16 December 2022
EMA/PDCO/903993/2022
Human Medicines Division

Paediatric Committee (PDCO)

Minutes for the meeting on 08-11 November 2022

Chair: Brian Aylward – Vice-Chair: Sylvie Benchetrit

Disclaimers

Some of the information contained in this set of minutes is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published in the PDCO Committee meeting reports (after the PDCO Opinion is adopted), and on the Opinions and decisions on paediatric investigation plans webpage (after the EMA Decision is issued).

Of note, this set of minutes is a working document primarily designed for PDCO members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
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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. Due to the current coronavirus (COVID-19) pandemic, and the associated EMA Business Continuity Plan (BCP), the meeting was held remotely.

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and on the topics in the agenda of the meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics.

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

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure. All decisions taken at this meeting were made in the presence of a quorum of members. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. Adoption of agenda

The agenda for 08-11 November 2022 meeting was adopted with amendments.

1.3. Adoption of the minutes

The minutes for 11-14 October 2022 meeting were adopted and will be published on the EMA website.

2. Opinions

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

2.1. Opinions on Products

2.1.1. Obefazimod - EMEA-003196-PIP01-22

Abivax; Treatment of ulcerative colitis / 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 the paediatric population from 2 years to less than 18 years of age, in the conditions of treatment of Crohn's disease, treatment of ulcerative colitis was adopted. The PDCO agreed on a waiver in a subset of children from birth to less than 2 years of age on the grounds of lack of significant benefit over existing treatments. The PDCO granted a deferral for the completion of this PIP.

2.1.2. Inclacumab - EMEA-003219-PIP01-22

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

Day 120 opinion

Haematology-Hemostaseology

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the PIP for the proposed medicine for children from birth to less than 6 months of age, in the condition of treatment of sickle cell disease was adopted. The PDCO agreed on a waiver in a subset of children on the grounds 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.

2.1.3. HIV-1 maturation inhibitor (GSK3640254) / dolutegravir - EMEA-003152-PIP01-21

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

Day 120 opinion

Infectious Diseases

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, the additional information provided by the applicant, the inclusion in the opinion of some key elements reflecting additional requirements made by the PDCO, a positive opinion for the PIP for the proposed medicine for the age subset from 2 years to less than 18 years of age, in the condition treatment of human immunodeficiency virus infection (HIV-1) was adopted. The PDCO agreed on a waiver in a subset of children on the grounds of that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments. The PDCO granted a deferral for the completion of this PIP. The estimated date of completion of the PIP is open to revision when the results of the pivotal adult studies for the treatment of virologically suppressed patients are available.

2.1.4. HIV-1 maturation inhibitor (GSK3640254) - EMEA-003153-PIP01-21

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

Day 120 opinion

Infectious Diseases

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, the additional information provided by the applicant, the inclusion in the opinion of some key elements reflecting additional requirements made by the PDCO, a positive opinion for the PIP for the proposed medicine for the age subset from 6 years to less than 18 years of age, in the condition treatment of human immunodeficiency virus infection was adopted. The PDCO agreed on a waiver in a subset of children on the grounds of clinical studies not feasible. The PDCO granted a deferral for the completion of this PIP.

2.1.5. Posoleucel - Orphan - EMEA-002908-PIP01-20

AlloVir International DAC; Treatment of viral diseases in haematopoietic stem cell transplantation

Day 120 opinion

Infectious Diseases

Summary of Committee discussion:

In the written response, and during an oral explanation before the Committee on 9 November 2022, 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 posoleucel for all paediatric age subsets, in the condition of treatment of viral diseases in haematopoietic stem cell transplantation was adopted.

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

Roche Registration GmbH; Treatment of spinal muscular atrophy

Day 120 opinion

Neurology

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 and adolescents from 2 months to less than 18 years of age, in the condition of spinal muscular atrophy was adopted. The PDCO agreed on a waiver in a subset of children on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s). The PDCO granted a deferral for the completion of this PIP.

2.1.7. Pridopidine (hydrochloride) - Orphan - EMEA-003174-PIP01-21

Prilenia Therapeutics B.V.; Treatment of Huntington disease (HD)

Day 120 opinion

Neurology

Summary of Committee discussion:

The PDCO discussed at Day 120, during the November 2022 plenary meeting, an application for a paediatric investigation plan, a waiver and a deferral for pridopidine (hydrochloride) for treatment of Huntington disease.
The Committee confirmed all conclusions reached at Day 90 and took into consideration further information provided by the applicant between Day 90 and Day 120.
The PDCO adopted a positive opinion on a paediatric investigation plan with a deferral and a waiver for children under the age of 2 years on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible in the treatment of Huntington's disease.

