21 January 2022
EMA/PDCO/780332/2021
Human Medicines Division

Paediatric Committee (PDCO)

Minutes for the meeting on 14-17 December 2021

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 14-17 December 2021 meeting was adopted.

1.3. Adoption of the minutes

The minutes for 9-12 November 2021 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. Aficamten - EMEA-002958-PIP01-21

Cytokinetics Inc.; Treatment of hypertrophic cardiomyopathy

Day 120 opinion

Cardiovascular Diseases

Summary of Committee discussion:

The PDCO discussed the application and a positive opinion was adopted for the PIP for aficamten (chemical name changed to the recommended INN at the request of the applicant) for treatment of hypertrophic cardiomyopathy in children from 6 years to less than 18 years of age.
A waiver was granted for children from birth to less than 6 years of age on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible. A deferral was granted for the quality study, clinical study and modelling and simulation studies.

2.1.2. Seralutinib - Orphan - EMEA-002972-PIP01-21

Gossamer Bio 002 Limited; Treatment of pulmonary arterial hypertension

Day 120 opinion

Cardiovascular Diseases

Note: Withdrawal request received on 24 November 2021

2.1.3. Single strain of non-genetically modified *Prevotella histicola* - EMEA-002933-PIP01-20

Evelo Biosciences, Inc.; Treatment of psoriasis

Day 120 opinion

Dermatology

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 children from 2 years to less than 18 years of age, in the condition treatment of psoriasis was adopted. The PDCO agreed on a waiver in a subset of children from birth to less than 2 years 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. 2-Amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-((1R,5S)-3-(tetrahydro-2H-pyran-4-yl)-3-azabicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide fumarate dihydrate (INCB-00928) - EMEA-002992-PIP01-21

Incyte Biosciences Distribution B.V; Treatment of fibrodysplasia ossificans progressiva

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 for the PIP for the proposed medicine for children from 2 years to less than 18 years of age, in the condition of treatment of fibrodysplasia ossificans progressiva was adopted. The PDCO agreed on a waiver in a subset of children from birth to less than 2 years on the grounds that the specific medicinal product is does not represent a significant therapeutic benefit over existing treatments for paediatric patients. The PDCO granted a deferral for the completion of this PIP.

2.1.5. Dienogest / ethinylestradiol - EMEA-002229-PIP02-21

Chemo Research; Treatment of hirsutism associated with polycystic ovary syndrome

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, the PDCO adopted a positive opinion on D120 for dienogest / ethinylestradiol for treatment of hirsutism associated with polycystic ovary syndrome in post-menarche adolescent girls (2 years post-menarche or above 14 years of age for girls with primary amenorrhea) and less than 18 years of age.
A waiver was granted for boys from birth to less than 18 years and premenarcheal girls on the ground that the condition does not occur in the specified paediatric subsets and a waiver for post-menarcheal girls less than 2 years post-menarche or below 14 years of age for girls with primary amenorrhea on the ground that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subsets.

2.1.6. Poly(oxy-1,2-ethanediyl), alpha-hydro-omega-methoxy, ether with N-[[[2-[[6-[[1-[3-[[3-(2,3-dihydroxypropoxy)propyl]amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]thio]hexyl]amino]ethyl]amino]carbonyl]-2-methylalanyl-teriparatide (2:1) (TransCon PTH)- Orphan - EMEA-002955-PIP01-21

Ascendis Pharma Bone Diseases A/S; Treatment of hypoparathyroidism

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 children from birth to less than 18 years of age in the condition of treatment of hypoparathyroidism was adopted. The PDCO granted a deferral for the completion of this PIP.

2.1.7. Tildacerfont - Orphan - EMEA-002970-PIP01-21

Spruce Biosciences, Inc.; Treatment of congenital adrenal hyperplasia

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

The PDCO re-discussed at day 120, during the December 2021 plenary meeting, a PIP application with a deferral and a waiver for tildacerfont for the treatment of congenital adrenal hyperplasia.
The PDCO confirmed all the conclusions reached at day 90, took into consideration the clarifications provided by the applicant between day 90 and day 120 and adopted a positive opinion on a paediatric investigation plan for the treatment of congenital adrenal hyperplasia with a deferral and a waiver for children from birth to less than 1 year of age on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2.1.8. Benralizumab - EMEA-001214-PIP07-21

AstraZeneca AB; Treatment of eosinophilic gastritis/eosinophilic gastroenteritis

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 for the PIP for the proposed medicine for children from 2 years to less than 18 years, in the condition of treatment of eosinophilic gastritis/gastroenteritis was adopted. The PDCO agreed on a waiver in a subset of children from birth to less than 2 years 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.

2.1.9. Izencitinib - EMEA-002757-PIP02-21

Theravance Biopharma Ireland Limited; Treatment of Crohn's disease

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 for the PIP for the proposed medicine for children from 2 years to less than 18 years, in the condition treatment of Crohn’s disease was adopted. The PDCO agreed on a waiver in a subset of children from birth to less than 2 years 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.

2.1.10. 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-PIP01-21

IMARA Inc; Treatment of sickle cell disease

Day 120 opinion

Haematology-Hemostaseology

Note: Withdrawal request received on 10 December 2021

2.1.11. Benralizumab - EMEA-001214-PIP04-19

AstraZeneca AB; Treatment of hypereosinophilic syndrome (HES)

Day 120 opinion

Haematology-Hemostaseology

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the applicant's modified proposal for a paediatric investigation plan. The applicant provided clarifications requested at day 90.
The PDCO thus granted a positive opinion on the paediatric plan proposed by the applicant.

2.1.12. Alectinib - EMEA-002431-PIP02-21

Roche Registration GmbH; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms)

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 alectinib for all paediatric patients from birth to less than 18 years of age in the condition of treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms) was adopted. The PDCO granted a deferral for the completion of this PIP.

