatry

3.3.15. Daprodustat - EMEA-001452-PIP01-13-M04

GlaxoSmithKline Trading Services Limited; Treatment of anaemia associated with chronic kidney disease

Day 30 discussion

Uro-nephrology / Haematology-Hemostaseology

3.3.16. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - EMEA-002330-PIP01-18-M02

Pfizer Europe MA EEIG; Prevention of disease caused by *Streptococcus pneumoniae*

Day 30 discussion

Vaccines

3.3.17. Hepatitis B (rDNA) surface antigen adjuvanted - EMEA-001127-PIP02-11-M02

Dynavax GmbH; Prevention of hepatitis B virus infection

Day 30 discussion

Vaccines

3.3.18. *Neisseria meningitidis* serogroup W polysaccharide conjugated to tetanus toxoid / *Neisseria meningitidis* serogroup Y polysaccharide conjugated to tetanus toxoid / *Neisseria meningitidis* serogroup C polysaccharide conjugated to tetanus toxoid / *Neisseria meningitidis* serogroup A polysaccharide conjugated to tetanus toxoid - EMEA-001930-PIP01-16-M04

Sanofi Pasteur; Prevention of invasive meningococcal disease

Day 30 discussion

Vaccines

3.3.19. Nirsevimab - EMEA-001784-PIP01-15-M04

AstraZeneca AB; Prevention of lower respiratory tract infection caused by respiratory syncytial virus

Day 30 discussion

Vaccines

3.3.20. NVX-CoV2373 - EMEA-002941-PIP01-20-M02

Novavax CZ, a.s.; Prevention of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Vaccines

3.3.21. Split influenza virus, inactivated containing antigens equivalent to the B-like strain (Yamagata lineage) / Split influenza virus, inactivated containing antigens equivalent to the B-like strain (Victoria lineage) / Split influenza virus, inactivated containing antigens equivalent to the A/H3N2-like strain / Split influenza virus, inactivated containing antigens equivalent to the A/H1N1-like strain - EMEA-002359-PIP01-18-M05

Sanofi Pasteur; Prevention of influenza infection

Day 30 discussion

Vaccines

4. Nominations

Information related to this section cannot be disclosed at the present time as it is deemed to contain commercially confidential information.

4.1. List of submissions of applications with start of procedure 25 April 2022 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

Summary of Committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

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

Information related to this section cannot be disclosed at the present time as it is deemed to contain commercially confidential information.

5.1. New Scientific Advice

5.2. Final Scientific Advice (Reports and Scientific Advice letters)

No item

6. Discussion on the applicability of class waivers

6.1. Discussions on the applicability of class waiver for products

No item

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. Mavacamten (SAR439152/MYK-461) - EMEA-002231-PIP01-17

Bristol-Myers Squibb Pharma EEIG; Treatment of hypertrophic cardiomyopathy

Proposed PIP indication: nonobstructive hypertrophic cardiomyopathy

Action: For adoption

Summary of Committee discussion:

The PDCO reviewed the request during the plenary meeting held on 19-22 April 2022. The PDCO was of the view that the proposed indication "treatment of non-obstructive hypertrophic cardiomyopathy", falls under the scope of Decision P/0106/2019, as the indication is considered to be covered by the condition "treatment of hypertrophic cardiomyopathy" listed in the Agency Decision.

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 membership

The PDCO Committee noted the nomination of Louisa Braun Exner as the new alternate of Denmark.

The PDCO Committee noted that mandates for Croatia for Milivoj Novak (member) and Arnes Resic (alternate) have expired.

9.1.2. Vote by Proxy

No item

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 list of the CHMP procedures with paediatric indications starting in March 2022, was presented to the PDCO members.

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

9.3.1. Non-clinical Working Group: D30 Products identified

PDCO member: Karen van Malderen

Summary of Committee discussion:

The Chair of the Non-clinical Working Group (NcWG) identified the products which will require evaluation by the newly formed Non-clinical Working Party (NcWP). NcWP will replace NcWG in the future.

9.3.2. Formulation Working Group

PDCO member: Brian Aylward

Summary of Committee discussion:

The Chair of the Formulation Working Group (FWG) identified the products which will require FWG evaluation and discussion.

