19 January 2024
EMA/PDCO/586488/2023
Human Medicines Division

Paediatric Committee (PDCO)

Minutes for the meeting on 12-15 December 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).

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1. Introductions

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

The Chair opened the meeting by welcoming all participants. 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.

1.2. Adoption of agenda

The agenda for 12-15 December 2023 meeting was adopted with amendments.

1.3. Adoption of the minutes

The minutes for the 7-10 November 2023 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. Obicetrapib - EMEA-003438-PIP02-23

NewAmsterdam Pharma BV; Treatment of elevated cholesterol

Day 120 opinion

Cardiovascular Diseases

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 Day 120 for obicetrapib for treatment of elevated cholesterol for paediatric patients from 6 years to less than 18 years of age.
A waiver was granted for paediatric population from birth to less than 6 years of age on the grounds of lack of significant therapeutic benefit over existing treatments.
The PDCO granted a deferral for one or more measures contained in this paediatric investigation plan.

2.1.2. Remibrutinib - EMEA-002582-PIP03-23

Novartis Europharm Limited; Treatment of chronic inducible urticaria

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 on a paediatric investigation plan (PIP) for remibrutinib in children from 6 years to less than 18 years of age was adopted by the PDCO in the condition of treatment of chronic inducible urticaria.
The Committee agreed on a waiver in children below 6 years of age on the grounds that the specific medicinal product is likely to be unsafe. The PDCO granted a deferral for the completion of this PIP.

2.1.3. Frexalimab - EMEA-002945-PIP03-23

Sanofi Winthrop Industrie; Treatment of type 1 diabetes mellitus

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

The PDCO adopted a positive opinion by consensus, on 15 December 2023, agreed on a paediatric investigation plan (PIP) and granted a waiver below the age of 1 year on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments and a deferral for one or more measures contained in the PIP for frexalimab for the condition of treatment of type 1 diabetes mellitus.

2.1.4. Semaglutide / fibroblast growth factor 21 analogue (NNC194-0499) - EMEA-003402-PIP01-23

Novo Nordisk A/S; Treatment of non-alcoholic steatohepatitis

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 paediatric investigation plan (PIP) for the proposed medicine for children from 8 years to less than 18 years of age, in the condition of treatment of non-alcoholic steatohepatitis, was adopted. The PDCO agreed on a waiver in a subset of children from birth to less than 8 years of age on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments. The PDCO granted a deferral for one or more measures contained in the PIP.

2.1.5. Tarperprumig - Orphan - EMEA-003432-PIP01-23

Alexion Europe SAS; Treatment of sickle cell disease (SCD)

Day 120 opinion

Haematology-Hemostaseology

Note: Withdrawal request received on 27 November 2023

2.1.6. EMEA-003271-PIP02-22

Treatment of epilepsy syndromes / Treatment of primary generalised tonic-clonic seizures

Day 120 opinion

Neurology

Note: Withdrawal request received on 8 December 2023

2.1.7. Dordaviprone - Orphan - EMEA-003389-PIP01-23

Chimerix IRL Limited; Treatment of glioma

Day 120 opinion

Oncology

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 paediatric investigation plan (PIP) for the proposed medicine for the paediatric population from birth to less than 18 years of age, in the condition of treatment of glioma was adopted. The PDCO granted a deferral for one or more measures contained in the PIP.

2.1.8. Trotabresib - EMEA-003361-PIP01-22

Treatment of malignant neoplasms of the central nervous system

Day 120 opinion

Oncology

Note: Withdrawal request received on 13 December 2023

2.1.9. Apitegromab - Orphan - EMEA-002951-PIP02-21

Scholar Rock, Inc.; Treatment of spinal muscular atrophy

Day 120 opinion

Other / Neurology

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the paediatric investigation plan (PIP) for the proposed medicine for children from 2 months to less than 18 years of age, in the condition of treatment of spinal muscular atrophy 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 one or more measures contained in the PIP.

2.1.10. Ferric citrate coordination complex (FCCC) - EMEA-001213-PIP03-23

Averoa SAS; Treatment of anaemias due to chronic kidney disorders

Day 120 opinion

Uro-nephrology

Summary of Committee discussion:

Based on the assessment of the applicant's responses at Day 60, and further discussions at the Paediatric Committee, the PDCO decided for a waiver below 6 months of age, based on lack of significant therapeutic benefit. The clinical studies were updated starting from 6 months of age and covering the paediatric population up to 18 years of age.
The PDCO therefore agreed on a paediatric investigation plan (PIP) with a waiver and a deferral for ferric citrate coordination complex (FCCC) for children from 6 months of age to less than 18 years of age in the condition of treatment of anaemias due to chronic kidney disorders. The PIP contains two quality studies, one non-clinical study and two clinical studies.

2.1.11. Zigakibart - Orphan - EMEA-003300-PIP01-22

Chinook Therapeutics, Inc.; Treatment of primary IgA nephropathy

Day 120 opinion

Uro-nephrology

Summary of Committee discussion:

The PDCO adopted a positive opinion for the paediatric investigation plan (PIP) in the condition of "treatment of primary IgA nephropathy" covering the paediatric age groups from 2 years to less than 18 years. A waiver was granted for the paediatric population from birth to less than 2 years of age on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible.

Deferrals were granted for the completion of some measures in the PIP (clinical study and modelling and simulation study).

2.1.12. MRNA encoding for the linked NTD and RBD domains of the spike glycoprotein of SARS-CoV-2 (mRNA-1283) - EMEA-003426-PIP01-23

Moderna Biotech Spain S.L; Prevention of coronavirus disease 2019 (COVID-19)

Day 120 opinion

Vaccines / Infectious Diseases

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the paediatric investigation plan (PIP) for the proposed medicine for children from birth to less than 18 years of age in the condition of prevention of COVID-19 was adopted. The PDCO granted a deferral for one or more measures contained in the PIP.