2.1.13. Nirogacestat hydrobromide - Orphan - EMEA-002971-PIP01-21

SpringWorks Therapeutics, Inc; Treatment of soft tissue sarcoma

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 the proposed medicine for children from 2 years to less than 18 years of age, in the condition of treatment of soft tissue sarcoma was

adopted. The PDCO agreed on a waiver in a subset of children on the grounds of lack of safety. The PDCO granted a deferral for the completion of this PIP.

2.1.14. Ribociclib - EMEA-002765-PIP02-21

Novartis Europharm Limited; Treatment of neuroblastoma

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 ribociclib for patients from 1 year to less than 18 years of age in the condition of treatment of neuroblastoma was adopted. The PDCO agreed on a waiver in a subset of children on the grounds of lack of significant therapeutic benefit.

2.1.15. Vorasidenib (as hemicitrate, hemihydrate salt) - EMEA-002932-PIP02-21

Les Laboratoires Servier (LLS); Treatment of low grade glioma

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 the proposed medicine for children from 12 to less than 18 years of age in the condition of treatment of low grade glioma was adopted. The PDCO agreed on a waiver in a subset of children on the grounds of lack of significant therapeutic benefit.

2.1.16. Derivative of 6-[2-(pyridin-2-yl)phenoxy]methyl}-1,2,3,4-tetrahydroisoquinoline - EMEA-003002-PIP01-21

Boehringer Ingelheim International GmbH; Treatment of chronic kidney disease

Day 120 opinion

Uro-nephrology

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 paediatric population from 6 months to less than 18 years, in the condition treatment of chronic kidney disease was adopted. The PDCO agreed on a waiver for children from birth to less than 6 months of age on the grounds that the proposed product is likely to be unsafe in this subset. The PDCO granted a deferral for the completion of this PIP.

2.1.17. ExPEC9V - EMEA-002996-PIP01-21

Janssen-Cilag International NV; Prevention of infections caused by extraintestinal pathogenic *Escherichia coli* (ExPEC)

Day 120 opinion

Vaccines

Summary of Committee discussion:

The PDCO adopted a positive opinion, including a waiver for children from birth to less than 6 weeks on the grounds that clinical studies with ExPEC9V cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s) and a deferral for all studies in the PIP.

2.1.18. Acetylsalicylic acid / rosuvastatin calcium - EMEA-002239-PIP02-21

Lanova Farmaceutici SRL; Prevention of cardiovascular events

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 agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for acetylsalicylic acid / rosuvastatin calcium for all subsets of the paediatric population (0 to 18 years of age) in the condition of prevention of cardiovascular events.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.19. Colchicine - EMEA-003101-PIP01-21

Pharmascience International Limited; Prevention of cardiovascular events

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 agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for colchicine for all subsets of the paediatric population (0 to 18 years of age) in the condition of prevention of cardiovascular events, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as studies are not feasible.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric

population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.20. Derivative of pyrrolopyrimidine - EMEA-003109-PIP01-21

AstraZeneca AB; Prevention of cardiovascular events in patients with heart failure

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 agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for derivative of pyrrolopyrimidine for all subsets of the paediatric population (0 to 18 years of age) in the condition of prevention of cardiovascular events in patients with heart failure.

2.1.21. Fostamatinib - EMEA-001196-PIP03-21

Instituto Grifols, S.A.; Treatment of autoimmune haemolytic anaemia

Day 60 opinion

Immunology-Rheumatology-Transplantation / 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 discussions at the Paediatric Committee the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for the proposed medicine for all subsets of the paediatric population (from birth to less than 18 years of age) for the condition treatment of autoimmune haemolytic anaemia on the grounds of lack of safety.
The PDCO recommended to grant the waiver for all pharmaceutical forms and all routes of administration to which the applicant agreed.

2.1.22. Gantenerumab - EMEA-003107-PIP01-21

Roche Registration GmbH; Prevention of Alzheimer's disease

Day 60 opinion

Neurology

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for gantenerumab for all subsets of the paediatric population (0 to 18 years of age) in the condition of prevention of Alzheimer's disease, on the grounds that the disease for which the specific medicinal product is intended does not occur in the

specified paediatric subset.
The PDCO recommended to grant the waiver for all pharmaceutical forms and all routes of administration to which the applicant agreed.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need.

2.1.23. Aumolertinib - EMEA-003106-PIP01-21

SFL Pharmaceuticals Deutschland GmbH; Treatment of lung 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 agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for aumolertinib for all subsets of the paediatric population (birth to less than 18 years of age) in the condition of treatment of lung cancer based on the ground that the disease does not occur in children. Since the agreed waiver ground is disease not occurring, the possibility to apply this to all pharmaceutical forms and all routes of administrations was agreed to by the applicant.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.24. Favezelimab / pembrolizumab - EMEA-003104-PIP01-21

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

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed at day 60, during the December 2021 plenary meeting, a product-specific waiver application for the fixed dose combination (FDC) favezelimab / pembrolizumab for the conditions ‘treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue)’ and ‘treatment of malignant neoplasms of the central nervous system’ based on lack of significant therapeutic benefit in the paediatric population.
The PDCO confirmed all conclusions reached at day 30, considered the information provided by the applicant between day 30 and day 60 and adopted a positive opinion on a product specific waiver for favezelimab / pembrolizumab for all subsets of the paediatric population (from birth to less than 18 years of age) in the conditions ‘treatment of all conditions

included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue and melanoma)' and 'treatment of malignant neoplasms of the central nervous system' based on the grounds that the medicinal product does not represent a significant therapeutic benefit over existing treatments in the paediatric population.

