EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 February 2023
EMA/PDCO/51475/2023
Human Medicines Division

Paediatric Committee (PDCO)

Minutes for the meeting on 17-20 January 2023

Chair: Brian Aylward – Vice-Chair: Sylvie Benchetrit

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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

Table of contents

1. Introductions

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

The Chair opened the meeting by welcoming all participants. Due to the coronavirus (COVID-19) pandemic, 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 on the topics in the agenda of the meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics.

Participants were asked to declare any changes, omissions or errors to their declared interests concerning the matters for discussion. No new or additional competing interests were declared. Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

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. All decisions taken at this meeting were made in the presence of a quorum of members. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The Chair welcomed the new member and thanked the departing member for her contributions to the Committee.

The Chair announced the start of the Swedish presidency of the Council of the European Union (EU).

1.2. Adoption of agenda

The agenda for 17-20 January 2023 meeting was adopted with amendments.

1.3. Adoption of the minutes

The minutes for 13-16 December 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. Zilebesiran (sodium) - EMEA-003218-PIP01-22

Alnylam Netherlands B.V.; Treatment of hypertension

Day 120 opinion

Cardiovascular Diseases

Summary of Committee discussion:

Based on the assessment of this application and the additional clarifications received from the applicant, and further discussions at the Paediatric Committee, all issues were considered resolved and a positive opinion including a deferral was adopted by the PDCO for the PIP for zilebesiran (sodium) for the paediatric population from 2 years to less than 18 years of age in the condition of treatment of hypertension.
The PDCO recommended granting a waiver for zilebesiran (sodium) for the paediatric population from birth to less than 2 years of age on the grounds that that the specific medicinal product is likely to be unsafe. A deferral was granted for most measures contained in this PIP.

2.1.2. Danuglipron - EMEA-002944-PIP02-22

Pfizer Europe MA EEIG; Treatment of obesity

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

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 years to less than 18 years of age in the condition of treatment of obesity was adopted. The PDCO agreed on a waiver in a subset of children on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments. The PDCO granted a deferral for most of the measures contained in the PIP.

2.1.3. Insulin lispro - EMEA-003166-PIP01-21

ADOCIA; Treatment of type 1 diabetes mellitus / Treatment of type 2 diabetes mellitus

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

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 insulin lispro (BC222) for the

paediatric population from 1 year to less than 18 years of age in the condition treatment of type 1 diabetes mellitus, and a positive opinion for the PIP for insulin lispro (BC222) for the paediatric population from 10 years to less than 18 years of age in the condition treatment of type 2 diabetes mellitus were adopted.
The PDCO agreed on a waiver in the paediatric population from birth to less than 1 year of age with type 1 diabetes mellitus, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset, and agreed on a waiver in the paediatric population from birth to less than 10 years of age with type 2 diabetes mellitus, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset.
The PDCO granted a deferral for some measures contained in this PIP.

2.1.4. (S)-2-hydroxy-6-((4-(2-(2-hydroxyethyl) nicotinoyl) morpholin-3-yl) methoxy) benzaldehyde - EMEA-003241-PIP01-22

Global Blood Therapeutics Netherlands B.V.; Treatment of sickle cell disease

Day 120 opinion

Haematology-Hemostaseology

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 children from 6 months to less than 18 years of age, in the condition of treatment of sickle cell disease was adopted. The PDCO agreed on a waiver in a subset of children on the grounds of lack of significant therapeutic benefit. The PDCO granted a deferral for most of the measures contained in this PIP.

2.1.5. Cemdisiran - Orphan - EMEA-003237-PIP01-22

Regeneron Ireland DAC; Treatment of myasthenia gravis

Day 120 opinion

Neurology

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO adopted a positive opinion on D120 for cemdisiran for treatment of myasthenia gravis for paediatric patients from 6 years to 18 years of age with a deferral for the completion of the study contained in the PIP.
A waiver was granted for paediatric population from birth to less than 6 years of age 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.

2.1.6. Pozelimab - EMEA-003238-PIP01-22

Regeneron Ireland DAC; Treatment of myasthenia gravis

Day 120 opinion

Neurology

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO adopted a positive opinion on D120 for pozelimab for treatment of myasthenia gravis for paediatric patients from 6 years to less than 18 years of age with a deferral of the completion of the study contained in this PIP.
A waiver was granted for paediatric population from birth to less than 6 years of age 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.

2.1.7. Lutetium (177Lu) edotreotide - Orphan - EMEA-003245-PIP01-22

ITM Solucin GmbH; Treatment of gastro-entero-pancreatic neuroendocrine tumours (GEP-NETs)

Day 120 opinion

Oncology

Summary of Committee discussion:

The PDCO discussed at Day 120, during the January 2023 plenary meeting, an application for a paediatric investigation plan for lutetium (177Lu) edotreotide for the treatment of gastro-entero-pancreatic neuroendocrine tumours.
The PDCO confirmed all conclusions reached at Day 90 and adopted a positive opinion at Day 120 on a paediatric investigation plan for the treatment of gastro-entero-pancreatic neuroendocrine tumours (GEP-NETs) with a deferral and a waiver for children less than 2 years of age on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for these paediatric patients.

2.1.8. Obecabtagene autoleucel - Orphan - EMEA-003171-PIP01-21

Autolus GmbH; Treatment of acute lymphoblastic leukaemia

Day 120 opinion

Oncology

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 obecabtagene autoleucel in patients from 6 kg of body weight to less than 18 years of age, in the condition of treatment of acute lymphoblastic leukaemia (ALL) was adopted. The PDCO agreed on a waiver in patients weighing less than 6 kg of bodyweight based on the ground that studies are not feasible. The PDCO granted a deferral for most of the measures contained in this PIP. The PDCO re-

emphasised that there is the expectation for the applicant to come back to modify PIP Study 3 once supportive results of Study 2 have been generated.