2.1.13. Obicetrapib / ezetimibe - EMEA-003514-PIP01-23

NewAmsterdam Pharma BV; Treatment of mixed hyperlipidaemia

Day 60 opinion

Cardiovascular Diseases

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for obicetrapib / ezetimibe for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of mixed hyperlipidaemia. 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.

2.1.14. Obicetrapib / ezetimibe - EMEA-003514-PIP02-23

NewAmsterdam Pharma BV; Treatment of elevated cholesterol

Day 60 opinion

Cardiovascular Diseases

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for obicetrapib / ezetimibe for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of elevated cholesterol.

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. The PDCO identified treatment of elevated cholesterol, especially in children with familial hypercholesterolaemia, as an unmet need, but this could be covered by the paediatric investigation plan submitted by the applicant for obicetrapib alone. 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.

2.1.15. Ruxolitinib (phosphate) - EMEA-002618-PIP04-23

Incyte Biosciences Distribution B.V.; Treatment of *Prurigo nodularis*

Day 60 opinion

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 ruxolitinib (phosphate) for all subsets of the paediatric population (birth to less than 18 years of age) in the condition "treatment of *Prurigo nodularis*".

2.1.16. Methyl (1-{[6-{[(1S)-1-cyclopropylethyl]amino}-2-(pyrazolo[5,1-b][1,3]thiazol-7-yl)pyrimidin-4-yl]carbonyl}piperidin-4-yl)carbamate mono(4-methylbenzenesulfonate) monohydrate - EMEA-003503-PIP01-23

NS Pharma, Inc.; Treatment of eosinophilic granulomatosis with polyangiitis

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of Committee discussion:

This is a waiver request for all paediatric subsets due to lack of safety and lack of significant therapeutic benefit as clinical studies are not feasible.
Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO concluded that the waiver is not currently justified by the application sufficiently. While the presented non-clinical findings are acknowledged and agreed to be concerning at least below 8 years of age, their clinical relevance as well as mechanisms for and reversibility of findings require further clarifications.
For the lack of significant benefit, the rarity of the disease does in itself not render paediatric development unfeasible, especially in light of the fact that there are two other agreed and ongoing paediatric investigation plans for the same condition.
The waiver request has therefore been refused by the PDCO.

2.1.17. Nipocalimab - Orphan - EMEA-002559-PIP09-23

Janssen-Cilag International NV; Prevention of foetal and neonatal alloimmune

thrombocytopenia

Day 60 opinion

Immunology-Rheumatology-Transplantation

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 nipocalimab (concentrate for solution for infusion, intravenous use) for post-menarchal females less than 18 years of age on the grounds of absence of significant clinical benefit due to clinical studies being not feasible, and a waiver for all male paediatric subjects and pre-menarchal female subjects on the grounds of the condition not occurring in these subsets, in the condition of prevention of foetal and neonatal alloimmune thrombocytopenia.
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. Cladribine - EMEA-000383-PIP04-23

Merck Europe B.V.; Treatment of myasthenia gravis

Day 60 opinion

Neurology

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 cladribine for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of treatment of myasthenia gravis on the grounds that the specific medicinal product is likely to be unsafe. The applicant agreed with extending the waiver to all pharmaceutical forms and all routes of administration.

2.1.19. Tifcemalimab - EMEA-003512-PIP01-23

Junshi Biosciences; Treatment of lung cancer (small cell and non-small cell lung cancer)

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO discussed at Day 60, during the December 2023 plenary meeting, a product-specific waiver request for tifcemalimab for the treatment of all conditions in the category of malignant neoplasms (except central nervous system (CNS), lymphoid and haematopoietic malignancies) on the grounds that the product would lack significant therapeutic benefit in

paediatric patients.
The PDCO confirmed all the conclusions reached at Day 30 and adopted a positive opinion at Day 60 for this product for the treatment of lung cancer (small cell and non-small cell lung cancer) on the grounds that the disease occurs only in adults.
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.
The applicant agreed for the waiver to be extended to all pharmaceutical forms and all routes of administration.

2.1.20. Tinengotinib (TT-00420) - EMEA-003504-PIP01-23

TransThera Sciences (Nanjing), Inc.; Treatment of cholangiocarcinoma

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 tinengotinib (TT-00420) for all subsets of the paediatric population (birth to less than 18 years of age) in the condition of treatment of cholangiocarcinoma based on the ground of lack of significant therapeutic benefit.
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.

2.1.21. Faricimab - EMEA-002817-PIP05-23

Roche Registration GmbH; Treatment of choroidal neovascularisation secondary to pathologic myopia

Day 60 opinion

Ophthalmology

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 faricimab for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of treatment of choroidal neovascularisation secondary to pathologic myopia on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not 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.

2.1.22. Rocatinlimab - EMEA-002886-PIP02-23

Amgen Europe BV; Treatment of *Prurigo nodularis*

Day 30 opinion

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 rocatinlimab for all subsets of the paediatric population (birth to 18 years of age) in the condition of treatment of *Prurigo nodularis* on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not 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.

2.2. Opinions on Compliance Check

2.2.1. Belimumab - EMEA-C-000520-PIP02-13-M04

Glaxo Group Limited; Treatment of systemic lupus erythematosus

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of Committee discussion:

The PDCO adopted on 15 December 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/0395/2022) of 9 September 2022.

2.2.2. Bosutinib - EMEA-C-000727-PIP01-09-M07

Pfizer Europe MA EEIG; Treatment of chronic myeloid leukaemia

Day 60 opinion

Oncology

Summary of Committee discussion:

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

- EMEA-C1-000727-PIP01-09-M06

The PDCO adopted on 15 December 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/0336/2023) of 7 August 2023.