2.1.25. (1R,2S,5S)-N-((1S)-1-Cyano-2-((3S)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido)butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide - EMEA-003081-PIP01-21

Pfizer Europe MA EEIG; Treatment of coronavirus disease 2019 (COVID-19) / Prevention of coronavirus disease 2019 (COVID-19)

Day 90 opinion

Infectious Diseases

Summary of Committee discussion:

In the written responses the applicant addressed the requests for modification adopted by the Committee at D60.
Based on the assessment of this application, the additional information provided by the applicant and the additional key elements implemented in the opinion, a positive opinion for the PIP for the proposed medicine for the paediatric population from birth to less than 18 years of age, in the conditions of treatment of coronavirus disease 2019 and prevention of coronavirus disease 2019 was adopted. The PDCO granted a deferral for the completion of this PIP.

2.1.26. Insulin efsitora alfa - EMEA-003105-PIP01-21

Eli Lilly and Company; Treatment of type 1 diabetes mellitus / Treatment of type 2 diabetes mellitus

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

Based on the assessment of this application and discussions at the Paediatric Committee the PDCO disagrees with the applicant's proposal for the paediatric investigation plan and deferral for treatment of type 1 diabetes mellitus and treatment of type 2 diabetes mellitus in T1DM patients aged 12 to < 18 years old and T2DM patients aged 10 to <18 years old, as the measures and timelines are not appropriate to ensure the generation of the necessary data determining the conditions in which the medicinal product may be used to treat the paediatric population or some subsets, nor to adapt a paediatric formulation, or do not bring expected significant therapeutic benefit. The PDCO agreed on an opinion on the refusal of the proposed paediatric investigation plan and deferral and agreed on the granting of a product/specific waiver for all subsets of the paediatric population of its own motion, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subsets of the paediatric population and on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

2.2. Opinions 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.

2.2.1. Tralokinumab - EMEA-C2-001900-PIP02-17-M05

LEO Pharma A/S; Treatment of atopic dermatitis

Day 60 letter

Dermatology

Summary of Committee discussion:

The PDCO considered the applicant's responses submitted after Day 30 satisfactory. Deviations from the PIP, detected during compliance check, are minor with no consequence on the scientific value of the generated data.
Therefore, the completed Study 1 (LP0162-1334) is considered compliant with the latest Agency's Decision (P/0292/2021) of 11 August 2021.
The PDCO finalised this partially completed compliance procedure on 17 December 2021.

2.2.2. Simeticone / macrogol 4000 / potassium chloride / sodium sulphate, anhydrous / sodium chloride / citric acid, anhydrous / sodium citrate - EMEA-C-001356-PIP02-12-M04

Alfasigma S.p.A.; Bowel cleansing prior to clinical procedures

Day 60 opinion

Gastroenterology-Hepatology

Summary of Committee discussion:

The PDCO adopted on 17 December 2021 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0134/2021) of 14 April 2021.

2.2.3. Peramivir - EMEA-C-001856-PIP02-16-M02

BioCryst Ireland Limited; Treatment of influenza

Day 60 opinion

Infectious Diseases

Summary of Committee discussion:

The PDCO took note of outcomes of preceding partial compliance check procedure EMEA-C1-001856-PIP02-16. The outcome of the D30 discussion was confirmed and Study 2 (BCX1812-305) was considered to have been completed in compliance with the latest Agency's Decision P/0257/2021 of 7 July 2021.
The PDCO adopted on an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0257/2021) of 7 July 2021.

2.2.4. Pneumococcal polysaccharide serotype 1 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 3 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 4 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 5 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 6A – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 6B – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 7F – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 9V – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 14 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 18C – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 19A – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 19F – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 22F – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 23F – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 33F – diphtheria CRM197 conjugate (15-valent pneumococcal polysaccharide conjugate vaccine [V114]) - EMEA-C-002215-PIP01-17-M03

Merck Sharp & Dohme (Europe), Inc.; Prevention of disease caused by *Streptococcus pneumoniae*

Day 60 opinion

Vaccines

Summary of Committee discussion:

The PDCO adopted on 17 December 2021 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0343/2021) of 9 August 2021.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Dupilumab - EMEA-001501-PIP02-13-M07

sanofi-aventis groupe; Treatment of asthma

Day 60 opinion

Dermatology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency’s latest decision (P/0361/2021 of 8 September 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.2. Mitapivat - Orphan - EMEA-002684-PIP01-19-M01

Agios Netherlands B.V.; Treatment of pyruvate kinase deficiency

Day 60 opinion

Haematology-Hemostaseology

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/0365/2020 of 9 September 2020).

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

2.3.3. Vadadustat - EMEA-001944-PIP01-16-M03

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

Day 60 opinion

Haematology-Hemostaseology

Summary of Committee discussion:

The PDCO re-discussed at day 60, during the December 2021 plenary meeting, a modification for vadadustat for the treatment of anaemia due to chronic disorders.
The applicant requests to postpone initiation of 4 studies.
The PDCO confirmed all the conclusions reached at day 30 and adopted a positive opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0401/2020 of 23 October 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.4. Allogeneic bone marrow derived mesenchymal stromal cells, ex-vivo expanded - Orphan - EMEA-002706-PIP01-19-M01

medac Gesellschaft für klinische Spezialpräparate mbH; Treatment of acute graft-versus-host disease

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of Committee discussion:

The PDCO noted that remaining issues were resolved after further consultation with the applicant on a draft opinion.

The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0453/2020 of 01/12/2020).