2.1.8. Vodobatinib - EMEA-003014-PIP01-21

Treatment of chronic myeloid leukaemia

Day 120 opinion

Oncology

Note: Withdrawal request received on 04 November 2022

2.1.9. Enzastaurin hydrochloride - Orphan - EMEA-003096-PIP02-22

Aytu BioPharma Inc.; Treatment of Ehlers-Danlos syndrome

Day 120 opinion

Other

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 adolescents from 12 years to less than 18 years of age in the condition of treatment of Ehlers-Danlos syndrome was adopted. The PDCO agreed on a waiver in a subset of children on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2.1.10. Depemokimab - EMEA-003051-PIP04-22

GlaxoSmithKline Trading Services Limited; Treatment of eosinophilic granulomatosis with polyangiitis (EGPA)

Day 120 opinion

Pneumology - Allergology

Summary of Committee discussion:

The PDCO discussed at Day 120, during the November 2022 plenary meeting, an application for a paediatric investigation plan with a deferral and a waiver for depemokimab for treatment of eosinophilic granulomatosis with polyangiitis (EGPA).
The Committee confirmed all conclusions reached at Day 90 and took into consideration further information provided by the applicant between Day 90 and Day 120.
The PDCO adopted a positive opinion on a paediatric investigation plan with a deferral and a waiver for children from birth to less than 6 years of age on grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible eosinophilic granulomatosis with polyangiitis.

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

Biocodex SA; Treatment of primary hyperoxaluria

Day 120 opinion

Uro-nephrology

Summary of Committee discussion:

Prior to Day 120, the applicant satisfactorily addressed the minor issues that were identified at Day 90. Therefore, the PDCO adopted a positive opinion. The agreed PIP for stiripentol for the treatment of primary hyperoxaluria covers all paediatric age-groups from birth to less than 18 years of age. The completion of the PIP is deferred.

2.1.12. Live, attenuated, dengue virus, serotype 4 (DENV4) / Live, attenuated, dengue virus, serotype 3 (DENV3) / Live, attenuated, chimeric dengue virus, serotype 2 (DENV2) / Live, attenuated, dengue virus, serotype 1 (DENV1) - EMEA-002999-PIP01-21

Merck Sharp & Dohme (Europe), Inc.; Prevention of dengue disease

Day 120 opinion

Vaccines

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed on a positive opinion for a PIP for live, attenuated, dengue virus, serotype 3 (DENV3) / live, attenuated, dengue virus, serotype 1 (DENV1) / live, attenuated, chimeric dengue virus, serotype 2 (DENV2) / live, attenuated, dengue virus, serotype 4 (DENV4) for all subsets of the paediatric population (0 to 18 years of age) in the condition of prevention of dengue disease in children from 2 months of age to less than 18 years of age.
The PIP contains five clinical studies, a deferral, and a waiver below 2 months of age on the grounds that the specific medicinal product is likely to be ineffective in this age group.

2.1.13. Rivaroxaban / acetylsalicylic acid - EMEA-003291-PIP01-22

PharOS Pharmaceutical Oriented Services Single Member Ltd; Prevention of atherothrombotic events

Day 60 opinion

Cardiovascular Diseases

Summary of Committee discussion:

The PDCO has rediscussed this application on D60.
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 rivaroxaban / acetylsalicylic acid for all subsets of the paediatric population (birth to 18 years of age) in the condition of prevention of atherothrombotic events. With the applicant’s agreement the PDCO granted the waiver for all pharmaceutical forms and routes of administration as the condition does not occur in children.
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. Eplerenone / torasemide - EMEA-003289-PIP01-22

WIN MEDICA S.A.; Treatment of heart failure

Day 60 opinion

Cardiovascular Diseases

Summary of Committee discussion:

The PDCO has rediscussed this application on D60.
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 eplerenone / torasemide for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of heart failure.
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.

2.1.15. Indapamide / valsartan - EMEA-003285-PIP01-22

KRKA, d.d., Novo mesto; Treatment of hypertension

Day 60 opinion

Cardiovascular Diseases

Summary of Committee discussion:

The PDCO has re-discussed this application on D60.
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 indapamide / valsartan for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of hypertension.
The PDCO emphasised that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.16. Rosuvastatin (calcium) / fenofibrate - EMEA-003295-PIP01-22

Althera Laboratories Ltd; Treatment of elevated cholesterol with elevated triglycerides

Day 60 opinion

Cardiovascular Diseases

Summary of Committee discussion:

The PDCO has rediscussed this application on D60.
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 rosuvastatin (calcium) / fenofibrate for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of elevated cholesterol with elevated triglycerides.
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.

2.1.17. Messenger RNA encoding Cas9 and single guide RNA targeting the human TTR gene - Orphan - EMEA-003298-PIP01-22

Intellia Therapeutics, Inc.; Treatment of transthyretin amyloidosis (ATTR)

Day 60 opinion

Cardiovascular Diseases / Neurology

Summary of Committee discussion:

The PDCO confirmed the outcome of Day 30 discussion and 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 messenger RNA encoding Cas9 and single guide RNA targeting the human TTR gene for all subsets of the paediatric population (from birth to less than 18 years of age) for the condition of treatment of transthyretin amyloidosis on the grounds that the specific medicinal product does not represent a

significant therapeutic benefit over existing treatments for the paediatric population.