2.2.3. Isatuximab - EMEA-C-002205-PIP01-17-M04

Sanofi-Aventis Recherche & Développement; Treatment of malignant neoplasms of the haematopoietic and lymphoid tissue

Day 60 opinion

Oncology

Summary of Committee discussion:

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

- EMEA-C1-002205-PIP01-17-M01

The PDCO adopted on 15 December 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/0144/2023) of 21 April 2023.

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

Les Laboratoires Servier; Treatment of low grade glioma

Day 30 opinion

Oncology

Summary of Committee discussion:

The PDCO adopted on 15 December 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/0007/2022) of 31 January 2022.

2.2.5. Remdesivir - EMEA-C-002826-PIP01-20-M04

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

Day 30 opinion

Infectious Diseases

Summary of Committee discussion:

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

- EMEA-C1-002826-PIP01-20-M01
- EMEA-C2-002826-PIP01-20-M01

The PDCO adopted on 15 December 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/0439/2023) of 28 October 2023.

2.2.6. *Dermatophagoides pteronyssinus / Dermatophagoides farinae* - EMEA-C-001258-PIP01-11-M08

ALK-Abelló A/S; Treatment of allergic rhinitis

Day 30 opinion

Pneumology - Allergology

Summary of Committee discussion:

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

- EMEA-C2-001258-PIP01-11-M06
- EMEA-C3-001258-PIP01-11-M08

The PDCO adopted on 15 December 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/0297/2022) of 10 August 2022.

2.2.7. Autologous tumour-infiltrating lymphocytes - EMEA-C2-002776-PIP01-20-M02

Iovance Biotherapeutics, Inc.; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms)

Day 30 letter

Oncology

Summary of Committee discussion:

The PDCO took note of the completed Study 1 (in vitro study to assess the feasibility of producing tumour infiltrating lymphocytes (TIL) from paediatric tumour samples using the same process used to manufacture TIL products from tumour tissue from adults to characterise the phenotype of paediatric TILs). The study was considered compliant with the latest Agency's Decision (P/0440/2023) of 2 November 2023.

The PDCO finalised this partially completed compliance procedure on 15 December 2023.

2.2.8. Rilpivirine - EMEA-C1-000317-PIP02-18-M01

Janssen-Cilag International NV; Treatment of human immunodeficiency virus (HIV-1) infection

Day 30 letter

Infectious Diseases

Summary of Committee discussion:

The PDCO concluded that the Study 1 is compliant with the latest Agency's Decision (P/0397/2022) of 9 September 2022.

The PDCO finalised this partially completed compliance procedure on 15 December 2023.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Tocilizumab - EMEA-000309-PIP07-21-M01

Roche Registration GmbH; Treatment of coronavirus disease 2019 (COVID-19)

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of Committee discussion:

In December 2023 the PDCO noted the responses of the applicant to the issues raised during the previous meeting and agreed to grant a waiver for all subsets of the paediatric population in treatment of coronavirus disease 2019 (COVID-19) of its own motion on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible in paediatric patients. The new PDCO opinion supersedes the previous PDCO opinion.

2.3.2. Etripamil - EMEA-002303-PIP01-17-M04

Milestone Pharmaceuticals, Inc.; Treatment of supraventricular arrhythmia

Day 60 opinion

Cardiovascular Diseases

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan (PIP), 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/0349/2022 of 10 August 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.3. Deucravacitinib - EMEA-002350-PIP01-18-M03

Bristol-Myers Squibb Pharma EEIG; Treatment of psoriasis

Day 60 opinion

Dermatology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan (PIP), the PDCO considered that the proposed changes could be accepted. Within this modification some elements of the statistical plan of Study 3 (a pharmacokinetic, safety and efficacy study in children and adolescents from 6 years to less than 18 years of age with moderate to severe psoriasis) were updated.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0278/2022 of 26 August 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.4. Tralokinumab - EMEA-001900-PIP02-17-M08

LEO Pharma A/S; Treatment of atopic dermatitis

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 (PIP), 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/0186/2023 of 5 June 2023).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.5. Regadenoson - EMEA-000410-PIP01-08-M06

GE Healthcare AS; Diagnosis of myocardial perfusion disturbances

Day 60 opinion

Diagnostic / Cardiovascular Diseases

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan (PIP), 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/0030/2019 of 29 January 2019).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.6. Pariglasgene brecaparvovec (DTX401) - Orphan - EMEA-002734-PIP01-19-M01

Ultragenyx Germany GmbH; Treatment of glycogen storage disease type Ia

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 (PIP), the PDCO considered that some of the proposed changes to timelines for Studies 1, 2 and 3 and the modifications to endpoints and statistical analysis for the clinical studies 2 and 3 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/0278/2021 of 8 July 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.7. Crizanlizumab - Orphan - EMEA-002141-PIP01-17-M04

Novartis Europharm Limited; Treatment of sickle cell disease

Day 60 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 (PIP), 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/0533/2021 of 9 December 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.8. Mozafancogene autotemcel - Orphan - EMEA-002578-PIP01-19-M01

Rocket Pharmaceuticals, Inc; Treatment of Fanconi anaemia subtype A

Day 60 opinion

Haematology-Hemostaseology

Summary of Committee discussion:

The PDCO re-discussed at Day 60, during the December 2023 plenary meeting, a request for modification for mozafancogene autotemcel for the treatment of Fanconi anaemia subtype A.
Based on the review of the documentation submitted by the applicant for modifying the agreed paediatric investigation plan (PIP), the PDCO considered that some of 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/0114/2020 of 18 March 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.9. Upadacitinib - EMEA-001741-PIP01-14-M07

AbbVie Ltd; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, spondyloarthritis 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 (PIP), 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/0237/2023 of 14 June 2023).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.10. Ceftobiprole medocaril sodium - EMEA-000205-PIP02-11-M06