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

2.3.5. Apremilast - EMEA-000715-PIP03-11-M07

Amgen Europe B.V.; Treatment of psoriasis

Day 60 opinion

Immunology-Rheumatology-Transplantation

Note: Withdrawal request received on 8 December 2021

2.3.6. Baricitinib - EMEA-001220-PIP01-11-M06

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:

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/0311/2021 of 11 August 2021). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.7. Atazanavir (sulphate) / cobicistat - EMEA-001465-PIP01-13-M04

Bristol-Myers Squibb Pharma EEIG; Treatment of human immunodeficiency virus (HIV-1) infection

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/0510/2020 of 22 December 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.8. Avibactam / ceftazidime - EMEA-001313-PIP01-12-M11

Pfizer Europe MA EEIG; Treatment of infections due to aerobic Gram-negative organisms / Treatment of urinary tract infections / Treatment of pneumonia / Treatment of intra-abdominal infections

Day 60 opinion

Infectious Diseases

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed

paediatric investigation plan, the PDCO considered that the proposed changes could be accepted. The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0027/2021 of 27 January 2021). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.9. Cabotegravir - EMEA-001418-PIP01-13-M04

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

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 some 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/0118/2021 of 17 March 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.10. Tenofovir alafenamide / rilpivirine / emtricitabine - EMEA-001679-PIP01-14-M01

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

Day 60 opinion

Infectious Diseases

Note: Withdrawal request received on 16 December 2021

2.3.11. Brivaracetam - Orphan - EMEA-000332-PIP02-17-M03

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

Day 60 opinion

Neurology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that 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/0173/2021 of 9 April 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.12. Onasemnogene abeparvovec - Orphan - EMEA-002168-PIP01-17-M04

Novartis Gene Therapy EU Limited; Treatment of spinal muscular atrophy

Day 60 opinion

Neurology

Summary of Committee discussion:

The PDCO re-discussed at day 60, during the December 2021 plenary meeting, a modification for onasemnogene abeparvovec for the treatment of spinal muscular atrophy. The applicant requested to delete two clinical studies from the PIP and to replace them with two new ones.
The PDCO confirmed most conclusions reached at day 30, took into consideration the clarifications provided by the applicant between day 30 and day 60 and adopted a positive opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0379/2020 of 9 September 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.13. Phenobarbital - EMEA-002532-PIP01-18-M02

Proveca Pharma Limited; Treatment of epilepsy

Day 60 opinion

Neurology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that 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/0301/2021 of 13 August 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.14. Avapritinib - Orphan - EMEA-002358-PIP02-18-M02

Blueprint Medicines (Netherlands) B.V.; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms)

Day 60 opinion

Oncology

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/0007/2020 of 6 January 2020.
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.15. Gemtuzumab ozogamicin - Orphan - EMEA-001733-PIP02-15-M02

Pfizer Europe MA EEIG; Treatment of acute myeloid leukaemia

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed at day 60, during the December 2021 plenary meeting, a modification for gemtuzumab ozogamicin for the treatment of acute myeloid leukaemia. The applicant requests a delay for the completion of one of the clinical studies, which will also result in a delay of PIP completion. The PDCO confirmed all the conclusions reached at day 30, took into consideration additional information provided between day 30 and day 60. 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/0326/2017 of 31 October 2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.16. Talimogene laherparepvec - EMEA-001251-PIP01-11-M05

Amgen Europe B.V.; Treatment of melanoma

Day 60 opinion

Oncology

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 including narrowing the condition to 'treatment of melanoma', 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/0187/2020 of 13 May 2020. The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.17. Cysteamine (hydrochloride) - Orphan - EMEA-000322-PIP01-08-M06

Recordati Rare Diseases SARL; Treatment of corneal cystine crystal deposits in cystinosis

Day 60 opinion

Ophthalmology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0172/2017 of 31 July 2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.18. Lanadelumab - Orphan - EMEA-001864-PIP01-15-M06

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

Day 60 opinion

Other

Summary of Committee discussion:

The PDCO adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0264/2021 of 7 July 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.19. Budesonide / glycopyrronium bromide / formoterol fumarate dihydrate - EMEA-002063-PIP01-16-M01

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/0384/2017 of 19 December 2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.20. Dexmedetomidine (hydrochloride) - EMEA-002758-PIP01-19-M01

BioXcel Therapeutics, Inc.; Treatment of bipolar disorder / 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 some of the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0019/2021 of 29 January 2021). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.4. Opinions on Re-examinations

2.4.1. Glycopyrronium bromide - EMEA-002383-PIP01-18-M01

Dr. August Wolff GmbH & Co. KG - Arzneimittel; Treatment of hyperhidrosis

Day 30 opinion

Dermatology

Summary of Committee discussion:

The planned oral explanation was cancelled. 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/0420/2020 of 23 October 2020).

2.4.2. Ravulizumab - EMEA-001943-PIP04-20

Alexion Europe SAS; Treatment of neuromyelitis optica spectrum disorders

Day 30 opinion

Neurology

Summary of Committee discussion:

The Paediatric Committee, having assessed the detailed grounds for re-examination recommends as set out in the appended summary report to maintain its opinion.

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. Cotadutide - EMEA-C1-002712-PIP01-19-M01

AstraZeneca AB; Treatment of non-alcoholic steatohepatitis (NASH)

Day 30 letter

Immunology-Rheumatology-Transplantation

2.7.2. Remimazolam (as besylate) - EMEA-C1-001880-PIP02-19-M03

PAION Deutschland GmbH; Sedation

Day 30 letter

Anaesthesiology

2.7.3. *Neisseria meningitidis* serogroup B recombinant lipoprotein (rLP2086; subfamily B; *Escherichia coli*) / *Neisseria meningitidis* serogroup B recombinant lipoprotein (rLP2086; subfamily A; *Escherichia coli*) / *Neisseria meningitidis* serogroup B recombinant lipoprotein (rLP2086; subfamily B) - EMEA-C3-001037-PIP02-11-M05

Pfizer Europe MA EEIG; Prevention of invasive meningococcal disease caused by *N. meningitidis* serogroup B

Day 30 letter

Vaccines

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. Phospholipid esters from herring roe - EMEA-003053-PIP01-21