2.1.18. Eplontersen - EMEA-003294-PIP01-22

AstraZeneca AB; Treatment of transthyretin amyloidosis

Day 60 opinion

Neurology

Summary of Committee discussion:

The PDCO confirmed the outcome of Day 30 discussion and 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 eplontersen for all subsets of the paediatric population (from birth to less than 18 years of age) for the condition of treatment of transthyretin amyloidosis on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for the paediatric population.

2.1.19. Unesbulin - Orphan - EMEA-003297-PIP01-22

PTC Therapeutics International; Treatment of soft tissue sarcoma

Day 60 opinion

Oncology

Note: Withdrawal request received on 11 November 2022

2.1.20. Treprostinil (palmitil) - EMEA-003204-PIP01-22

Insmed Netherlands B.V.; Treatment of pulmonary hypertension due to lung disease and/or hypoxia

Day 60 opinion

Pneumology - Allergology

Summary of Committee discussion:

This application has been re-discussed by the PDCO on D60.
Based on the assessment of this application and further discussions at the Paediatric Committee including assessment of the clarifications from the applicant, the PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for treprostinil (palmitil) for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of pulmonary hypertension due to lung disease and/or hypoxia as the 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. The PDCO identified treatment of pulmonary arterial hypertension as an additional unmet 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. Tozinameran, tozinameran / famtozinameran - EMEA-002861-PIP02-20-M05

Prevention of coronavirus disease 2019 (COVID-19)

Day 30 opinion

Infectious Diseases

The PDCO adopted the opinion by written procedure on 04 November 2022

2.1.22. Ezeprogind - Orphan - EMEA-003320-PIP01-22

Alzprotect S.A.S., France; Treatment of progressive supranuclear palsy

Day 30 opinion

Neurology

Summary of Committee discussion:

The PDCO discussed at Day 30, during the November 2022 plenary meeting, an application for a full waiver for ezeprogind for treatment of progressive supranuclear palsy.
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 ezeprogind for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of treatment of progressive supranuclear palsy.
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 Niemann-Pick disease type C (NPC) or neurodegeneration with brain iron accumulation (NBIA) as an unmet 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. Edoxaban tosilate - EMEA-C-000788-PIP02-11-M11

Daiichi Sankyo Europe GmbH; Treatment of venous thromboembolism

Day 30 opinion

Cardiovascular Diseases / Haematology-Hemostaseology

Summary of Committee discussion:

The PDCO agreed that all studies were conducted in compliance with the PIP.

2.2.2. Baricitinib - EMEA-C-001220-PIP03-16-M02

Eli Lilly and Company; Treatment of atopic dermatitis

Day 30 opinion

Dermatology

Summary of Committee discussion:

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

- EMEA-C1-001220-PIP01-11
- EMEA-C1-001220-PIP03-16
- EMEA-C2-001220-PIP01-11-M06
- EMEA-C2-001220-PIP03-16-M01
- EMEA-C3-001220-PIP03-16-M02

The PDCO adopted on 11 November 2022 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's decision (P/0311/2021) of 11 August 2021.

2.2.3. Recombinant 10 kDa culture filtrate protein of *Mycobacterium tuberculosis* (rCFP-10) / recombinant dimer of *Mycobacterium tuberculosis* 6 kDa early secretory antigenic target (rdESAT-6) - EMEA-C-001156-PIP01-11-M07

Vakzine Projekt Management GmbH; Diagnosis of tuberculosis

Day 30 opinion

Diagnostic

Summary of Committee discussion:

PDCO concluded with adoption of a positive opinion on the compliance check confirming all studies have been performed in compliance with the latest PIP decision.

2.2.4. Alogliptin - EMEA-C-000496-PIP01-08-M08

Takeda Development Centre Europe Ltd; Treatment of type 2 diabetes mellitus

Day 30 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

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

- EMEA-C1-000496-PIP01-08-M02

The PDCO adopted on 11 November 2022 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's decision (P/0257/2020) of 15 July 2020.
The PDCO considers that the following studies could be considered significant:
Study 4, (SYR-322_104)
Study 5, (SYR-322_309).

2.2.5. Denosumab - EMEA-C1-000145-PIP02-12-M04

Amgen Europe B.V.; Treatment of osteoporosis

Day 30 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

The PDCO confirmed the completed Study 3 and considered that it is compliant with the latest Agency's decision (P/0213/2021) of 21 May 2021.
The PDCO finalised this partially completed compliance procedure on 11 November 2022.

2.2.6. Naloxegol (as naloxegol oxalate) - EMEA-C-001146-PIP01-11-M07

Kyowa Kirin Pharmaceutical Development Limited; Treatment of opioid-induced constipation

Day 30 opinion

Gastroenterology-Hepatology

Summary of Committee discussion:

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

- EMEA-C1-001146-PIP01-11

The PDCO adopted on 11 November 2022 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's decision (P/0493/2021) of 3 December 2021.