Basilea Pharmaceutica Deutschland GmbH; Treatment of pneumonia

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 (PIP), 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/0529/2021 of 3 December 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.11. Ivosidenib - Orphan - EMEA-002247-PIP03-17-M01

Les Laboratoires Servier; Treatment of acute myeloid leukaemia

Day 60 opinion

Oncology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan (PIP), the PDCO considered that the proposed changes consisting of extending the waiver to cover the subset of the paediatric population from 2 years to less than 18 years of age could be accepted.
Based on the lack of interests shown by the investigators in carrying out paediatric studies with this product and the extreme rarity of the disease, the PDCO concluded that the studies that may be carried in paediatric patients with acute myeloid leukaemia (AML) harbouring isocitrate dehydrogenase (IDH) mutations are not expected to generate the necessary data to establish a benefit/risk of the product in paediatric patients with AML.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0280/2018 of 12 September 2018).
The waiver was granted for paediatric population from 2 years to less than 18 years of age based on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible.
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.12. Odronextamab - Orphan - EMEA-003149-PIP01-21-M02

Regeneron Ireland DAC; Treatment of mature B cell malignancies

Day 60 opinion

Oncology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan (PIP), 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/0197/2023 of 15 May 2023).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.13. Bupivacaine - EMEA-000877-PIP03-17-M05

Pacira Ireland Ltd; Postsurgical analgesia

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 (PIP), 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/0438/2022 of 28 October 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.14. Pegcetacoplan - Orphan - EMEA-002600-PIP03-21-M01

Apellis Ireland Limited; Treatment of glomerulonephritis and nephrotic syndrome

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 (PIP), the PDCO considered that the proposed changes in study timelines 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/0284/2022 of 11 August 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.15. Dengue tetravalent vaccine (live, attenuated) / Dengue tetravalent vaccine (live, attenuated) / Dengue tetravalent vaccine (live, attenuated) / Dengue tetravalent vaccine (live, attenuated) - EMEA-001888-PIP01-15-M02

Takeda Vaccines, Inc.; Prevention of dengue fever

Day 60 opinion

Vaccines

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan (PIP), 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/0429/2020 of 30 October 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.16. Gadopiclenol - EMEA-001949-PIP01-16-M06

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

Day 30 opinion

Diagnostic

Summary of Committee discussion:

This modification proposes the removal of the age-staggered approach from Study 5 to accelerate recruitment. Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan (PIP), 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/0126/2023 of 28 April 2023). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.17. Gadopiclenol - EMEA-001949-PIP02-18-M04

Guerbet; Detection and visualisation of disorders or lesions with suspected abnormal vascularity in various body regions for diagnostic purposes

Day 30 opinion

Diagnostic

Summary of Committee discussion:

This modification proposes the removal of the age-staggered approach from Study 5 to accelerate recruitment. Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan (PIP), 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/0143/2023 of 21 April 2023). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.18. Haematopoietic stem cells and blood progenitors umbilical cord-derived expanded with (1R,4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexane-1,4-diamine dihydrobromide dihydrate (ECT-001-CB) - Orphan - EMEA-003025-PIP03-23-M01

ExCellThera; Treatment in allogeneic haematopoietic stem cell transplantation in patients with haematological malignancies

Day 30 opinion

Immunology-Rheumatology-Transplantation / Oncology / Haematology-Hemostaseology

Summary of Committee discussion:

The PDCO discussed at Day 30, during the December 2023 plenary meeting, a request for modification for haematopoietic stem cells and blood progenitors umbilical cord-derived expanded with (1R,4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexane-1,4-diamine dihydrobromide dihydrate (ECT-001-CB) for the treatment in allogeneic haematopoietic stem cell transplantation in patients with haematological malignancies.
Based on the review of the documentation submitted by the applicant for modifying the agreed paediatric investigation plan (PIP), the PDCO considered that some of 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/0426/2023 of 27 October 2023).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.19. (R)-1-(1-acryloylpiperidin-3-yl)-4-amino-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one - EMEA-002566-PIP01-19-M01

Sanofi Winthrop Industrie; Treatment of multiple sclerosis

Day 30 opinion

Neurology

Summary of Committee discussion:

This application proposes a roughly one-year postponement of the PIP studies, caused by a delay in the adult development. Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan (PIP), 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/0310/2020 of 14 August 2020). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.20. Tolvaptan - EMEA-001231-PIP02-13-M11

Otsuka Pharmaceutical Netherlands B.V.; Treatment of polycystic kidney disease

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism / Uro-nephrology

Note: Withdrawal request received on 12 December 2023

2.3.21. Apremilast - EMEA-000715-PIP02-11-M07

Amgen Europe B.V.; Treatment of juvenile psoriatic arthritis (JPsA) / Treatment of juvenile idiopathic arthritis (JIA)

Day 60 opinion

Immunology-Rheumatology-Transplantation

Note: Withdrawal request received on 28 November 2023

2.3.22. Chikungunya virus, strain CHIKV LR2006-OPY1, live attenuated - EMEA-002873-PIP01-20-M01

Valneva Austria GmbH; Prevention of chikungunya disease

Day 30 opinion

Vaccines

The PDCO adopted the opinion by written procedure on 23 November 2023

2.3.23. Birch bark extract - Orphan - EMEA-001299-PIP03-17-M03

Amryt Pharmaceuticals DAC; Treatment of epidermolysis bullosa

Day 01 opinion

Dermatology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan (PIP), the PDCO considered that the proposed changes concerning the administrative modification were acceptable. The new PIP decision will no longer include a linking article to the PIP covering non-orphan conditions.

The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0243/2023 of 16 June 2023).

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

2.4. Opinions on Re-examinations

2.4.1. Amlitelimab - EMEA-003233-PIP01-22

Sanofi Winthrop Industrie; Treatment of atopic dermatitis

Day 30 opinion

Dermatology

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion on a paediatric investigation plan (PIP) for amlitelimab in children from 6 months to less than 18 years of age was adopted by the PDCO in the condition of treatment of atopic dermatitis.