9.4. Cooperation within the EU regulatory network

9.4.1. European Network of Paediatric Research (Enpr) - European Medicines Agency (EMA)

No item

9.5. Cooperation with International Regulators

9.5.1. Report from the Paediatric Cluster Teleconference

No item

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

No item

9.7. PDCO work plan

No item

9.8. Planning and reporting

No item

10. Any other business

10.1. ALADDIN - Educational program on regulatory science in paediatric oncology

Summary of Committee discussion:

This item was postponed to the next PDCO meeting of May 2022.

10.2. COVID-19 update

Summary of Committee discussion:

The Committee was updated on clinical aspects of COVID-19 relevant to paediatrics.

10.3. Innovation Task Force (ITF) annual report 2021

Summary of Committee discussion:

The Regulatory Science and Innovation Task Force – Research and Innovation (TRS-RNI) presented 2021/2022 PDCO relevant stakeholder interactions on innovative developments and a trend analysis including:

- Patient-customised oligonucleotides for the treatment of patients with rare genetic mutations causing brain or eye diseases
- Real-world data collection infrastructure for natural history studies in genetic rare dilated cardiomyopathies
- New infection models to evaluate the impact of various pertussis vaccines on protection against colonisation.

The PDCO welcomed the update and acknowledged the relevance of the ITF platform. The next update is planned for 2023.

10.4. Marketing Authorisation Applications (MAAs) 3-year forecast report

Summary of Committee discussion:

The PDCO Committee was presented with a summary of the initial marketing authorisation applications expected to be submitted in the next 3 years (up to December 2024). The report highlighted key features of the pipeline and has annexed the full list of expected MAAs and listing of post authorisations submissions.

10.5. Paediatric addendum for antibacterial agents

PDCO member: Maria Fernandez Cortizo

Summary of Committee discussion:

The draft addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections to address paediatric-specific clinical data requirements was proposed for formal adoption by the PDCO. The draft guidance was agreed by the Infectious Disease Working Party (IDWP) in mid-2021, with the pandemic being the main reason justifying the delay in the proposal for adoption. The document needed to be adopted by the PDCO and by the CHMP. The Biological Health Threats and Vaccines Strategy and former member of the IDWP Secretariat attended the discussion and informed the PDCO that it will be proposed for adoption by the CHMP at the next PROM meeting in May 2022.

During the discussion which followed a short presentation by the rapporteur of the addendum (Maria Fernandez Cortizo), some members expressed concerns in relation to the extrapolation of safety, based on matching the systemic exposure of adult subjects, in particular when off-target effects are present and/or in case of new families of antibacterial agents. It was clarified that the wording of the addendum indicates that safety data may need to be generated in the paediatric population or in specific age subsets if there are emerging concerns from the available non-clinical and/or (e.g., adult) clinical data that are especially relevant to the paediatric population. The relevance of the non-clinical data (off-target effects) was highlighted and it was clarified that by no means the wording of the addendum in what refers to safety aspects (Section 7) was intended to suggest that juvenile studies should never be required.

Attending to the above, the PDCO formally adopted the paediatric addendum on antibacterial agents in its April 2022 meeting.

10.6. Complex clinical trials (CCT) Questions & Answers document

Summary of Committee discussion:

The PDCO received an update of the complex clinical trials Q&A, that was presented as a Joint European Commission-EMA-Head of Medicines Agencies (EC-EMA-HMA) document. The Q&A essentially integrates regulators' concerns across the trial lifecycle (before CTA and includes MA) and identifies what sponsors need to take into account for planning, conduct, using a CCT. It was highlighted that the Q&A is about evolving approaches and relies on limited experience of the network for MA. The clinical-methodological issues need collaboration with stakeholders to evaluate and mitigate the proposals.

PDCO members were invited to review and share any major comments on the draft by 28 April 2022 to Tomasz Grybek (representative of PDCO within the CTEG).

The CCT Q&A is under the remit of the CT EU Steering Group (EC, HMA, EMA) to adopt and publish the Q&A (in May 2022).

10.7. Reflection of extrapolation in PIP opinions

Summary of Committee discussion:

The PDCO Committee was informed about the recent publication of the extrapolation guidance document, which is in line with the framework of ICH E11A. The PDCO discussed adequate reflection of the use of extrapolation in the PIP opinions, taking into consideration the objective of the extrapolation plan.