2.2.7. Dabrafenib - EMEA-C-001147-PIP01-11-M07

Novartis Europharm Limited; Treatment of melanoma

Day 30 opinion

Oncology

Summary of Committee discussion:

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

- EMEA-C1-001147-PIP01-11
- EMEA-C2-001147-PIP01-11-M01
- EMEA-C3-001147-PIP01-11-M07

The PDCO adopted on 11 November 2022 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's decision (P/0410/2020) of 23 October 2020.

2.2.8. Trametinib - EMEA-C-001177-PIP01-11-M06

Novartis Europharm Limited; Treatment of melanoma

Day 30 opinion

Oncology

Summary of Committee discussion:

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

- EMEA-C1-001177-PIP01-11-M01
- EMEA-C2-001177-PIP01-11-M06

The PDCO adopted on 11 November 2022 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's decision (P/0392/2020) of 23 October 2020.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Baricitinib - EMEA-001220-PIP03-16-M03

Eli Lilly and Company Limited; Treatment of atopic dermatitis

Day 60 opinion

Dermatology

Note: Withdrawal request received on 24 October 2022

2.3.2. Dupilumab - EMEA-001501-PIP04-19-M02

Regeneron Ireland DAC; Treatment of eosinophilic esophagitis

Day 60 opinion

Gastroenterology-Hepatology

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/0361/2021 of 8 September 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.3. Linaclotide - EMEA-000927-PIP01-10-M07

AbbVie Deutschland GmbH & Co KG; Treatment of functional constipation

Day 60 opinion

Gastroenterology-Hepatology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as

set in the Agency's latest decision (P/0216/2021 of 8 June 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.4. Odevixibat - Orphan - EMEA-002054-PIP03-20-M02

Albireo AB; Treatment of Alagille syndrome

Day 60 opinion

Gastroenterology-Hepatology

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/0368/2022 of 9 September 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.5. Upadacitinb - EMEA-001741-PIP02-16-M02

AbbVie Ltd; Treatment of ulcerative colitis

Day 60 opinion

Gastroenterology-Hepatology

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/0068/2019 of 22 March 2019).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.6. (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 / ritonavir - EMEA-003081-PIP01-21-M02

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

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 application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The opinion was also updated to include the fixed-dose combination of (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 (PF-07321332) / ritonavir as part of the PIP.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0566/2021 of 21 December 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.7. Doravirine - EMEA-001676-PIP01-14-M05

Merck Sharp & Dohme (Europe), Inc.; Treatment of human immunodeficiency virus-1 (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 some of the proposed changes could be accepted.
A postponement in the date of completion of the PIP from January 2026 to November 2029 was requested by the applicant which was not fully justified in the view of the PDCO who agreed that completion date of the PIP should not be prolonged beyond November 2028.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0177/2021 of 12 April 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.8. Lefamulin - EMEA-002075-PIP01-16-M03

Nabriva Therapeutics DAC; Treatment of community-acquired pneumonia

Day 60 opinion

Infectious Diseases

Summary of Committee discussion:

In the written response the applicant addressed some of 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/0066/2019 of 22 March 2019).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.9. Tecovirimat monohydrate - Orphan - EMEA-001205-PIP02-19-M02

SIGA Technologies, Inc.; Treatment of the following viral infections in adults and children with body weight at least 13 kg: smallpox, monkeypox, cowpox. Also indicated to treat complications due to replication of vaccinia virus following vaccination against smallpox in

adults and children with body weight at least 13 kg

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 some of the proposed changes to the dates of the studies and to the deferral could not be accepted. The PDCO also decided to delete Study 8 as it is not the definitive relative bioavailability study.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0496/2021 of 3 December 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.10. Tenofovir disoproxil fumarate / lamivudine / doravirine - EMEA-001695-PIP01-14-M05

Merck Sharp & Dohme (Europe), Inc.; Treatment of human immunodeficiency virus-1 (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 some of the proposed changes could be accepted. Regarding the proposed conclusion date of the clinical Study 5, common to EMEA-001676-PIP01-14-M05 the PDCO convened that the study should not be protracted beyond December 2027 (the applicant had initially proposed November 2029). Therefore, this was agreed as a conclusion date.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0176/2021 of 12 April 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.11. Givinostat - Orphan - EMEA-000551-PIP04-21-M01

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

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 some 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/0062/2022 of 11 March 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.12. Ofatumumab - EMEA-002397-PIP01-18-M03

Novartis Ireland Limited; Treatment of multiple sclerosis

Day 60 opinion

Neurology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that 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/0121/2022 of 15 April 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.13. Siponimod (hemifumarate) - EMEA-000716-PIP01-09-M05