The Committee agreed on a waiver in children below 6 months 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(s).

The PDCO granted a deferral for the completion of this PIP.

2.4.2. Cedazuridine / decitabine - EMEA-003071-PIP02-23

Otsuka Pharmaceutical Netherlands B.V.; Treatment of myelodysplastic syndromes

Day 30 opinion

Oncology / Haematology-Hemostaseology

Summary of Committee discussion:

The re-examination consisted of requesting a deferral for the initiation of Study 2 to allow the submission of an upcoming regulatory application for an adult indication.

Based on the review of the grounds for re-examination and taking also into account that the study is planned to be started as originally agreed, the PDCO concluded that the amendment of opinion was acceptable.

A positive opinion for the paediatric investigation plan (PIP) for the proposed medicine for patients from 3 months to less than 18 years of age, in the condition of treatment of myelodysplastic syndromes, including juvenile myelomonocytic leukaemia 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 one or more measures contained in the PIP.

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. Botaretigene sparoparvovec - EMEA-C1-002827-PIP01-20-M02

Janssen-Cilag International N.V.; Treatment of retinitis pigmentosa

Day 30 letter

Ophthalmology

2.7.2. Chikungunya virus, strain CHIKV LR2006-OPY1, live attenuated - EMEA-C1-002873-PIP01-20

Valneva Austria GmbH; Prevention of chikungunya disease

Day 30 letter

Vaccines

Note: Withdrawal received on 23 November 2023

2.7.3. Remibrutinib - EMEA-C2-002582-PIP01-19-M03

Novartis Europharm Limited; Treatment of chronic spontaneous urticaria

Day 30 letter

Dermatology

2.7.4. Iptacopan - EMEA-C2-002705-PIP03-20

Novartis Europharm Limited; Treatment of paroxysmal nocturnal haemoglobinuria

Day 30 letter

Other / Haematology-Hemostaseology

2.7.5. Tozinameran, tozinameran / famtozinameran - EMEA-C1-002861-PIP02-20-M06

BioNTech Manufacturing GmbH; Prevention of coronavirus disease 2019 (COVID-19)

Day 30 letter

Infectious Diseases

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. Upadacitinib - EMEA-001741-PIP10-23

Treatment of alopecia areata

Day 90 discussion

Dermatology

3.1.2. Orforglipron - EMEA-003299-PIP02-22

Treatment of obesity

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.3. Sepiapterin - Orphan - EMEA-003027-PIP02-23

PTC Therapeutics International; Treatment of hyperphenylalaninaemia

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.4. Synthetic double-stranded siRNA oligonucleotide directed against apolipoprotein C-III mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues - Orphan - EMEA-003420-PIP01-23

Arrowhead Pharmaceuticals, Inc.; Treatment of familial chylomicronemia syndrome (FCS)

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.5. Dupilumab - EMEA-001501-PIP12-23

Treatment of eosinophilic gastritis / gastroenteritis

Day 90 discussion

Gastroenterology-Hepatology

3.1.6. Ianalumab - EMEA-002338-PIP04-23

Treatment of autoimmune haemolytic anaemia

Day 90 discussion

Haematology-Hemostaseology

3.1.7. Belumosudil - Orphan - EMEA-003425-PIP01-23

Sanofi Winthrop Industrie; Transplant complications / Treatment of graft versus host disease (GVHD)

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.8. Blinatumomab - Orphan - EMEA-000574-PIP03-23

Amgen Europe B.V.; Treatment of B-lymphoblastic leukaemia/lymphoma

Day 90 discussion

Oncology

3.1.9. Clobetasol - EMEA-003458-PIP01-23

Treatment of inflammation and pain associated with ocular surgery

Day 90 discussion

Ophthalmology

3.1.10. Tinlarebant - Orphan - EMEA-003225-PIP01-22

Belite Bio, Inc; Treatment of Stargardt disease

Day 90 discussion

Ophthalmology

3.1.11. Venglustat - Orphan - EMEA-001716-PIP08-23

Sanofi B.V.; Treatment of Fabry disease

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.12. EMEA-003513-PIP01-23

Treatment of coeliac disease

Day 60 discussion

Gastroenterology-Hepatology

3.1.13. Mezagitamab - EMEA-003502-PIP01-23

Treatment of immune thrombocytopenia (ITP)

Day 60 discussion

Haematology-Hemostaseology

3.1.14. Recombinant humanised IgG1, kappa light chain, long-acting monoclonal antibody - EMEA-003510-PIP01-23

Prevention of hereditary angioedema attacks

Day 60 discussion

Haematology-Hemostaseology

3.1.15. Zunsemetinib - EMEA-003511-PIP01-23

Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, and juvenile idiopathic arthritis)

Day 60 discussion

Immunology-Rheumatology-Transplantation

Note: Withdrawal request received on 10 January 2024

3.1.16. Humanised IgG1K monoclonal antibody against interferon beta - Orphan - EMEA-003089-PIP02-23

Pfizer Europe MA EEIG; Treatment of idiopathic inflammatory myopathy (ICD11 4A41)

Day 60 discussion

Immunology-Rheumatology-Transplantation / Dermatology

3.1.17. Contezolid - EMEA-003508-PIP01-23

Acute bacterial skin and skin structure infection (ABSSSI) / Moderate to severe diabetic foot infection (DFI) without concomitant osteomyelitis

Day 60 discussion

Infectious Diseases

3.1.18. Contezolid acefosamil - EMEA-003509-PIP01-23

Acute bacterial skin and skin structure infection (ABSSSI) / Moderate to severe diabetic foot infection (DFI) without concomitant osteomyelitis