Treatment of psoriasis

Day 90 discussion

Dermatology

3.1.2. Efgartigimod alfa - Orphan - EMEA-002597-PIP04-21

argenx BV; Treatment of immune thrombocytopenia

Day 90 discussion

Haematology-Hemostaseology

3.1.3. Recombinant humanized anti-blood dendritic cell antigen 2 (BDCA2) monoclonal antibody - EMEA-002555-PIP02-21

Treatment of lupus erythematosus

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.4. Acetyl-L-leucine ((s)-(acetylamino)-4-methylpentanoic acid) - Orphan - EMEA-002796-PIP01-20

IntraBio Ltd.; Treatment of Niemann-Pick disease type C

Day 90 discussion

Neurology

3.1.5. Firazorexton sesquihydrate - EMEA-002993-PIP01-21

Treatment of narcolepsy

Day 90 discussion

Neurology

3.1.6. Givinostat - Orphan - EMEA-000551-PIP04-21

Italfarmaco S.p.A.; Treatment of Duchenne muscular dystrophy

Day 90 discussion

Neurology

3.1.7. Viltolarsen - Orphan - EMEA-002853-PIP01-20

NS Pharma, Inc.; Treatment of Duchenne muscular dystrophy

Day 90 discussion

Neurology

3.1.8. Pemigatinib - Orphan - EMEA-002370-PIP02-21

Incyte Biosciences Distribution B.V.; Treatment of myeloid/lymphoid neoplasms with FGFR1 rearrangement

Day 90 discussion

Oncology

3.1.9. Zamtocabtagene autoleucel - Orphan - EMEA-003009-PIP01-21

Miltenyi Biomedicine GmbH; Treatment of mature B cell neoplasms

Day 90 discussion

Oncology

3.1.10. Pabinafusp alfa - Orphan - EMEA-003033-PIP01-21

JCR Pharmaceuticals Co., Ltd.; Mucopolysaccharidosis type II

Day 90 discussion

Other

3.1.11. EMEA-003052-PIP01-21

Treatment of cystic fibrosis

Day 90 discussion

Pneumology - Allergology

3.1.12. EMEA-002946-PIP01-20

Treatment of major depressive disorder

Day 90 discussion

Psychiatry

3.1.13. Ralmitaront - EMEA-003003-PIP01-21

Treatment of schizophrenia

Day 90 discussion

Psychiatry

3.1.14. L-Carnitine / glucose / calcium chloride dihydrate / magnesium chloride hexahydrate / sodium lactate / sodium chloride - EMEA-003049-PIP01-21

Treatment of patients in need of peritoneal dialysis

Day 90 discussion

Uro-nephrology

3.1.15. COVID-19 vaccine (recombinant, adjuvanted) - EMEA-002987-PIP01-21

Prevention of coronavirus disease 2019 (COVID-19)

Day 90 discussion

Vaccines

3.1.16. *Neisseria meningitidis* serogroup B fHbp subfamily B / *Neisseria meningitidis* serogroup B fHbp subfamily A / *Neisseria meningitidis* group Y polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group W-135 polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group C polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group A polysaccharide conjugated to tetanus toxoid carrier protein - EMEA-002814-PIP02-21

Invasive disease caused by *Neisseria meningitidis* group A, B, C, W and Y from 2 months of

age

Day 90 discussion

Vaccines

3.1.17. Pudexacianinium - EMEA-003099-PIP01-21

Visualization of ureter

Day 60 discussion

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

3.1.18. Efruxifermin - EMEA-003114-PIP01-21

Treatment of non-alcoholic fatty liver disease including non-alcoholic steatohepatitis

Day 60 discussion

Gastroenterology-Hepatology

3.1.19. Omfiloctocog alfa - EMEA-003113-PIP01-21

Perioperative management / Control and prevention of bleeding

Day 60 discussion

Haematology-Hemostaseology

3.1.20. Cenerimod - EMEA-003108-PIP01-21

Treatment of systemic lupus erythematosus (SLE)

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.21. Adeno-associated virus serotype hu68 containing the human GLB1 gene - Orphan - EMEA-003102-PIP01-21

Passage Bio, Inc.; Treatment of GM1 gangliosidosis

Day 60 discussion

Neurology

3.1.22. Corticotropin - EMEA-003097-PIP01-21

Treatment of infantile spasms

Day 60 discussion

Neurology

3.1.23. Humanised monoclonal IgG1-based antibody - EMEA-003100-PIP01-21

Treatment of spinal muscular atrophy

Day 60 discussion

Neurology

3.1.24. Amifampridine - EMEA-003103-PIP01-21

Lambert-Eaton myasthenic syndrome

Day 60 discussion

Other

3.1.25. A 2'-O-(2'-methoxyethyl) modified antisense oligonucleotide targeting prekallikrein (PKK) mRNA - EMEA-003112-PIP01-21

Hereditary angioedema / Prevention of hereditary angioedema

Day 60 discussion

Pneumology - Allergology / Haematology-Hemostaseology

3.1.26. Troriluzole - EMEA-003084-PIP02-21

Treatment of obsessive-compulsive disorder

Day 60 discussion

Psychiatry

3.1.27. EMEA-003098-PIP01-21

Treatment of proteinuric chronic kidney disease

Day 60 discussion

Uro-nephrology

3.1.28. Bardoxolone - EMEA-002488-PIP02-21

Treatment of autosomal dominant polycystic kidney disease (ADPKD)

Day 60 discussion

Uro-nephrology

3.1.29. Pegcetacoplan - Orphan - EMEA-002600-PIP03-21

Apellis Ireland Limited; Treatment of glomerulonephritis and nephrotic syndrome

Day 60 discussion

Uro-nephrology

3.1.30. Vibegron - EMEA-001415-PIP02-21

Treatment of myoneurogenic bladder disorders

Day 60 discussion

Uro-nephrology

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

Prevention of RSV-associated lower respiratory tract illness

Day 60 discussion

Vaccines

3.1.32. EMEA-003120-PIP01-21

Prevention of cardiovascular events in patients with chronic heart failure

Day 30 discussion

Cardiovascular Diseases

3.1.33. Ex vivo expanded autologous human keratinocytes containing epidermal stem cells transduced with a LAMB3-encoding retroviral vector - Orphan - EMEA-003137-PIP01-21