Novartis Europharm Ltd; Treatment of multiple sclerosis

Day 60 opinion

Neurology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that 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/0119/2022 of 13 April 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.14. Entospletinib - Orphan - EMEA-002058-PIP01-16-M01

Kronos Bio Inc.; Treatment of acute myeloid leukaemia

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed at Day 60, during the November 2022 plenary meeting, a request for modification for entospletinib for the treatment of acute myeloid leukaemia.
The applicant requested to delete the requirement to perform certain non-clinical assays in two non-clinical studies and to substantially delay their completion.
Based on the review of the documentation submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be acceptable. Therefore, the PDCO adopted a positive opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0285/2017 of 4 October 2017). The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.15. Imetelstat - Orphan - EMEA-001910-PIP03-20-M01

Geron Corporation; Treatment of acute myeloid leukaemia (AML) / Treatment of myelodysplastic syndromes (MDS), including juvenile myelomonocytic leukaemia (JMML)

Day 60 opinion

Oncology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0099/2021 of 19 March 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.16. Lenvatinib - EMEA-001119-PIP03-19-M03

Eisai GmbH; Treatment of all conditions included in the category of malignant neoplasms except haematopoietic and lymphoid tissue neoplasms, papillary thyroid cancer, follicular thyroid cancer and osteosarcoma

Day 60 opinion

Oncology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0154/2022 of 13 May 2022).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.17. Characterised peanut powder - EMEA-001753-PIP02-15-M01

Cambridge Allergy Ltd; Treatment of peanut allergy

Day 60 opinion

Other

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/0151/2016 of 14 June 2016).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.18. Setrusumab - Orphan - EMEA-002169-PIP01-17-M02

Mereo Biopharma 3 Ltd; Treatment of osteogenesis imperfecta

Day 60 opinion

Other

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that most of the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0241/2018 of 15 August 2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.19. Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extract of *Betula alba* pollen (birch pollen) - EMEA-000630-PIP02-09-M05

LETI Pharma GmbH; Treatment of allergic rhinitis / rhino-conjunctivitis

Day 60 opinion

Pneumology - Allergology

Summary of Committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed.
The PDCO adopted a negative opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0013/2014 of 22 January 2014).
Therefore, the measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver remain unchanged.

2.3.20. Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extract of birch pollen - EMEA-000837-PIP01-10-M02

LETI Pharma GmbH; Treatment of allergic rhinitis / rhino-conjunctivitis

Day 60 opinion

Pneumology - Allergology

Summary of Committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed.
The PDCO therefore adopted a negative opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0004/2012 of 23 January 2012). The measures and timelines of the agreed paediatric investigation plan and the subset of the paediatric population and condition covered by the waiver remain unchanged.

2.3.21. Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extracts of birch, alder and hazel pollen - EMEA-000662-PIP02-09-M05

LETI Pharma GmbH; Treatment of allergic rhinitis / rhino-conjunctivitis

Day 60 opinion

Pneumology - Allergology

Summary of Committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed.
The PDCO therefore adopted a negative opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0014/2014 of 22 January 2014).
Therefore, the measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver remain unchanged.

2.3.22. Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extracts of birch, alder and hazel pollen - EMEA-000838-PIP01-10-M02

LETI Pharma GmbH; Treatment of allergic rhinitis / rhino-conjunctivitis

Day 60 opinion

Pneumology - Allergology

Summary of Committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed.
The PDCO therefore adopted a negative opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0005/2012 of 23 January 2012). The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver remain unchanged.

2.3.23. Modified vaccinia Ankara - Bavarian Nordic virus (smallpox) - EMEA-001161-PIP02-11-M02

Bavarian Nordic A/S; Prevention of smallpox, monkeypox and disease caused by vaccinia virus

Day 60 opinion

Vaccines

Summary of Committee discussion:

In line with the Day 30 discussion, the PDCO accepted most of the changes proposed by the applicant.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0038/2012 of 24 February 2012).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.24. COVID-19 vaccine (Ad26.COV2-S [recombinant]) - EMEA-002880-PIP01-20-M01

Janssen-Cilag International N.V.; Prevention of coronavirus disease 2019 (COVID-19)

Day 60 opinion

Vaccines / Infectious Diseases

Summary of Committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO agreed with the applicant's request to modify the PIP into a waiver for the entire paediatric population based on the grounds of lack of significant therapeutic benefit over existing vaccines. This was based on the consideration that it will be not feasible to clearly define/quantify the risk of thrombosis with thrombocytopenia syndrome in the paediatric population, the course of COVID-19 is generally mild in the paediatric population, and other vaccines with a better known safety profile, are authorised in the paediatric population.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0059/2021 of 5 February 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.4. Opinions on Re-examinations