2.1.9. Humanised IgG2 monoclonal antibody against interleukin-6 - EMEA-003215-PIP01-22

Roche Registration GmbH; Treatment of uveitic macular oedema

Day 120 opinion

Ophthalmology

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 humanised IgG2 monoclonal antibody against interleukin-6 (RO7200220) for patients from 2 years of age to less than 18 years of age the condition of treatment of uveitic macular oedema was adopted by majority. The PDCO agreed on a waiver in children less than 2 years of age on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2.1.10. Clazakizumab - EMEA-001371-PIP03-22

CSL Behring GmbH; Prevention of cardiovascular events in patients with atherosclerosis

Day 60 opinion

Cardiovascular Diseases / Uro-nephrology

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 clazakizumab for all subsets of the paediatric population (birth to less than 18 years of age) in the condition of prevention of cardiovascular events in patients with atherosclerosis on the ground of lack of significant therapeutic benefit in children from birth to less than 18 years of age, as clinical trials would not be feasible. 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.

2.1.11. Sodium(4-{(E)-3-(4-fluorophenyl)-3-[4-(3-morpholin-4-yl-prop-1-ynyl)phenyl]allyloxy}-2-methylphenoxy)acetate - Orphan - EMEA-003331-PIP01-22

Reneo Pharmaceuticals Inc; Treatment of primary mitochondrial disorders

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Note: Withdrawal request received on 17 January 2023

2.1.12. Enpatoran - EMEA-003342-PIP01-22

Merck Europe B.V.; Treatment of cutaneous lupus erythematosus

Day 60 opinion

Immunology-Rheumatology-Transplantation / Dermatology

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 enpatoran for all subsets of the paediatric population (0 to less than 18 years of age) in the condition of "treatment of cutaneous lupus erythematosus" based 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).
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.

2.1.13. Pembrolizumab - EMEA-001474-PIP03-22

Merck, Sharp & Dohme (Europe) Inc; Treatment of Hodgkin lymphoma / Treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue)

Day 60 opinion

Oncology

Summary of Committee discussion:

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 pembrolizumab solution for injection for subcutaneous use for all subsets of the paediatric population (from birth to less than 18 years of age) in the conditions of 'treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue)' and 'treatment of Hodgkin lymphoma' based 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).
The PDCO emphasised that the granting of a waiver for the conditions 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.

2.1.14. Sotorasib - EMEA-002690-PIP02-22

Amgen Europe BV; Treatment of colorectal carcinoma

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed at Day 60, during the January 2023 plenary meeting, a request for a product-specific waiver for sotorasib for the treatment of colorectal carcinoma on the grounds that the disease does not occur in paediatric patients.
The PDCO confirmed all conclusions reached at Day 30 and 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 conditions of "treatment of colorectal carcinoma" on the grounds that the disease occurs only in adult populations.
The applicant agreed for the waiver to be extended to all pharmaceutical forms and all routes of administration.

2.1.15. Upifitamab rilsodotin - EMEA-003340-PIP01-22

Mersana Therapeutics Inc.; Treatment of ovarian cancer / Treatment of fallopian tube cancer / Treatment of primary peritoneal cancer

Day 60 opinion

Oncology

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 upifitamab rilsodotin for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of treatment of primary peritoneal cancer and the condition of treatment of fallopian tube cancer, both based on the ground that the disease does not occur in children. And the condition of treatment of ovarian cancer based on the ground of disease not occurring in boys/male patients of all ages (from birth to less than 18 years of age) and girls/female patients from birth to less than 12 years of age. And based on the ground of lack of significant therapeutic benefit in girls/young female patients age 12 years and above to less than 18 years of age.
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.

2.1.16. Camlipixant - EMEA-003334-PIP01-22

Bellus Health Cough, Inc.; Treatment of unexplained or chronic refractory cough

Day 60 opinion

Pneumology - Allergology

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 discussions at the Paediatric Committee the PDCO members agreed with the applicant's request for a waiver.

The PDCO recommended granting a waiver for the proposed medicine for all subsets of the paediatric population (from birth to less than 18 years of age) for 'treatment of unexplained or chronic refractory cough' 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).

2.1.17. Varicella virus OKA strain (live, attenuated) / rubella virus Wistar RA 27/3 strain (live, attenuated) / measles virus Schwarz strain (live, attenuated) / mumps virus RIT 4385 strain, derived from Jeryl Lynn strain (live, attenuated) - EMEA-003341-PIP01-22

GlaxoSmithKline Biologicals SA; Prevention of measles, mumps, rubella and varicella

Day 60 opinion

Vaccines / Infectious Diseases

Summary of Committee discussion:

The PDCO agreed that a waiver can be granted to all subsets of the paediatric population from birth to less than 18 years of age on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as the needs are already covered. 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 rubella virus Wistar RA 27/3 strain (live, attenuated) / varicella virus OKA strain (live, attenuated), mumps virus RIT 4385 strain, derived from Jeryl Lynn strain (live, attenuated) / measles virus Schwarz strain (live, attenuated) for all subsets of the paediatric population (0 to 18 years of age) in the condition of prevention of measles, mumps, rubella and varicella.
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.

2.1.18. Varicella virus OKA strain (live, attenuated) - EMEA-003317-PIP02-22

GlaxoSmithKline Biologicals SA; Prevention of varicella

Day 30 opinion

Vaccines / Infectious Diseases

Summary of Committee discussion:

The PDCO was presented with the updated request for a waiver included in this PIP submission and the applicant plan for the clinical development and marketing in the EU. The submission is considered to be late according to the Paediatric Regulation as a clinical trial in children has already started enrolling.
The PDCO agreed that a waiver can be granted to all subsets of the paediatric population from birth to less than 18 years of age on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as the needs are already covered.

2.1.19. Clascoterone - EMEA-003330-PIP01-22

Cassiopea S.p.A; Treatment of acne vulgaris

Day 60 opinion

Dermatology

Summary of Committee discussion:

Based on the assessment of this application and the additional clarifications received from the applicant, and further discussions at the Paediatric Committee, all issues were considered resolved and a positive opinion was adopted by the PDCO for the PIP for clascoterone for the paediatric population from 9 years to less than 18 years of age in the condition of treatment of acne vulgaris. The late submission of the PIP containing only completed studies was noted which did not allow a prospective discussion of the plan.
The PDCO recommended granting a waiver for clascoterone for the paediatric population from birth to less than 9 years of age on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset.
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. *Neisseria meningitidis* serogroup B fHbp subfamily B / *Neisseria meningitidis* serogroup B fHbp subfamily A / *Neisseria meningitidis* group A polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group W-135 polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group Y polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group C polysaccharide conjugated to tetanus toxoid carrier protein - EMEA-C1-002814-PIP02-21

Pfizer Europe MA EEIG; Treatment of invasive disease caused by *Neisseria meningitidis* group A, B, C, W and Y from 2 months of age

Day 60 letter

Vaccines

Summary of Committee discussion:

The PDCO agreed that the number of subjects included in the Study 1 is compliant with the key binding elements (KBE).
It was also agreed that of lack of data for the 6 months follow up after booster vaccinations, included in the KBE among others secondary endpoints, is acceptable and would not jeopardise the overall scientific value of the study. The PDCO noted that the applicant is planning to include this analysis in the final study report.