Holostem Terapie Avanzate s.r.l.; Treatment of junctional epidermolysis bullosa (JEB)

Day 30 discussion

Dermatology

3.1.34. Tezepelumab - EMEA-001613-PIP04-21

Treatment of chronic spontaneous urticaria

Day 30 discussion

Dermatology

3.1.35. Avexitide - Orphan - EMEA-003125-PIP01-21

EigerBio Europe Limited; Treatment of postbariatric hypoglycaemia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.36. Elamipretide - Orphan - EMEA-003128-PIP01-21

Stealth BioTherapeutics Inc.; Treatment of Barth syndrome

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.37. A nonreplicating, recombinant adeno-associated virus (AAV) serotype 9 (AAV9) gene transfer vector that contains a modified human ATP7B coding sequence - Orphan - EMEA-003131-PIP01-21

Ultragenyx Germany GmbH; Treatment of Wilson disease

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.38. Parsaclisib - Orphan - EMEA-002696-PIP02-21

Incyte Biosciences Distribution B.V.; Treatment of autoimmune haemolytic anaemia

Day 30 discussion

Haematology-Hemostaseology

3.1.39. Human normal immunoglobulin - EMEA-003121-PIP01-21

Treatment of post-polio syndrome

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.40. EMEA-003116-PIP01-21

Treatment of coeliac disease

Day 30 discussion

Immunology-Rheumatology-Transplantation / Gastroenterology-Hepatology

3.1.41. Ibrexafungerp citrate - EMEA-002535-PIP04-21

Invasive candidiasis

Day 30 discussion

Infectious Diseases

3.1.42. Nifurtimox - EMEA-003134-PIP01-21

Treatment of Chagas disease

Day 30 discussion

Infectious Diseases

3.1.43. Ivermectin - EMEA-003136-PIP01-21

Topical treatment of head lice infestations / Treatment of head lice infestations

Day 30 discussion

Infectious Diseases / Dermatology

3.1.44. Self-complementary adeno-associated viral vector serotype 9 containing the human CLN3 gene - Orphan - EMEA-003124-PIP01-21

Amicus Therapeutics Europe Limited; Neuronal ceroid lipofuscinosis - CLN3

Day 30 discussion

Neurology

3.1.45. EMEA-003129-PIP01-21

Treatment of osteosarcoma

Day 30 discussion

Oncology

3.1.46. Ceralasertib - EMEA-003127-PIP01-21

Treatment of lung carcinoma (small cell and non-small cell carcinoma)

Day 30 discussion

Oncology

3.1.47. Cosibelimab - EMEA-003041-PIP01-21

Treatment of cutaneous squamous cell carcinoma

Day 30 discussion

Oncology

3.1.48. Nemtabrutinib - EMEA-003135-PIP01-21

Treatment of mature B cell malignancies

Day 30 discussion

Oncology

3.1.49. Sunvozertinib - EMEA-003132-PIP01-21

Treatment of non-small cell lung cancer (NSCLC)

Day 30 discussion

Oncology

3.1.50. Tarlatamab - EMEA-003138-PIP01-21

Treatment of neuroendocrine prostate cancer (NEPC) / Treatment of small cell lung cancer (SCLC)

Day 30 discussion

Oncology

3.1.51. Tucatinib - EMEA-002242-PIP02-21

Treatment of solid tumours / Treatment of malignant neoplasms with HER2 alterations

Day 30 discussion

Oncology

3.1.52. Vimseltinib - Orphan - EMEA-002802-PIP02-21

Deciphera Pharmaceuticals; Treatment of tenosynovial giant cell tumour

Day 30 discussion

Oncology

3.1.53. Bemcentinib - EMEA-003123-PIP01-21

Treatment of acute myeloid leukaemia

Day 30 discussion

Oncology / Haematology-Hemostaseology

3.1.54. (R)-tetrahydrofuran-3-yl 4-(6-(5-(4-ethoxy-1-isopropylpiperidin-4-yl)pyridin-2-yl)pyrrolo[1,2-b]pyridazin-4-yl)piperazine-1-carboxylate sesquisuccinate - Orphan - EMEA-003133-PIP01-21

Ipsen Pharma; Fibrodysplasia ossificans progressiva / Treatment of fibrodysplasia ossificans progressiva

Day 30 discussion

Other

3.1.55. Anti TL1a mAb - EMEA-003111-PIP02-21

Treatment of asthma

Day 30 discussion

Other

3.1.56. Azelastine hydrochloride / mometasone furoate - EMEA-003122-PIP01-21

Seasonal allergic rhinitis

Day 30 discussion

Oto-rhino-laryngology

3.1.57. EMEA-001649-PIP02-21

Treatment of fibrosing interstitial lung diseases (ILD)

Day 30 discussion

Pneumology - Allergology

3.1.58. Zuranolone - EMEA-003119-PIP01-21

Treatment of postpartum depression

Day 30 discussion

Psychiatry

3.1.59. *Borrelia* outer surface protein A (OspA) serotypes (ST1-6) lipidated, fusion protein vaccine - EMEA-003130-PIP01-21

Prevention of Lyme disease

Day 30 discussion

Vaccines

3.1.60. Recombinant COVID-19 subunit nanoparticle - EMEA-003115-PIP01-21

Prevention of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Vaccines

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. Nirsevimab - EMEA-C2-001784-PIP01-15-M03