Day 60 discussion

Infectious Diseases

3.1.19. Sonrotoclax - EMEA-003489-PIP02-23

Treatment of malignant solid tumours

Day 60 discussion

Oncology

3.1.20. Multivalent, recombinant, N-terminal surface protein vaccine, containing the alpha-like proteins Rib, AlpC, Alp1, Alp 2/3 antigens of *Streptococcus agalactiae* - EMEA-003505-PIP01-23

Prevention of group B streptococcal invasive disease in infants through maternal immunisation

Day 60 discussion

Vaccines

3.1.21. Doruxapapogenum ralaplasmidum (pGX3024) - Orphan - EMEA-003506-PIP01-23

Inovio, Inc.; Treatment of papilloma viral infections

Day 60 discussion

Vaccines / Infectious Diseases

3.1.22. Pegtibatinase - Orphan - EMEA-003518-PIP01-23

Travere Therapeutics Ireland Limited; Treatment of classical homocystinuria / Classical homocystinuria due to CBS-deficiency

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.23. Nomacopan - Orphan - EMEA-003517-PIP01-23

Akari Malta Ltd; Treatment in haematopoietic stem cell transplantation

Day 30 discussion

Haematology-Hemostaseology

3.1.24. Ensitrelvir - EMEA-003192-PIP02-23

Treatment of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Infectious Diseases

3.1.25. Lenacapavir - EMEA-002740-PIP02-23

Prevention of human immunodeficiency virus (HIV-1) infection

Day 30 discussion

Infectious Diseases

3.1.26. EMEA-003515-PIP01-23

Treatment of Parkinson's disease

Day 30 discussion

Neurology

3.1.27. Iptacopan - EMEA-002705-PIP06-23

Treatment of generalised myasthenia gravis (gMG)

Day 30 discussion

Neurology

3.1.28. IgG-like T cell engager binding to DLL3 and CD3 - EMEA-003516-PIP01-23

Treatment of neuroendocrine carcinoma / Treatment of small cell lung carcinoma

Day 30 discussion

Oncology

3.1.29. Interferon gamma / tumour necrosis factor-alpha / granulocyte colony-stimulating factor / interleukin-1 beta, human / interleukin-2 - EMEA-003523-PIP01-23

Treatment of squamous cell carcinoma of the head and neck (SCCHN)

Day 30 discussion

Oncology

3.1.30. Isatuximab - EMEA-002205-PIP02-23

Treatment of malignant neoplasms of the haematopoietic and lymphoid tissue

Day 30 discussion

Oncology

3.1.31. Volrustomig - EMEA-003423-PIP02-23

Treatment of head and neck epithelial malignant neoplasms

Day 30 discussion

Oncology

3.1.32. Zanzalintinib - EMEA-003522-PIP01-23

Treatment of colorectal cancer / Treatment of renal cell carcinoma / Treatment of head and neck squamous cell carcinoma

Day 30 discussion

Oncology

3.1.33. Zenocutuzumab - EMEA-003519-PIP01-23

Treatment of pancreatic cancer / Treatment of lung cancer

Day 30 discussion

Oncology

3.1.34. EMEA-003520-PIP01-23

Treatment of dry eye disease

Day 30 discussion

Ophthalmology

3.1.35. Adeno-associated viral vector serotype 8 containing the 3' human otoferlin coding sequence / adeno-associated viral vector serotype 8 containing the 5' human otoferlin coding sequence - Orphan - EMEA-003524-PIP01-23

Sensorion SA; Treatment of otoferlin gene-mediated hearing loss

Day 30 discussion

Other

3.1.36. Mirdametinib - Orphan - EMEA-003525-PIP01-23

Springworks Therapeutics Ireland Limited; Treatment of neurofibromatosis type 1 - plexiform neurofibroma

Day 30 discussion

Other

3.1.37. Vosoritide - EMEA-002033-PIP02-23

Treatment of hypochondroplasia

Day 30 discussion

Other

3.1.38. Recombinant varicella zoster virus glycoprotein E adjuvanted - EMEA-003526-PIP01-23

Prevention of herpes zoster

Day 30 discussion

Vaccines

3.1.39. Single-stranded 5' capped mRNA encoding the HAs of the influenza virus and the N-terminal domain (NTD) and receptor binding domain (RBD) of the SARS-CoV-2 spike glycoprotein - EMEA-003521-PIP01-23

Prevention of influenza and 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. Pegfilgrastim - EMEA-C-002671-PIP02-20

Accord Healthcare S.L.U.; Prevention of chemotherapy-induced febrile neutropenia

Day 30 discussion

Haematology-Hemostaseology

3.2.2. Casirivimab - EMEA-C-002964-PIP01-21-M02

Roche Registration GmbH; Prevention of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Infectious Diseases

3.2.3. Imdevimab - EMEA-C-002965-PIP01-21-M02

Roche Registration GmbH; Prevention of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Infectious Diseases

3.2.4. Talimogene laherparepvec - EMEA-C-001251-PIP01-11-M06

Amgen Europe B.V.; Treatment of melanoma

Day 30 discussion

Oncology

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Difelikefalin - EMEA-002565-PIP02-19-M01

Vifor Fresenius Medical Care Renal Pharma France; Treatment of chronic kidney disease associated pruritus

Day 30 discussion

Dermatology

3.3.2. Azilsartan medoxomil - EMEA-000237-PIP01-08-M12

Takeda Development Centre Europe Ltd; Treatment of hypertension

Day 30 discussion

Cardiovascular Diseases

3.3.3. Sodium zirconium cyclosilicate - EMEA-001539-PIP01-13-M06

AstraZeneca AB; Treatment of hyperkalaemia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.4. Eluxadoline - EMEA-001579-PIP01-13-M06