2.2.2. Ivacaftor [N-(2,4-Di-tert-butyl-5-hydroxyphenyl)-1,4-dihydro-4- oxoquinoline-3-carboxamide] - EMEA-C-000335-PIP01-08-M15

Vertex Pharmaceuticals (Ireland) Limited; Treatment of cystic fibrosis

Day 30 opinion

Other

Summary of Committee discussion:

The PDCO took note of outcomes of preceding partial compliance check procedures:

- EMEA-C1-000335-PIP01-08-M04
- EMEA-C2-000335-PIP01-08-M07
- EMEA-C4-000335-PIP01-08-M09
- EMEA-C5-000335-PIP01-08-M09
- EMEA-C6-000335-PIP01-08-M09
- EMEA-C7-000335-PIP01-08-M10
- EMEA-C8-000335-PIP01-08-M12
- EMEA-C9-000335-PIP01-08-M13
- EMEA-C10-000335-PIP01-08-M14

The PDCO adopted on 20 January 2023 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0002/2023) of 6 January 2023.

2.2.3. Tenofovir (disoproxil fumarate) - EMEA-C-000533-PIP01-08-M11

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

Day 30 opinion

Infectious Diseases

Summary of Committee discussion:

The PDCO took note of outcomes of preceding partial compliance check procedures:

- EMEA-C1-000533-PIP01-08
- EMEA-C2-000533-PIP01-08-M02
- EMEA-C3-000533-PIP01-08-M02
- EMEA-C4-000533-PIP01-08-M07
- EMEA-C5-000533-PIP01-08-M10

The PDCO adopted an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0073/2022) of 11 March 2022.

2.2.4. Fluticasone furoate / vilanterol - EMEA-C-000431-PIP01-08-M12

Glaxo Group Limited; Treatment of asthma

Day 30 opinion

Pneumology - Allergology

Summary of Committee discussion:

The PDCO took note of outcomes of preceding partial compliance check procedures:

- EMEA-C1-000431-PIP01-08-M04
- EMEA-C2-000431-PIP01-08-M04
- EMEA-C3-000431-PIP01-08-M09
- EMEA-C4-000431-PIP01-08-M12

The PDCO adopted on 20 January 2023 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0092/2021) of 19 March 2021.

2.2.5. Vortioxetine - EMEA-C-000455-PIP02-10-M09

H. Lundbeck A/S; Treatment of major depressive disorder

Day 30 opinion

Psychiatry

Summary of Committee discussion:

The PDCO took note of outcomes of preceding partial compliance check procedures:

- EMEA-C1-000455-PIP02-10-M01

The PDCO adopted an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0337/2022) of 10 August 2022.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Crinecerfont; 2-thiazolamine, 4-(2-chloro-4-methoxy-5-methylphenyl)-N-[(1S)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-N-2-propyn-1-yl; NBI-74788 - Orphan - EMEA-002700-PIP01-19-M01

Neurocrine Therapeutics Ltd.; Treatment of congenital adrenal hyperplasia

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 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/0104/2021 of 17 March 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.2. Drospirenone / estetrol monohydrate - EMEA-001332-PIP01-12-M06

Estetra SRL; Prevention of pregnancy

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 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/0561/2021 of 31 December 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.3. Evinacumab - EMEA-002298-PIP01-17-M05

Ultragenyx Germany GmbH; Treatment of elevated cholesterol

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

Between Day 30 and Day 60 the applicant addressed all the issues identified at Day 30 satisfactorily. Therefore, based on the review of the rationale submitted by the application 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/0394/2022 of 9 September 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.4. Ibutamoren mesilate - Orphan - EMEA-003032-PIP01-21-M01

Lumos Pharma, Inc.; Treatment of growth hormone deficiency

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 changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0151/2022 of 13 May 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.5. Baricitinib - EMEA-001220-PIP01-11-M07

Eli Lilly and Company Limited; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis)

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of Committee discussion:

The PDCO confirmed the outcome of the discussion at Day 30 and, 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/0004/2022 of 31 January 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.6. Baloxavir marboxil - EMEA-002440-PIP01-18-M04

Roche Registration GmbH; Treatment of influenza / Prevention of influenza

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/0383/2022 of 9 September 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.7. Relebactam monohydrate / cilastatin sodium / imipenem monohydrate - EMEA-001809-PIP01-15-M03

Merck Sharp & Dohme (Europe), Inc.; Treatment of infections caused by gram-negative organisms

Day 60 opinion

Infectious Diseases

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 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/0279/2020 of 24 July 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.8. Fremanezumab - EMEA-001877-PIP01-15-M03

Teva GmbH; Prevention of migraine headaches

Day 60 opinion

Neurology

Note: Withdrawal request received on 11 January 2023

2.3.9. Glycopyrronium bromide - EMEA-001366-PIP01-12-M03

Proveca Pharma Limited; Treatment of sialorrhoea

Day 60 opinion

Neurology

Note: Withdrawal request received on 19 January 2023

2.3.10. Quizartinib - Orphan - EMEA-001821-PIP01-15-M06

Daiichi Sankyo Europe GmbH; Treatment of acute myeloid leukaemia

Day 60 opinion

Oncology

Summary of Committee discussion:

In the written response, the applicant provided the Committee with the clarifications requested at D30. 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/0281/2021 of 16 July 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.11. Gilteritinib (as fumarate) - Orphan - EMEA-002064-PIP01-16-M04