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

Day 30 discussion

Infectious Diseases

3.2.2. Nivolumab - EMEA-C-001407-PIP01-12-M03

Bristol-Myers Squibb Pharma EEIG; Treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue)

Day 30 discussion

Oncology

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Delgocitinib - EMEA-002329-PIP02-20-M01

LEO Pharma A/S; Treatment of chronic hand eczema

Day 30 discussion

Dermatology

3.3.2. Spesolimab - EMEA-002475-PIP02-19-M02

Boehringer Ingelheim International GmbH; Prevention of generalized pustular psoriasis / Treatment of generalized pustular psoriasis

Day 30 discussion

Dermatology

3.3.3. Tralokinumab - EMEA-001900-PIP02-17-M06

LEO Pharma A/S; Treatment of atopic dermatitis

Day 30 discussion

Dermatology

3.3.4. Dienogest / ethinyl estradiol - EMEA-002229-PIP01-17-M03

Chemo Research; Prevention of pregnancy

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.5. Pegvaliase - Orphan - EMEA-001951-PIP01-16-M02

BioMarin International Limited; Treatment of hyperphenylalaninaemia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.6. Etrasimod L-arginine - EMEA-002713-PIP01-19-M01

Arena Pharmaceuticals, Inc.; Treatment of ulcerative colitis

Day 30 discussion

Gastroenterology-Hepatology

3.3.7. Guselkumab - EMEA-001523-PIP05-19-M01

Janssen-Cilag International N.V.; Treatment of Crohn's disease

Day 30 discussion

Gastroenterology-Hepatology

3.3.8. Mirikizumab - EMEA-002208-PIP01-17-M02

Eli Lilly and Company; Treatment of Crohn’s disease / Treatment of ulcerative colitis

Day 30 discussion

Gastroenterology-Hepatology

3.3.9. Efanesoctocog alfa - Orphan - EMEA-002501-PIP01-18-M02

Bioverativ Therapeutics, Inc., a Sanofi Company; Treatment of haemophilia A

Day 30 discussion

Haematology-Hemostaseology

3.3.10. Glutamine - Orphan - EMEA-001996-PIP02-16-M01

Emmaus Medical Europe Ltd.; Treatment of sickle cell disease

Day 30 discussion

Haematology-Hemostaseology

3.3.11. Apremilast - EMEA-000715-PIP02-11-M05

Amgen Europe B.V.; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.12. Imlifidase - Orphan - EMEA-002183-PIP01-17-M01

Hansa Biopharma AB; Prevention of graft rejection following solid organ transplantation

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.13. Casirivimab - EMEA-002964-PIP01-21-M01

Regeneron Ireland DAC; Prevention of coronavirus disease 2019 (COVID-19) / Treatment of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Infectious Diseases

3.3.14. Cilgavimab (AZD1061) - EMEA-002925-PIP01-20-M01

AstraZeneca AB; Prevention or treatment of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Infectious Diseases

3.3.15. Fostemsavir (tromethamine) - EMEA-001687-PIP01-14-M06

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

Day 30 discussion

Infectious Diseases

3.3.16. Imdevimab - EMEA-002965-PIP01-21-M01

Regeneron Ireland DAC; Treatment of coronavirus disease 2019 (COVID-19) / Prevention of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Infectious Diseases

3.3.17. Ridinilazole (hydrate) - EMEA-002250-PIP02-17-M01

Summit Limited; Treatment of *Clostridioides difficile* infection

Day 30 discussion

Infectious Diseases

3.3.18. Tedizolid phosphate - EMEA-001379-PIP01-12-M06

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

Day 30 discussion

Infectious Diseases

3.3.19. Tenofovir disoproxil - EMEA-000533-PIP01-08-M11

Gilead Sciences International Limited; Treatment of chronic viral hepatitis B / Treatment of human immunodeficiency virus (HIV-1) infection

Day 30 discussion

Infectious Diseases

3.3.20. Tixagevimab (AZD8895) - EMEA-002900-PIP01-20-M01

AstraZeneca AB; Prevention or treatment of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Infectious Diseases

3.3.21. Efinaconazole - EMEA-001627-PIP01-14-M01

Almirall, S.A.; Treatment of onychomycosis

Day 30 discussion

Infectious Diseases / Dermatology

3.3.22. Isoflurane - EMEA-002320-PIP01-17-M02

Sedana Medical AB; Sedation of mechanically ventilated patients

Day 30 discussion

Neonatology - Paediatric Intensive Care

3.3.23. Delandistrogene moxeparvovec - Orphan - EMEA-002677-PIP01-19-M01

Roche Registration GmbH; Duchenne muscular dystrophy

Day 30 discussion

Neurology

3.3.24. Eculizumab - Orphan - EMEA-000876-PIP05-15-M05

Alexion Europe SAS; Treatment of myasthenia gravis

Day 30 discussion

Neurology

3.3.25. Eptinezumab - EMEA-002243-PIP01-17-M02

H. Lundbeck A/S; Prevention of migraine headaches

Day 30 discussion

Neurology

3.3.26. Dinutuximab beta - Orphan - EMEA-001314-PIP01-12-M01

EUSA Pharma (Netherlands) BV; Neuroblastoma

Day 30 discussion

Oncology

3.3.27. Ex vivo expanded autologous human corneal epithelium cells containing stem cells - Orphan - EMEA-001082-PIP02-11-M03

Holostem Terapie Avanzate S.r.l.; Limbal stem cell deficiency due to ocular burns