AbbVie Limited; Treatment of diarrhoea-predominant irritable bowel syndrome

Day 30 discussion

Gastroenterology-Hepatology

3.3.5. Mepolizumab - EMEA-000069-PIP01-07-M08

GSK Trading Services Limited; Treatment of hypereosinophilic syndrome

Day 30 discussion

Haematology-Hemostaseology

3.3.6. Recombinant human A disintegrin and metalloprotease with thrombospondin type-1 motifs 13 (rADAMTS13) - Orphan - EMEA-001160-PIP01-11-M04

Takeda Pharmaceuticals International AG; Treatment of thrombotic thrombocytopenic purpura

Day 30 discussion

Haematology-Hemostaseology

3.3.7. Upadacitinib - EMEA-001741-PIP04-17-M05

AbbVie Ltd; Treatment of atopic dermatitis

Day 30 discussion

Immunology-Rheumatology-Transplantation / Dermatology

3.3.8. Oritavancin (diphosphate) - EMEA-001270-PIP01-12-M07

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

skin structure infections

Day 30 discussion

Infectious Diseases

3.3.9. Acetyl-L-leucine ((s)-(acetylamino)-4-methylpentanoic acid) - Orphan - EMEA-002796-PIP01-20-M02

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

Day 30 discussion

Neurology

3.3.10. Fordadistrogene movaparvovec - Orphan - EMEA-002741-PIP01-20-M02

Pfizer Europe MA EEIG; Treatment of Duchenne muscular dystrophy

Day 30 discussion

Neurology

3.3.11. Givinostat - Orphan - EMEA-000551-PIP04-21-M03

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

Day 30 discussion

Neurology

3.3.12. Abemaciclib - EMEA-002342-PIP01-18-M04

Eli Lilly and Company Limited; Treatment of Ewing's sarcoma

Day 30 discussion

Oncology

3.3.13. Abemaciclib - EMEA-002342-PIP02-18-M03

Eli Lilly and Company Limited; Treatment of glioma

Day 30 discussion

Oncology

3.3.14. Dinutuximab beta - Orphan - EMEA-001314-PIP01-12-M02

Recordati Netherlands B.V.; Treatment of neuroblastoma

Day 30 discussion

Oncology

3.3.15. Midostaurin - Orphan - EMEA-000780-PIP01-09-M07

Novartis Europharm Limited; Treatment of acute myeloid leukaemia / Treatment of mast cell leukaemia / Treatment of malignant mastocytosis

Day 30 discussion

Oncology

3.3.16. Atropine sulfate - EMEA-002744-PIP01-19-M01

Nevakar Inc.; Treatment of myopia

Day 30 discussion

Ophthalmology

3.3.17. Molgramostim - Orphan - EMEA-002282-PIP01-17-M02

Savara Aps; Treatment of pulmonary alveolar proteinosis

Day 30 discussion

Pneumology - Allergology

3.3.18. Nedosiran - Orphan - EMEA-002493-PIP01-18-M06

Novo Nordisk A/S; Treatment of primary hyperoxaluria

Day 30 discussion

Uro-nephrology

3.3.19. Purified rabies virus, WISTAR PM/WI 38-1503-3M strain (inactivated) - EMEA-002234-PIP01-17-M02

Sanofi Pasteur; Prevention of rabies disease / Treatment of exposure to rabies virus

Day 30 discussion

Vaccines

3.3.20. Recombinant SARS-CoV-2 spike protein - EMEA-002915-PIP01-20-M03

Sanofi Pasteur; Prevention of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Vaccines

3.3.21. Chikungunya virus virus-like particle vaccine / aluminum hydroxide - EMEA-002656-PIP01-19-M01

Bavarian Nordic A/S; Prevention of chikungunya disease

Day 30 discussion

Vaccines / Infectious Diseases

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 03 January 2024 for Nomination of Rapporteur and Peer reviewer

Summary of Committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

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

Summary of Committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

4.3. Nominations for other activities

Summary of Committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

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

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

5.1. New Scientific Advice

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

6. Discussion on the applicability of class waivers

6.1. Discussions on the applicability of class waiver for products

6.1.1. Alvelestat - EMEA-10-2023

Mereo BioPharma Ireland Limited; All classes of medicinal products for treatment of chronic obstructive pulmonary disease (COPD) (excluding chronic lung diseases associated with long-term airflow limitation, such as asthma, bronchopulmonary dysplasia, primary cilia dyskinesia, obstructive lung disease related to graft-versus-host disease after [bone-marrow] transplantation) / Treatment of severe alpha-1 antitrypsin deficiency associated lung disease (AATD-LD), specifically emphysema

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 not confirmed.

This was based on the consideration that the proposed indication will fall within the treatment of AATD and not within the treatment of COPD.

Other potential paediatric interests of this medicine suggested by PDCO: treatment of congenital alpha-1 antitrypsin deficiency (including in particular patients with liver disease).

6.1.2. Mitiperstat - EMEA-12-2023

AstraZeneca AB; All classes of medicinal products for treatment of chronic obstructive pulmonary disease (COPD) (excluding chronic lung diseases associated with long-term airflow limitation, such as asthma, bronchopulmonary dysplasia, primary cilia dyskinesia, obstructive lung disease related to graft-versus-host disease after [bone-marrow] transplantation) / Treatment of COPD with a history of exacerbations

Summary of Committee discussion:

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

Other potential paediatric interests of this medicine suggested by PDCO: non-alcoholic steatohepatitis.

6.1.3. Adeno-associated virus serotype R100 containing VEGF-C and aflibercept transgene - EMEA-13-2023

4D Molecular Therapeutics, Inc.; All classes of medicinal products for treatment of age-related macular degeneration and diabetic macular oedema / Treatment of age-related

macular degeneration (AMD) and diabetic macular oedema (DME)

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.

6.1.4. JNJ-64042056 - EMEA-14-2023

Janssen-Cilag International NV; All classes of medicinal products for treatment of Alzheimer's disease / Treatment of preclinical Alzheimer's disease

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

None

9.1.2. Vote by Proxy

None

9.1.3. Strategic Review and Learning Meeting (SRLM) - Leuven, Belgium 16-17 May 2024

PDCO member: Karen van Malderen

Summary of Committee discussion:

The Committee was updated on the SRLM meeting to be held in Leuven, Belgium.