Astellas Pharma Europe B.V.; Treatment of acute myeloid leukaemia

Day 60 opinion

Oncology / 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/0110/2021 of 17 March 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.12. Inotuzumab ozogamicin - Orphan - EMEA-001429-PIP01-13-M07

Pfizer Europe MA EEIG; Treatment of B cell acute lymphoblastic leukaemia

Day 60 opinion

Oncology / Haematology-Hemostaseology

Summary of Committee discussion:

The PDCO re-discussed at Day 60, during the January 2023 plenary meeting, a request for modification for inotuzumab ozogamicin for the treatment of B cell acute lymphoblastic leukaemia.
The modification involves delaying the initiation and completion of a clinical study.
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/0398/2022 of 9 September 2022). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.13. Afamelanotide - Orphan - EMEA-000737-PIP02-11-M02

Clinuvel Europe Limited; Treatment of erythropoietic protoporphyria

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 applicant requested changes to the timelines for all studies delaying the overall completion date of the PIP from June 2022 to March 2028, due to delays on the development of the planned paediatric formulation, which had a flow-on effect on the timing of the rest of studies.
The PDCO adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0292/2011 of 2 December 2011).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.14. Selexipag - EMEA-000997-PIP01-10-M06

Janssen-Cilag International NV; Treatment of pulmonary arterial hypertension

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 and having taken into account additional clarifications provided by the company, the PDCO considered that the proposed changes including the addition of a comparative pharmacodynamics study between adults and children based on 3 studies 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/0328/2021 of 13 August 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.15. Begelomab - Orphan - EMEA-001744-PIP01-14-M02

ADIENNE S.r.l SU; Treatment of acute graft-versus-host disease (aGvHD)

Day 60 opinion

Other / 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/0226/2015 of 2 October 2015).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.16. Methoxyflurane - EMEA-000334-PIP01-08-M11

Medical Developments UK Ltd; Treatment of acute pain

Day 60 opinion

Pain

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/0525/2021 of 3 December 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.17. Budesonide / glycopyrronium bromide / formoterol fumarate dihydrate - EMEA-002063-PIP01-16-M02

AstraZeneca AB; Treatment of 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/0013/2022 of 31 January 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.18. Cariprazine hydrochloride - EMEA-001652-PIP01-14-M04

Gedeon Richter Plc.; Treatment of schizophrenia

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 the PDCO considered that the proposed changes could currently not be accepted.
While there is no principal objection against extrapolation of efficacy per se, it can only be approved on a case-by-case basis, having assessed the underlying data, assumptions, model reliability and conclusiveness of the results. An exposure-response-model could be developed based on adult (and other) data that subsequently may be applied to children. If the predicted and observed data in children are similar extrapolation may be justified. Criteria for this similarity, i.e. which differences between observed and predicted data are acceptable, will need to be predefined and justified. For the development of the model CHMP Scientific Advice is available.
The PDCO therefore adopted a negative opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0105/2021 of 17 March 2021). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.19. Lumasiran - Orphan - EMEA-002079-PIP01-16-M03

Alnylam UK Limited; Treatment of hyperoxaluria

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/0505/2021 of 3 December 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.20. Hydroxypropyl-β-cyclodextrin (HPβCD) - Orphan - EMEA-002839-PIP01-20-M01

Cyclo Therapeutics Inc; Treatment of Niemann pick disease type C

Day 30 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 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/0162/2021 of 14 April 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.21. Exagamglogene autotemcel - Orphan - EMEA-002730-PIP04-21-M01

Vertex Pharmaceuticals (Ireland) Limited; Treatment of beta-thalassemia intermedia and major

Day 30 opinion

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/0549/2021 of 31 December 2021).

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

2.3.22. Cefepime / enmetazobactam - EMEA-002240-PIP02-17-M02

Allecra Therapeutics GmbH; Treatment of infections caused by gram-negative organisms

Day 30 opinion

Infectious Diseases

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes to amend the scope of the PIP to update the condition and to amend the pharmaceutical form 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/0340/2022 of 10 August 2022).

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

2.3.23. Brivaracetam - EMEA-000332-PIP02-17-M04

UCB Pharma S.A.; Treatment of paediatric epilepsy syndromes / Treatment of neonatal seizures

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/0003/2022 of 18 January 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.24. Eladocagene exuparvovec - Orphan - EMEA-002435-PIP01-18-M03

PTC Therapeutic International Limited; Treatment of aromatic L-amino acid decarboxylase deficiency

Day 30 opinion

Neurology

Summary of Committee discussion:

The PDCO discussed at Day 30, during the January 2023 plenary meeting, a request for modification for eladocagene exuparvovec for the treatment of aromatic L-amino acid decarboxylase deficiency.
The modification involves changes in the non-clinical and clinical studies.
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/0074/2021 of 17 March 2021). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.25. Methylphenidate hydrochloride - EMEA-003189-PIP01-22-M01

Laboratorios Lesvi, S.L.; Treatment of attention-deficit hyperactivity disorder

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/0203/2022 of 10 June 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.26. Risdiplam - Orphan - EMEA-002070-PIP01-16-M07

Roche Registration GmbH; Treatment of spinal muscular atrophy

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/0470/2021 of 26 November 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.27. Respiratory syncytial virus stabilised prefusion F subunit vaccine - EMEA-002795-PIP02-21-M01

Pfizer Europe MA EEIG; Prevention of lower respiratory tract disease caused by respiratory syncytial virus

Day 30 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/0255/2022 of 8 July 2022).
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. Tapentadol - EMEA-C1-000325-PIP01-08-M10

Grünenthal GmbH; Treatment of chronic pain

Day 30 letter

Pain

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. Pudexacianinium - EMEA-003099-PIP01-21

Visualisation of ureter

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Diagnostic / Oncology / Gastroenterology-Hepatology / Uro-nephrology

3.1.2. Cilgavimab / tixagevimab - EMEA-003079-PIP01-22

Treatment of coronavirus disease 2019 (COVID-19) / Prevention of coronavirus disease 2019 (COVID-19)

Day 90 discussion

Infectious Diseases

3.1.3. Vilobelimab - EMEA-003080-PIP03-22

Treatment of severe coronavirus disease 2019 (COVID-19)