No item

2.5. Opinions on Review of Granted Waivers

No item

2.6. Finalisation and adoption of Opinions

No item

2.7. Partial Compliance Checks completed by EMA

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

2.7.1. *N. meningitidis* serogroup A polysaccharide conjugated to tetanus toxoid / *N. meningitidis* serogroup C polysaccharide conjugated to tetanus toxoid / *N. meningitidis* serogroup W polysaccharide conjugated to tetanus toxoid / *N. meningitidis* serogroup Y polysaccharide conjugated to tetanus toxoid - EMEA-C3-001930-PIP01-16-M04

Sanofi Pasteur; Prevention of invasive meningococcal disease

Day 30 letter

Vaccines

2.7.2. Live, attenuated dengue virus, serotype 2 / Live, attenuated, chimeric dengue virus, serotype 4 / Live, attenuated, chimeric dengue virus, serotype 3 / Live, attenuated, chimeric dengue virus, serotype 1 - EMEA-C2-001888-PIP01-15-M01

Takeda Vaccines, Inc.; Prevention of dengue fever

Day 30 letter

Vaccines

2.7.3. Nivolumab - EMEA-C4-001407-PIP02-15-M05

Bristol-Myers Squibb Pharma EEIG; Treatment of malignant neoplasms of lymphoid tissue

Day 30 letter

Oncology

2.7.4. Nirsevimab - EMEA-C3-001784-PIP01-15-M04

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

Day 30 letter

Infectious Diseases

2.7.5. Migalastat hydrochloride - EMEA-C2-001194-PIP01-11-M05

Amicus Therapeutics Europe Limited; Treatment of Fabry disease

Day 30 letter

Endocrinology-Gynaecology-Fertility-Metabolism

2.7.6. Enmetazobactam / cefepime - EMEA-C1-002240-PIP02-17-M01

Allecra Therapeutics GmbH; Treatment of urinary tract infections

Day 30 letter

Infectious Diseases

2.7.7. Tezacaftor / ivacaftor / elexacaftor - EMEA-C4-002324-PIP01-17-M03

Vertex Pharmaceuticals (Ireland) Limited; Treatment of cystic fibrosis

Day 30 letter

Other

2.7.8. Fidanacogene elaparvovec - EMEA-C1-002362-PIP02-19-M02

Pfizer Europe MA EEIG; Treatment of congenital factor IX deficiency (haemophilia B)

Day 30 letter

Haematology-Hemostaseology

2.7.9. Lisocabtagene maraleucel - EMEA-C3-001995-PIP01-16-M03

Bristol-Myers Squibb Pharma EEIG; Treatment of mature B cell neoplasms

Day 30 letter

Oncology

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. Asundexian - EMEA-003144-PIP01-21

Prevention of arterial thromboembolism

Day 90 discussion

Cardiovascular Diseases

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

Treatment of familial chylomicronaemia syndrome

Day 90 discussion

Cardiovascular Diseases

3.1.3. Perflubutane - EMEA-003037-PIP02-22

Diagnostic evaluation of focal hepatic lesions

Day 90 discussion

Diagnostic / Oncology

3.1.4. Avexitide acetate - Orphan - EMEA-003125-PIP02-21

EigerBio Europe Limited; Treatment of congenital hyperinsulinism

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.5. Triheptanoin - Orphan - EMEA-001920-PIP04-19

Ultragenyx Germany GmbH; Treatment of long-chain fatty acid oxidation disorders (LC-FAOD)

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.6. Depemokimab - EMEA-003051-PIP05-22

Treatment of hypereosinophilic syndrome (HES)

Day 90 discussion

Haematology-Hemostaseology

3.1.7. Satralizumab - Orphan - EMEA-001625-PIP04-22

Roche Registration GmbH; Treatment of autoimmune encephalitis

Day 90 discussion

Neurology

3.1.8. Troriluzole (hydrochloride) - Orphan - EMEA-003084-PIP03-22

Biohaven Pharmaceutical Ireland DAC; Treatment of hereditary spinocerebellar ataxia

Day 90 discussion

Neurology

3.1.9. Autologous CD4+ and CD8+ T cells transduced with lentiviral vector encoding a chimeric antigen receptor (CAR) directed against CD19 and preserving the T cell phenotype of the leukapheresis starting material - EMEA-003212-PIP01-22

Treatment of mature B cell neoplasms

Day 90 discussion

Oncology

3.1.10. Fianlimab - EMEA-003207-PIP01-22

Treatment of melanoma

Day 90 discussion

Oncology

3.1.11. Naxitamab - Orphan - EMEA-002346-PIP01-18

Y-mAbs Therapeutics A/S; Short-term symptomatic treatment of pain / Treatment of

neuroblastoma

Day 90 discussion

Oncology

3.1.12. Tirzepatide - EMEA-002360-PIP02-22

Treatment of obesity

Day 90 discussion

Other

3.1.13. Dexmedetomidine - EMEA-003283-PIP01-22

Sedation

Day 60 discussion

Anaesthesiology

3.1.14. EMEA-003286-PIP01-22

Treatment of atopic dermatitis

Day 60 discussion

Dermatology

3.1.15. Isotretinoin - EMEA-003303-PIP01-22

Treatment of congenital ichthyosis

Day 60 discussion

Dermatology

3.1.16. EMEA-003301-PIP01-22

Treatment of psoriasis

Day 60 discussion

Dermatology

3.1.17. Spesolimab - EMEA-002475-PIP03-22

Treatment of Netherton syndrome

Day 60 discussion

Dermatology

3.1.18. EMEA-003299-PIP01-22

Treatment of type 2 diabetes mellitus

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.19. EMEA-003299-PIP02-22

Treatment of obesity

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.20. Wharton’s jelly derived mesenchymal stromal cells - EMEA-003287-PIP01-22