11. Breakout sessions

11.1. Neonatology

Summary of Committee discussion:

Members discussed product related developments for neonates.

11.2. Paediatric oncology

Summary of Committee discussion:

Members were informed about upcoming paediatric oncology meetings.

11.3. Vaccines

Summary of Committee discussion:

The discussion was focussed on proposals and considerations on primary series, boosters, and variant COVID vaccines.

The Chair thanked all 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 19-22 April 2022.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Koenraad Norga	Chair	Belgium	No interests declared	
Karl-Heinz Huemer	Member	Austria	No interests declared	
Marleen Renard	Member	Belgium	No participation in discussion, final deliberations and voting on:	2.3.4. Posaconazole - EMEA-000468-PIP02-12-M07
Karen Van Malderen	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Zena Gunther	Member	Cyprus	No interests declared	
Tereza Bazantova	Alternate	Czechia	No interests declared	
Nanna Borup Johansen	Member	Denmark	No interests declared	
Louisa Braun Exner	Alternate	Denmark	No interests declared	
Irja Lutsar	Member	Estonia	No interests declared	
Jana Lass	Alternate	Estonia	No interests declared	
Pauliina Lehtolainen-Dalkilic	Member	Finland	No interests declared	
Anne Paavola	Alternate	Finland	No interests declared	
Sylvie Benchetrit	Member	France	No interests declared	
Dominique Ploin	Alternate	France	No interests declared	
Sabine Scherer	Member (Vice-Chair)	Germany	No interests declared	
Yuansheng Sun	Alternate	Germany	No interests declared	
Eleni Katsomiti	Member	Greece	No interests declared	
Ágnes Gyurasics	Member (CHMP alternate)	Hungary	No interests declared	
Robert Porszasz	Alternate (CHMP member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	
Sara Galluzzo	Member	Italy	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Dina Apele-Freimane	Member	Latvia	No participation in discussion, final deliberations and voting on:	3.3.19. Nirsevimab - EMEA-001784-PIP01-15-M04
Dovile Zacharkiene	Member	Lithuania	No interests declared	
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No restrictions applicable to this meeting	
Herbert Lenicker	Alternate	Malta	No interests declared	
Roderick Houwen	Member	Netherlands	No restrictions applicable to this meeting	
Maaike van Dartel	Alternate	Netherlands	No interests declared	
Siri Wang	Member	Norway	No interests declared	
Anette Solli Karlsen	Alternate	Norway	No interests declared	
Marek Migdal	Member	Poland	No restrictions applicable to this meeting	
Helena Fonseca	Member	Portugal	No interests declared	
Hugo Tavares	Alternate	Portugal	No interests declared	
Dana Gabriela Marin	Member (CHMP alternate)	Romania	No interests declared	
Peter Sisovsky	Member	Slovakia	No interests declared	
Peter Szitanyi	Alternate	Slovakia	No interests declared	
Stefan Grosek	Member	Slovenia	No interests declared	
Fernando de Andrés Trelles	Member	Spain	No interests declared	
Maria Jesus Fernández Cortizo	Alternate	Spain	No interests declared	
Eva Agurell	Member	Sweden	No interests declared	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Fernando Cabanas	Member	Healthcare Professionals' Representative	No participation in final deliberations and voting on:	3.3.19. Nirsevimab - EMEA-001784-PIP01-15-M04
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Catherine Cornu	Alternate	Healthcare Professionals' Representative	No participation in final deliberations and voting on:	3.3.19. Nirsevimab - EMEA-001784-PIP01-15-M04
Jaroslav	Member	Patients'	No restrictions	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Sterba		Organisation Representative	applicable to this meeting	
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Tomasz Grybek	Alternate	Patients' Organisation Representative	No interests declared	
Michal Odermarsky	Alternate	Patients' Organisation Representative	No restrictions applicable to this meeting	
María Estela Moreno Martín	Expert - via telephone*	Spain	No interests declared	
Maija Tarkkanen	Expert - via telephone*	Finland	No interests declared	
Celine Chu	Expert - via telephone*	France	No interests declared	
Kristin Karlsson	Expert - via telephone*	Finland	No restrictions applicable to this meeting	
A representative from the European Commission attended the meeting Meeting run with support from relevant EMA staff				
*Experts were 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/