Day 30 discussion

Ophthalmology

3.3.28. Vosoritide - Orphan - EMEA-002033-PIP01-16-M02

BioMarin International Limited; Treatment of achondroplasia

Day 30 discussion

Other

3.3.29. Adrenaline (epinephrine) - EMEA-002749-PIP01-19-M01

ARS Pharmaceuticals IRL, Limited; Treatment of allergic reactions

Day 30 discussion

Pneumology - Allergology

3.3.30. Modified allergen extract of birch pollen - EMEA-000932-PIP01-10-M02

ROXALL Medizin GmbH; Treatment of allergic rhinitis / rhino-conjunctivitis

Day 30 discussion

Pneumology - Allergology

3.3.31. 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-M04

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 letters of intent received for submission of applications with start of procedure 4 January 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

No item

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

6.1.1. Lutetium (^{177}Lu) edotreotide - EMEA-15-2021

ITM Solucin GmbH; The classes of androgen receptor modulator, of oestrogen receptor modulator, of growth and sex hormone as well as their releasing or inhibiting factors, and of sex hormone-metabolism modulators medicinal products for treatment of breast malignant neoplasms, prostate malignant neoplasms and neuroendocrine malignant neoplasms / Treatment of gastroenteropancreatic neuroendocrine tumours (GEP-NETs)

The applicability of the class waiver as referred to in the Agency's Decision CW/0001/2015 to the planned therapeutic indication was not confirmed.

Other potential paediatric interests of this medicine suggested by PDCO: gliomas, meningiomas, medulloblastomas

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

No item

9.1.2. Vote by proxy

No item

9.1.3. Strategic Review and Learning Meeting (SRLM) – Paris, 31 March – 1 April 2022

PDCO member: Sylvie Benchetrit

Summary of Committee discussion:

PDCO members were invited to the next strategic review and learning meeting in Paris and the draft agenda was presented.

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 procedures with paediatric indications to be evaluated by the CHMP, starting in November 2021, 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 NcWG evaluation and discussion.

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)

Pan-European paediatric clinical trial network – Conect4children

Summary of Committee discussion:

Representatives of c4c (conect4children) presented an update on the strategic feasibility advice, including public patient involvement (PPI) that the network can offer to applicants (currently only to partners of the c4c consortium). Moreover, an update was provided on multi-stakeholder meetings to define unmet needs and clinical research approaches in different therapeutic areas, as well as on clinical trial site finding and feasibility as well as data standards and education/training.

9.5. Cooperation with International Regulators

No item

9.5.1. Report from the Paediatric Cluster Teleconference

Summary of Committee discussion:

The minutes 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

9.7.1. Development of Therapeutic Areas strategies - update

PDCO member: Sylvie Benchetrit

Summary of Committee discussion:

The PDCO was updated on different initiatives to progress on the scientific and regulatory debate underpinning paediatric development of different agent in Duchenne muscular dystrophy (DMD). Scientific article is under preparation.

9.8. Planning and reporting

9.8.1. EMA Business Pipeline activity and Horizon scanning

Q4/2021 Update of the Business Pipeline report for the human scientific committees

Summary of Committee discussion:

The Business Pipeline report for Q4/2021 was provided for information.

10. Any other business

10.1. COVID-19 update

Summary of Committee discussion:

The Committee was updated on the latest developments of COVID vaccines and treatments that are relevant to paediatrics.

10.2. Extrapolation project – presentation of results and conclusions

Summary of Committee discussion:

The Committee was updated about results from an internal research project on the status quo of reflection of extrapolation in PIP opinions.

10.3. Lifecycle regulatory submissions metadata (LRSM)

Summary of Committee discussion:

An EMA project that looks at tools to facilitate the identification and investigation of unstructured documents in support of Committee members and assessors was presented to the Committee. There was strong support by the Committee in the potential of this concept for PDCO work, as opposed to only relying on human memory. Ideas were shared about elements (metadata) of particular interest to PDCO members.

10.4. PIP-related CHMP procedures – discussion on monitoring – call for volunteers

PDCO member: Sabine Scherer

Summary of Committee discussion:

The PDCO was informed about the out-come of the discussion on this topic during the internal operations break-out session in November. A call for volunteers was issued in order to continue the discussion in a smaller group.

11. Breakout sessions

11.1. Internal PDCO Operations

Summary of Committee discussion:

The PDCO discussed topics relating to internal PDCO operations.

11.2. Neonatology

Summary of Committee discussion:

The breakout session was cancelled as no topic of relevance was identified.

11.3. Paediatric oncology

Summary of Committee discussion:

The PDCO was informed about upcoming meetings with relevance to paediatric oncology.

11.4. Vaccines

Summary of Committee discussion:

The population size of COVID vaccine studies was analysed across different PIPs and members discussed the requirements for the safety dataset size of COVID vaccines in paediatrics.

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 14-17 December 2021 meeting.

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 restrictions applicable to this meeting	
Karen Van Malderen	Alternate	Belgium	No interests declared	
Tereza Bazantova	Alternate	Czechia	No interests declared	
Nanna Borup Johansen	Member	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 member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	
Sara Galluzzo	Member	Italy	No interests declared	
Dina Apele-Freimane	Member	Latvia	No participation in discussions, final deliberations and voting on:	3.2.2. Nirsevimab - EMEA-C2-001784-PIP01-15-M03
Dovile Zacharkiene	Member	Lithuania	No interests declared	
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No interests declared	
Herbert Lenicker	Alternate	Malta	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
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:	3.2.2. Nirsevimab - EMEA-C2-001784-PIP01-15-M03
Doina Plesca	Alternate	Healthcare Professionals' Representative	No interests declared	
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:	3.2.2. Nirsevimab - EMEA-C2-001784-PIP01-15-M03
Jaroslav Sterba	Member	Patients' Organisation Representative	No interests declared	
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	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
María Estela Moreno Martín	Expert - via telephone*	Spain	No interests declared	
Lutz Wiesner	Expert - via telephone*	Germany	No interests declared	
Gaby Wangorsch	Expert - via telephone*	Germany	No interests declared	
Susanne Kaul	Expert - via telephone*	Germany	No interests declared	
Birgit Ahrens	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/