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 November 2023, was presented to the PDCO members.

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

An overview of discussions on PIP-related procedures, held by the CHMP in November 2023, was provided by a CHMP / PDCO member.

9.2.2. Reflection paper on primary biliary cholangitis (PBC) / primary sclerosing cholangitis (PSC)

PDCO member: Peter Szitanyi

Summary of Committee discussion:

The latest version of the reflection paper on the paediatric section was presented to the Committee.

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

9.3.4. Upcoming Innovation Task Force (ITF) meetings

Summary of Committee discussion:

Two upcoming meetings were presented to the Committee for information.

9.3.5. Methodology Working Party (MWP) - Presentation of reflection paper on use of real-world data to generate real-world evidence in non-interventional studies

Expert: Stine Hasling Mogensen

Summary of Committee discussion:

The PDCO members noted that this draft reflection paper is one of the deliverables related to real-world evidence (RWE) included in the MWP work plan 2022-2024. A summary of the structure and content of the reflection paper was presented to PDCO with an invitation to review the document and share their feedback at the latest by 12 January 2024.

The PDCO members welcomed the reflection paper and asked questions/clarifications regarding the scope of the reflection paper. It was clarified that the reflection paper focuses on the use of real-world data (RWD) in non-interventional studies. The use of RWD in clinical trials is not in scope, though it might be the subject of further RWE guidance.

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 ad hoc 18 December 2023 agenda of the cluster was 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. Work plan for 2024

PDCO Chair: Brian Aylward

Summary of Committee discussion:

The PDCO work plan for 2024 was adopted and has been published.

9.8. Planning and reporting

9.8.1. EMA Business Pipeline activity and Horizon scanning

Q4/2023 Update of the Business Pipeline report for the human scientific committees

Summary of Committee discussion:

The business pipeline report for Q4/2023 was provided for information.

10. Any other business

10.1. Real World Evidence update, including DARWIN EU®

Summary of Committee discussion:

The quarterly update on Real World Evidence, including DARWIN EU was presented to the Committee, for information. This included a summary of the Data Partners within the DARWIN EU Network, which has expanded the network to approximately 128 million active patients across the EU. An overview of the DARWIN EU studies was presented. DARWIN EU study results of interest to the plenary were presented, including treatment patterns of drugs used in adult and paediatric populations with lupus and natural history of dermatomyositis and polymyositis in adult and paediatric populations.

10.2. Research project in paediatric oncology - from PIP to MA - lessons learnt

Summary of Committee discussion:

The findings of the ALADDIN oncology project, carried out during a 6-month rotation project at the EMA, were presented to the Committee.

10.3. First-line tuberculosis products for paediatric patients - EC initiative

PDCO Chair: Brian Aylward

Summary of Committee discussion:

The Committee noted the EC initiative to speed up the development, availability and access to anti-tuberculosis medicines for children.

11. Breakout sessions

11.1. Internal PDCO Operations

Summary of Committee discussion:

Matters related to internal PDCO operations were discussed.

11.2. Paediatric oncology

Summary of Committee discussion:

The group discussed ongoing paediatric procedures. In addition, the 12th Paediatric Strategy Forum for Medicinal Product Development of CDK4/6, CDK 7 and CDK 9 Inhibitors in children and adolescents was reported.

11.3. Neonatology

Summary of Committee discussion:

The group discussed topics for revision of the neonatal guideline.

11.4. HIV

Summary of Committee discussion:

The group discussed ongoing paediatric procedures in the therapeutic area.

11.5. Vaccines

Summary of Committee discussion:

The recent advances in the development in paediatric age appropriate first line tuberculosis medicines were discussed.

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 12-15 December 2023 meeting PDCO meeting, which was held remotely.

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	
Johanna Wernsperger	Member	Austria	No interests declared	
Agnes Gyurasics	Alternate	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 restrictions applicable to this meeting	
Maria Eleni Avraamidou	Alternate	Cyprus	No interests declared	
Tereza Bazantova	Member	Czechia	No interests declared	
Pavlina Chladová	Alternate	Czechia	No interests declared	
Louisa Braun Exner	Member	Denmark	No interests declared	
Jana Lass	Member	Estonia	No interests declared	
Liisa Saare	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	
Sara Galluzzo	Member	Italy	No interests declared	
Cinzia Ciceroni	Alternate	Italy	No interests declared	
Dina Apele-Freimane	Member	Latvia	No participation in discussion, final deliberations and voting on:	2.3.12. Ceftobiprole medocaril sodium - EMEA-000205-PIP02-11-M06
Greta	Alternate	Lithuania	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Budukeviciute				
Carola de Beaufort	Member	Luxembourg	No restrictions applicable to this meeting	
Olivier Moes	Alternate	Luxembourg	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	
Sara Vennberg	Member	Sweden	No interests declared	
David Khan	Alternate	Sweden	No restrictions applicable to this meeting	
Johannes Taminiau	Alternate	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	
Tomasz Grybek	Member	Patients' Organisation Representative	No interests declared	
Jaroslav Sterba	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
Viviana Giannuzzi	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Patricia Felgueiras Seabra Durao	Alternate	Patients' Organisation Representative	No restrictions applicable to this meeting	
Victoria Romero Pazos	Alternate	Patients' Organisation Representative	No interests declared	
Celine Chu	Expert	France	No interests declared	
María Estela Moreno Martín	Expert	Spain	No interests declared	
Stine Hasling Mogensen	Expert	Denmark	No interests declared	
Olga Kholmanskikh	Expert	Belgium	No interests declared	
Maja Sommerfelt Grønvold	Expert	Norway	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/