Treatment of type 1 diabetes mellitus

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.21. Crofelemer - Orphan - EMEA-003296-PIP01-22

Napo Therapeutics S.p.A.; Treatment of short bowel syndrome

Day 60 discussion

Gastroenterology-Hepatology

3.1.22. Dirloctocogene samoparvovec - Orphan - EMEA-003290-PIP01-22

Spark Therapeutics Ireland Limited; Treatment of haemophilia A

Day 60 discussion

Haematology-Hemostaseology

3.1.23. Mocravimod - Orphan - EMEA-003304-PIP01-22

Priothera SAS; Treatment in haematopoietic stem cell transplantation (HSCT)

Day 60 discussion

Haematology-Hemostaseology

3.1.24. Adintrevimab - EMEA-003118-PIP02-22

Treatment of coronavirus disease 2019 (COVID-19)

Day 60 discussion

Infectious Diseases

3.1.25. Ensitrelvir - EMEA-003192-PIP01-22

Treatment of coronavirus disease 2029 (COVID-19)

Day 60 discussion

Infectious Diseases

3.1.26. EMEA-003288-PIP01-22

Treatment of developmental and epileptic encephalopathies and other seizure syndromes

Day 60 discussion

Neurology

3.1.27. Humanised VHH-type bispecific antibody against complement component 5 and serum albumin - EMEA-003302-PIP01-22

Treatment of acetylcholine receptor-antibody positive generalised myasthenia gravis

Day 60 discussion

Neurology

3.1.28. Vesleteplirsen - EMEA-003305-PIP01-22

Treatment of Duchenne muscular dystrophy

Day 60 discussion

Neurology

3.1.29. Obinutuzumab - Orphan - EMEA-001207-PIP06-22

Roche Registration GmbH; Prevention of cytokine release syndrome induced by anti CD20/CD3 antibodies

Day 60 discussion

Oncology

3.1.30. Humanised IgG4 monoclonal antibody against A proliferation-inducing ligand - Orphan - EMEA-003300-PIP01-22

Chinook Therapeutics, Inc.; Treatment of IgA nephropathy

Day 60 discussion

Uro-nephrology

3.1.31. Furosemide - EMEA-003316-PIP01-22

Treatment of fluid retention

Day 30 discussion

Cardiovascular Diseases

3.1.32. Landiolol - EMEA-001150-PIP03-22

Treatment of ventricular arrhythmias

Day 30 discussion

Cardiovascular Diseases

3.1.33. Ziltivekimab - EMEA-002840-PIP02-22

Treatment of heart failure

Day 30 discussion

Cardiovascular Diseases

3.1.34. Barzolvolimab - EMEA-003327-PIP01-22

Treatment of chronic spontaneous urticaria

Day 30 discussion

Dermatology

3.1.35. Efgartigimod alfa - EMEA-002597-PIP09-22

Treatment of bullous pemphigoid

Day 30 discussion

Dermatology

3.1.36. Povorcitinib - EMEA-003313-PIP01-22

Treatment of hidradenitis suppurativa

Day 30 discussion

Dermatology

3.1.37. Rilzabrutinib - EMEA-002438-PIP03-22

Treatment of atopic dermatitis

Day 30 discussion

Dermatology

3.1.38. Ritlecitinib - EMEA-002451-PIP03-22

Treatment of vitiligo

Day 30 discussion

Dermatology

3.1.39. Upadacitinib - EMEA-001741-PIP07-22

Treatment of vitiligo

Day 30 discussion

Dermatology

3.1.40. Recombinant human glutamic acid dexarboxylase (rhGAD65) - EMEA-000609-PIP02-22

Prevention or delay of clinical type 1 diabetes mellitus / Prevention of type 1 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.41. Setanaxib - Orphan - EMEA-003310-PIP01-22

Calliditas Therapeutics France SAS; Treatment of primary biliary cholangitis

Day 30 discussion

Gastroenterology-Hepatology

3.1.42. Acetylsalicylic acid / rivaroxaban - EMEA-003308-PIP01-22

Prevention of atherothrombotic events

Day 30 discussion

Haematology-Hemostaseology

3.1.43. Ciraparantag - EMEA-003321-PIP01-22

Treatment of FXa inhibitor-associated haemorrhage / Prevention of FXa inhibitor-associated haemorrhage