Day 90 discussion

Infectious Diseases

3.1.4. Zilovertamab vedotin - Orphan - EMEA-003257-PIP01-22

Merck Sharp & Dohme (Europe) Inc.; Treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic, and lymphoid tissue) / Treatment of malignant neoplasms of haematopoietic and lymphoid tissue

Day 90 discussion

Oncology

3.1.5. Recombinant human ectonucleotide pyrophosphatase/phosphodiesterase 1 fused to the Fc fragment of IgG1 - Orphan - EMEA-003232-PIP01-22

Inozyme Pharma Ireland Limited; Treatment of ectonucleotide pyrophosphatase / phosphodiesterase 1 (ENPP1) deficiency

Day 90 discussion

Other / Endocrinology-Gynaecology-Fertility-Metabolism / Cardiovascular Diseases

3.1.6. ABNCoV2 (AV2-cVLP-RBD SARS-CoV-2) - EMEA-003184-PIP01-22

Prevention of coronavirus disease 2019 (COVID-19)

Day 90 discussion

Vaccines / Infectious Diseases

3.1.7. Encaleret - Orphan - EMEA-003348-PIP01-22

Calcilytix Therapeutics, Inc a BridgeBio Company; Treatment of hypoparathyroidism

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.8. Recombinant human tissue nonspecific alkaline phosphatase (TNSALP) fragment crystallizable (Fc) deca aspartate fusion protein - EMEA-003343-PIP01-22

Treatment of hypophosphatasia

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.9. EMEA-003002-PIP03-22

Treatment of portal hypertension with compensated cirrhosis

Day 60 discussion

Gastroenterology-Hepatology

3.1.10. EMEA-003090-PIP02-22

Treatment of hereditary angioedema

Day 60 discussion

Haematology-Hemostaseology

3.1.11. Enpatoran - EMEA-003342-PIP02-22

Treatment of systemic lupus erythematosus

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.12. Trimodulin (human IgM, IgA, IgG solution) - EMEA-002883-PIP02-22

Treatment of coronavirus disease 2019 (COVID-19)

Day 60 discussion

Neonatology - Paediatric Intensive Care / Infectious Diseases

3.1.13. Recombinant human arylsulfatase A - Orphan - EMEA-002050-PIP02-22

Takeda Pharmaceuticals International AG Ireland Branch; Treatment of metachromatic leukodystrophy

Day 60 discussion

Neurology

3.1.14. Sodium ({(2S)-1,4-bis[2-(4-chloro-3-fluorophenoxy)acetamido]bicyclo [2.2.2]octan-2-yl}oxy)methyl hydrogen phosphate-2-amino-2-(hydroxymethyl) propane-1,3-diol (1/1/1) - Orphan - EMEA-003344-PIP01-22

Calico Life Sciences LLC; Treatment of vanishing white matter disease

Day 60 discussion

Neurology

3.1.15. Hemopexin, human - Orphan - EMEA-003333-PIP01-22

CSL Behring GmbH; Treatment of sickle cell disease

Day 60 discussion

Other

3.1.16. EMEA-003347-PIP01-22

Treatment of glomerulonephritis and nephrotic syndrome

Day 60 discussion

Uro-nephrology

3.1.17. Single-stranded 5' capped mRNA encoding the HAs of the influenza virus - EMEA-003346-PIP01-22

Prevention of influenza disease

Day 60 discussion

Vaccines

3.1.18. Zapomeran - EMEA-003349-PIP01-22

Prevention of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Vaccines

3.1.19. Nizaracianine - EMEA-003367-PIP01-22

Enhancement of the ureters during surgery

Day 30 discussion

Diagnostic

3.1.20. Venglustat - Orphan - EMEA-001716-PIP07-22

Genzyme Europe B.V.; Treatment of Gaucher disease

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.21. Pyridoxal 5'-phosphate monohydrate - Orphan - EMEA-002404-PIP02-22

Medicure Pharma Europe Limited; Treatment of pyridox(am)ine 5'-phosphate oxidase (PNPO) deficiency

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Neurology

3.1.22. Govorestat - Orphan - EMEA-003365-PIP01-22

Applied Therapeutics, Inc; Treatment of galactosemia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Ophthalmology / Neurology

3.1.23. Fazirsiran - Orphan - EMEA-003355-PIP01-22

Takeda Pharma A/S; Treatment of alpha-1 antitrypsin deficiency-associated liver disease

Day 30 discussion

Gastroenterology-Hepatology

3.1.24. Inhibitor of receptor-interacting protein kinase 1 - EMEA-003356-PIP01-22

Treatment of ulcerative colitis

Day 30 discussion

Gastroenterology-Hepatology

3.1.25. Efzofitimod - EMEA-003352-PIP01-22

Treatment of sarcoidosis

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.26. Ruzotolimod - EMEA-003363-PIP01-22

Treatment of chronic hepatitis B

Day 30 discussion

Infectious Diseases

3.1.27. Xalnesiran - EMEA-003362-PIP01-22

Treatment of chronic hepatitis B

Day 30 discussion

Infectious Diseases

3.1.28. Tozorakimab - EMEA-003360-PIP01-22

Treatment of acute respiratory failure

Day 30 discussion

Infectious Diseases / Pneumology - Allergology

3.1.29. Clonidine - EMEA-003198-PIP02-22

Treatment of attention deficit hyperactivity disorder

Day 30 discussion

Neurology

3.1.30. Utreloxastat - EMEA-003369-PIP01-22

Treatment of amyotrophic lateral sclerosis

Day 30 discussion

Neurology

3.1.31. EMEA-003271-PIP02-22

Treatment of primary generalised tonic-clonic seizures

Day 30 discussion

Neurology

3.1.32. EMEA-003358-PIP01-22

Treatment of breast malignant neoplasms

Day 30 discussion

Oncology

3.1.33. Lutetium 177-labelled radiohybrid prostate-specific membrane antigen-10.1 (177Lu) rhPSMA-10.1 - EMEA-003353-PIP01-22

Treatment of PSMA-expressing prostate cancer

Day 30 discussion

Oncology

3.1.34. Naxitamab - EMEA-002346-PIP02-22

Treatment of osteosarcoma

Day 30 discussion

Oncology

3.1.35. Nemvaleukin alfa - EMEA-003357-PIP01-22

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

Day 30 discussion

Oncology

3.1.36. Tamibarotene - Orphan - EMEA-003329-PIP02-22

Syros Pharmaceutical (Ireland) Limited; Treatment of RARA-positive patients with acute myeloid leukaemia (AML) / Treatment of RARA-positive patients with myelodysplastic syndromes (MDS)

Day 30 discussion

Oncology

3.1.37. Trotabresib - EMEA-003361-PIP01-22

Treatment of malignant neoplasms of the central nervous system

Day 30 discussion

Oncology

3.1.38. Acoltremon - EMEA-003351-PIP01-22

Treatment of dry eye disease

Day 30 discussion

Ophthalmology

3.1.39. Ciclosporin - EMEA-003366-PIP01-22

Treatment of dry eye disease (DED)

Day 30 discussion

Ophthalmology

3.1.40. Pabinafusp alfa - Orphan - EMEA-003033-PIP02-22

JCR Pharmaceuticals Co., Ltd.; Treatment of mucopolysaccharidosis II (Hunter´s syndrome)

Day 30 discussion

Other

3.1.41. Cannabidiol - Orphan - EMEA-003176-PIP02-22

Zynerba Pharmaceuticals Inc; Treatment of fragile X syndrome (FXS)

Day 30 discussion

Psychiatry

3.1.42. Inaxaplin - Orphan - EMEA-003368-PIP01-22

Vertex Pharmaceuticals (Ireland) Limited; Treatment of APOL1-mediated kidney disease

Day 30 discussion

Uro-nephrology

3.1.43. Meningococcal group Y oligosaccharide conjugated to *Corynebacterium diphteriae* CRM197 protein (MenY-CRM) / meningococcal group W-135 oligosaccharide conjugated to *Corynebacterium diphteriae* CRM197 protein (MenW-CRM) / meningococcal group C oligosaccharide conjugated to *Corynebacterium diphteriae* CRM197 protein (MenC-CRM) / meningococcal group A oligosaccharide conjugated to *Corynebacterium diphteriae* CRM197 protein (MenA-CRM) - EMEA-000032-PIP02-22

Prevention of meningococcal disease

Day 30 discussion

Vaccines

3.1.44. Meningococcal group Y oligosaccharides conjugated to *Corynebacterium diphtheriae* CRM197 protein / meningococcal group W-135 oligosaccharides conjugated to *Corynebacterium diphtheriae* CRM197 protein / meningococcal group C oligosaccharides conjugated to *Corynebacterium diphtheriae* CRM197 protein / meningococcal group A oligosaccharides conjugated to *Corynebacterium diphtheriae* CRM197 protein / outer membrane vesicles (OMV) from *N. meningitidis* / recombinant *Neisseria meningitidis* group B fHbp 2-3-1.13NB fusion protein / recombinant *Neisseria meningitis* group B protein 961c / recombinant *Neisseria meningitis* group B Protein 287-953 / recombinant *Neisseria meningitis* group B protein 936-741 - EMEA-003359-PIP01-22

Prevention of meningococcal disease

Day 30 discussion

Vaccines

3.1.45. An acellular tubular graft composed of human collagen types I and III and other extracellular matrix proteins, including fibronectin and vitronectin - EMEA-003345-PIP01-22

Treatment of vascular injuries

Day 60 discussion

Other

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. Beremagene geperpavec - EMEA-C-002472-PIP03-22

Krystal Biotech Netherlands B.V.; Treatment of dystrophic epidermolysis bullosa

Day 30 discussion

Dermatology

3.2.2. Alirocumab - EMEA-C-001169-PIP01-11-M05

sanofi-aventis recherche & développement; Treatment of elevated cholesterol

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.2.3. Dasiglucagon - EMEA-C1-002233-PIP01-17-M01

Zealand Pharma a/s; Treatment of hypoglycaemia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.2.4. Bezlotoxumab - EMEA-C-001645-PIP01-14-M04

Merck Sharp & Dohme (Europe), Inc.; Prevention of recurrence of *Clostridioides difficile* infection

Day 30 discussion

Infectious Diseases

3.2.5. Satralizumab - EMEA-C2-001625-PIP01-14-M06

Roche Registration GmbH; Treatment of neuromyelitis optica

Day 30 discussion

Neurology

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Remimazolam - EMEA-001880-PIP02-19-M04

PAION Deutschland GmbH; General anaesthesia / Sedation

Day 30 discussion

Anaesthesiology

3.3.2. Sotatercept - Orphan - EMEA-002756-PIP01-19-M02

Merck Sharp & Dohme B.V.; Treatment of pulmonary arterial hypertension

Day 30 discussion

Cardiovascular Diseases

3.3.3. Delgocitinib - EMEA-002329-PIP02-20-M02

LEO Pharma A/S; Treatment of chronic hand eczema

Day 30 discussion

Dermatology

3.3.4. Lebrikizumab - EMEA-002536-PIP01-18-M03

Eli Lilly and Company Limited; Treatment of atopic dermatitis

Day 30 discussion

Dermatology

3.3.5. Remibrutinib - EMEA-002582-PIP01-19-M02

Novartis Europharm Limited; Treatment of chronic spontaneous urticaria

Day 30 discussion

Dermatology

3.3.6. Denosumab - EMEA-000145-PIP02-12-M05

Amgen Europe B.V.; Treatment of osteoporosis

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.7. Glucagon analogue linked to a human immunoglobulin Fc fragment - Orphan - EMEA-003170-PIP01-21-M01

Hanmi Pharm. Co., Ltd.; Treatment of congenital hyperinsulinism

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.8. Osilodrostat - Orphan - EMEA-000315-PIP02-15-M03

Recordati Rare Diseases SARL; Treatment of adrenal cortical hyperfunction

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.9. Obeticholic Acid - Orphan - EMEA-001304-PIP02-13-M06

Advanz Pharma Limited; Treatment of primary biliary cirrhosis / Treatment of biliary atresia

Day 30 discussion

Gastroenterology-Hepatology

3.3.10. Andexanet alfa - EMEA-001902-PIP01-15-M07

AstraZeneca AB; Prevention of factor Xa inhibitor associated haemorrhage / Treatment of factor Xa inhibitor associated haemorrhage

Day 30 discussion

Haematology-Hemostaseology

3.3.11. Synthetic double-stranded siRNA oligonucleotide directed against antithrombin mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues - Orphan - EMEA-001855-PIP01-15-M04

Genzyme Europe B.V.; Treatment of congenital haemophilia A / Treatment of congenital haemophilia B

Day 30 discussion

Haematology-Hemostaseology

3.3.12. Filgotinib - EMEA-001619-PIP04-17-M02

Galapagos NV; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis, and juvenile idiopathic arthritis)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.13. Tofacitinib citrate - EMEA-000576-PIP01-09-M14

Pfizer Europe MA EEIG; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.14. Lamivudine / dolutegravir - EMEA-001940-PIP01-16-M05

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

Day 30 discussion

Infectious Diseases

3.3.15. Oritavancin (diphosphate) - EMEA-001270-PIP01-12-M06

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

Day 30 discussion

Infectious Diseases

3.3.16. Tedizolid phosphate - EMEA-001379-PIP01-12-M07

Merck Sharp & Dohme (Europe), Inc.; Treatment of acute bacterial skin and skin structure

infections

Day 30 discussion

Infectious Diseases

3.3.17. Eculizumab - Orphan - EMEA-000876-PIP03-14-M06

Alexion Europe SAS; Treatment of neuromyelitis optica spectrum disorders

Day 30 discussion

Neurology

3.3.18. Rimegepant - EMEA-002812-PIP02-20-M02

Biohaven Pharmaceutical Ireland DAC; Treatment of migraine headaches

Day 30 discussion

Neurology

3.3.19. Satralizumab - Orphan - EMEA-001625-PIP02-21-M01

Roche Registration GmbH; Treatment of myasthenia gravis

Day 30 discussion

Neurology

3.3.20. Acalabrutinib - Orphan - EMEA-001796-PIP03-16-M03

Acerta Pharma, BV; Treatment of mature B cell neoplasms

Day 30 discussion

Oncology

3.3.21. Carfilzomib - Orphan - EMEA-001806-PIP04-19-M01

Amgen Europe BV; Treatment of acute lymphoblastic leukaemia

Day 30 discussion

Oncology

3.3.22. Selpercatinib - EMEA-002544-PIP01-18-M02

Eli Lilly and Company; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms)

Day 30 discussion

Oncology

3.3.23. Temozolomide - EMEA-002634-PIP01-19-M02

Accord Healthcare S.L.U.; Treatment of malignant glioma, such as glioblastoma multiforme or anaplastic astrocytoma

Day 30 discussion

Oncology

3.3.24. Botaretigene sparoparvovec - Orphan - EMEA-002827-PIP01-20-M01

Janssen-Cilag International NV; Treatment of retinitis pigmentosa

Day 30 discussion

Ophthalmology

3.3.25. Patiromer sorbitex calcium - EMEA-001720-PIP01-14-M03

Vifor Fresenius Medical Care Renal Pharma France; Treatment of hyperkalaemia

Day 30 discussion

Other

3.3.26. Zilucoplan - Orphan - EMEA-002747-PIP01-20-M01

UCB Pharma SA; Treatment of myasthenia gravis

Day 30 discussion

Other / Neurology

3.3.27. Defatted powder of peanuts - EMEA-001734-PIP01-14-M06

Aimmune Therapeutics Inc; Treatment of peanut allergy

Day 30 discussion

Pneumology - Allergology

3.3.28. Ravulizumab (ALXN1210) - EMEA-001943-PIP02-20-M02

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

Day 30 discussion

Uro-nephrology / Haematology-Hemostaseology

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 30 January 2023 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

5.1.1. Committee representatives at SAWP: call for re-nomination

Summary of Committee discussion:

The PDCO noted the presentation and call for re-nomination. In accordance with the SAWP mandate, the SAWP composition will be reviewed and the members/alternates as well as the Committee representatives re-nominated for an adoption of the new composition at the CHMP plenary in March 2023. The criteria for the re-nomination was presented and the call for expression of interests among the Committees was launched.

6. Discussion on the applicability of class waivers

6.1. Discussions on the applicability of class waiver for products

6.1.1. (4R)-1-[(5-chloro-1H-1,2,4-triazol-1-yl)methyl]-4-(3,4,5-trifluorophenyl)pyrrolidin-2-one - EMEA-08-2022

AbbVie Ltd; All classes of medicinal products for treatment of Alzheimer's disease;

Treatment of dementia of the Alzheimer's type

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: cognitive impairment in major depressive disorder and schizophrenia.

6.1.2. Evorpacept - EMEA-10-2022

ALX Oncology, Inc; The class of Her- / epidermal growth factor-receptor antibody medicinal products for treatment of intestinal malignant neoplasms; The class of pyrimidine- and pyrimidine analogue-containing medicinal products AND the class of first- and second-generation platinum-containing medicinal products for treatment of head and neck epithelial malignant neoplasms in combination with HER2-targeted therapy, ramucirumab and paclitaxel for the treatment of patients with HER2-overexpressing advanced gastric or gastro-oesophageal junction adenocarcinoma with disease progression on or after prior HER2-targeted therapy and fluoropyrimidine or platinum-containing chemotherapy AND in combination with pembrolizumab, platinum and fluorouracil for the 1st line treatment of patients with metastatic or with unresectable, recurrent head and neck squamous cell carcinoma

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 indications was not confirmed as the product does not belong to any of the classes of medicinal products for the treatment of head and neck epithelial malignant neoplasms and for the treatment intestinal malignant neoplasms.

Other potential paediatric interests of this medicine suggested by PDCO: acute myeloid leukaemia, solid tumours, Non-Hodgkin lymphoma.

6.1.3. Lonsurf - EMEA-04-2022

Les Laboratoires Servier; The class of pyrimidine- and pyrimidine analogue-containing medicinal products for treatment of breast malignant neoplasms, intestinal malignant neoplasms, lung malignant neoplasms, pancreatic malignant neoplasms, head and neck epithelial malignant neoplasms, skin malignant neoplasms and actinic keratosis; Lonsurf is indicated in combination with bevacizumab for the treatment of adult patients with

metastatic colorectal cancer (CRC) who have received two prior anticancer treatment regimens

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 identified at this stage.

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

No item

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 Chair welcomed Adrienn Horváth, as the new member for Hungary.

The Chair thanked Agnes Gyurasics for her contribution as a member for Hungary.

9.1.2. Vote by Proxy

None

9.1.3. Strategic Review and Learning Meeting (SRLM) - Uppsala, 7-8 June 2023

PDCO member: Kristin Karlsson

Summary of Committee discussion:

PDCO members were informed about the date of the next strategic review and learning meeting in Uppsala.

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 PIP-related CHMP procedures starting in December 2022, was presented to the PDCO members.

Feedback on ongoing CHMP procedures was provided to the Committee by the PDCO experts involved.

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

9.3.1. Non-clinical Working Party: D30 Products identified

PDCO member: Karen van Malderen

Summary of Committee discussion:

The Vice-Chair of the Non-clinical Working Party (NcWP) identified the products which will require NcWP evaluation and discussion.

9.3.2. Formulation Working Group

PDCO member: Brian Aylward (*ad ínterim*)

Summary of Committee discussion:

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

9.3.3. Patients and Consumers Working Party (PCWP)/Healthcare Professionals Working Party (HCPWP)

No item

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. Paediatric Cluster Teleconference

Summary of Committee discussion:

The January 2023 agenda of the cluster were shared with the PDCO members for information.

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

9.8.1. EMA Business Pipeline activity and Horizon scanning

No item

10. Any other business

10.1. Regulatory and scientific virtual conference on RNA based medicines

Summary of Committee discussion:

PDCO members were informed about the upcoming regulatory and scientific virtual conference on RNA based medicines.

10.2. COVID-19 update

Summary of Committee discussion:

The update was cancelled.

10.3. Report on the conclusions of the Workshop on 'Toward Consensus on Best Practices for the Design and Conduct of Pediatric Obesity Pharmacotherapy Clinical Trials'

PDCO member: Helena Fonseca

Summary of Committee discussion:

PDCO member Helena Fonseca presented on the Roundtable Conference "Toward Consensus on Best Practices for the Design and Conduct of Pediatric Obesity Pharmacotherapy Clinical Trials". The roundtable took place in San Diego, USA, in November 2022 and addressed essential issues relevant to the design and conduct of paediatric anti-obesity medication clinical trials.

10.4. Revision of the guideline on clinical investigation of medicinal products in the treatment or prevention of diabetes mellitus

PDCO member: Carine de Beaufort

Summary of Committee discussion:

The guideline on clinical investigation of medicinal products in the treatment or prevention of diabetes mellitus is under revision, and a second revision of paediatric specificities was performed by the PDCO accounting with the latest updates in this evolving field. Following the plenary discussion, the PDCO conclusions will be shared with the drafting group.

10.5. Upcoming Innovation Task Force (ITF) meetings

Summary of Committee discussion:

Two ITF meetings taking place in January and February 2023 were presented for information.

10.6. Update on the EMA funded study on spinal muscular atrophy

Summary of Committee discussion:

EMA provided feedback on the EMA-funded study on spinal muscular atrophy (SMA). The procedural steps and the study plan were presented. PDCO will be kept informed of the progress and outcome of the study.

10.7. Q&A on change of propellants for pressurised metered dose inhalers

Chair of the Respiratory Drafting Group: Karolina Törneke

Summary of Committee discussion:

The Chair of the drafting group (DG) presented the draft Q&As document and addressed the questions and comments raised by PDCO members. It was agreed that PDCO members could send comments on the draft to the DG Chair in writing by 1 February 2023.

11. Breakout sessions

11.1. Internal PDCO Operations

Summary of Committee discussion:

Members of the PDCO discussed operational matters.

11.2. HIV

Summary of Committee discussion:

Members progressed in the discussion, focussing on experience related to procedures for the treatment of HIV under discussion.

11.3. Paediatric oncology

Summary of Committee discussion:

The BOS was cancelled.

11.4. Neonatology

Summary of Committee discussion:

Members discussed organisational matters for the planned review of the neonatal guideline.

11.5. Vaccines

Summary of Committee discussion:

The BOS was cancelled.

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 17-20 January 2023 meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Brian Aylward	Chair	Ireland	No interests declared	
Karl-Heinz Huemer	Member	Austria	No interests declared	
Marleen Renard	Member	Belgium	No restrictions applicable to this meeting	
Karen Van Malderen	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No participation in final deliberations and voting on:	3.3.29. Patiromer sorbitex calcium - EMEA-001720-PIP01-14-M03
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 (Vice-Chair)	France	No interests declared	
Sabine Scherer	Member	Germany	No interests declared	
Yuansheng Sun	Alternate	Germany	No interests declared	
Eleni Katsomiti	Member	Greece	No interests declared	
Anastasia Mountaki	Alternate	Greece	No interests declared	
Adrienn Horváth	Member	Hungary	No interests declared	
Dina Apele-Freimane	Member	Latvia	No restrictions applicable to this meeting	
Carola de Beaufort	Member	Luxembourg	No restrictions applicable to this meeting	
Olivier Moes	Alternate	Luxembourg	No interests declared	
John-Joseph	Member	Malta	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Borg				
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	
Kristin Karlsson	Member	Sweden	No restrictions applicable to this meeting	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Fernando Cabanas	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Jose Ignacio Malagon Calle	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Jaroslav Sterba	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomasz Grybek	Member	Patients' Organisation Representative	No interests declared	
María Estela Moreno Martín	Expert - via telephone*	Spain	No interests declared	
Sara Galluzzo	Expert - via telephone*	Italy	No interests declared	
Outi Mäki-Ikola	Expert - via telephone*	Finland	No restrictions applicable to this meeting	
André Elferink	Expert - via telephone*	Netherlands	No interests declared	
Marion Haberkamp	Expert - via telephone*	Germany	No interests declared	
Taina Mattila	Expert - via telephone*	Netherlands	No interests declared	
Karolina Törneke	Expert - via telephone*	Netherlands	No interests declared	
Georgios Aislaitner	Expert - via telephone*	Germany	No interests declared	
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/