Day 30 discussion

Haematology-Hemostaseology

3.1.44. Izokibep - EMEA-003325-PIP01-22

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

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.45. EMEA-003326-PIP01-22

Treatment of infections caused by gram-negative organisms / Complicated urinary tract infections (cUTI) / Hospital associated pneumonia or ventilator associated pneumonia

Day 30 discussion

Infectious Diseases

3.1.46. Lenacapavir / bictegravir - EMEA-003324-PIP01-22

Treatment of human immunodeficiency virus (HIV-1) infection

Day 30 discussion

Infectious Diseases

3.1.47. Luminol - EMEA-003322-PIP01-22

Treatment of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Infectious Diseases

3.1.48. Posoleucel - Orphan - EMEA-002908-PIP02-22

Allovir International DAC; Prevention of viral disease in haematopoietic stem cell transplantation (HCT)

Day 30 discussion

Infectious Diseases

3.1.49. RNA replicase inhibitor - EMEA-003306-PIP01-22

Treatment of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Infectious Diseases

3.1.50. Icerguastat - Orphan - EMEA-003312-PIP01-22

InFlectis BioScience S.A.S; Treatment of amyotrophic lateral sclerosis

Day 30 discussion

Neurology

3.1.51. Retifanlimab - Orphan - EMEA-002798-PIP03-22

Incyte Biosciences Distribution B.V.; Treatment of Merkel cell carcinoma

Day 30 discussion

Oncology

3.1.52. Uproleselan - Orphan - EMEA-003307-PIP01-22

GlycoMimetics, Inc.; Treatment of acute myeloid leukaemia

Day 30 discussion

Oncology

3.1.53. Vutrisiran - Orphan - EMEA-002425-PIP02-22

Alnylam Netherlands B.V.; Treatment of Stargardt disease

Day 30 discussion

Ophthalmology

3.1.54. Dersimelagon - EMEA-002850-PIP03-22

Treatment of systemic sclerosis

Day 30 discussion

Other

3.1.55. mRNA encoding modified human ornithine transcarbamylase - Orphan - EMEA-003315-PIP01-22

Arcturus Therapeutics Europe B.V.; Treatment of ornithine transcarbamylase deficiency / Treatment of ornithine transcarbamylase deficiency, which is characterised by episodes of hyperammonemia and consequent sequelae

Day 30 discussion

Other

3.1.56. Dexpramipexole - EMEA-003328-PIP01-22

Treatment of asthma

Day 30 discussion

Pneumology - Allergology

3.1.57. Pamrevlumab - EMEA-002979-PIP04-22

Treatment of interstitial lung diseases with fibrosis

Day 30 discussion

Pneumology - Allergology

3.1.58. EMEA-003319-PIP01-22

Treatment of borderline personality disorder (BPD)

Day 30 discussion

Psychiatry

3.1.59. EMEA-003319-PIP02-22

Treatment of major depressive disorder (MDD)

Day 30 discussion

Psychiatry

3.1.60. EMEA-003319-PIP03-22

Treatment of post-traumatic stress disorder (PTSD)

Day 30 discussion

Psychiatry

3.1.61. Influenza recombinant H7 haemagglutinin - EMEA-003314-PIP01-22

Prevention of influenza infection

Day 30 discussion

Vaccines

3.1.62. Phuket modRNA / Darwin modRNA / Austria modRNA / Wisconsin modRNA - EMEA-003318-PIP01-22

Prevention of influenza disease

Day 30 discussion

Vaccines

3.1.63. Single-stranded 5' capped mRNA encoding the respiratory syncytial virus glycoprotein F stabilised in the prefusion conformation - EMEA-003309-PIP01-22

Prevention of lower respiratory tract illness (LRTI) caused by respiratory syncytial virus (RSV)

Day 30 discussion

Vaccines

3.1.64. Tetanus toxoid - EMEA-003311-PIP01-22

Prevention of infectious disease caused by *Clostridium tetani*

Day 30 discussion

Vaccines

3.1.65. Live attenuated varicella virus - EMEA-003317-PIP01-22

Prevention of varicella

Day 30 discussion

Vaccines / Infectious Diseases

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. Ivacaftor [N-(2,4-Di-tert-butyl-5-hydroxyphenyl)-1,4-dihydro-4-oxoquinoline-3-carboxamide] - EMEA-C-000335-PIP01-08-M14

Vertex Pharmaceuticals (Ireland) Limited; Treatment of cystic fibrosis

Day 30 discussion

Other

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Macitentan - Orphan - EMEA-001032-PIP01-10-M05

Janssen-Cilag International NV; Treatment of systemic sclerosis / Treatment of pulmonary arterial hypertension / Treatment of idiopathic pulmonary fibrosis

Day 30 discussion

Cardiovascular Diseases

3.3.2. Human, recombinant, non-fucosylated IgG1k monoclonal antibody targeting OX-40 receptor on activated T cells - EMEA-002886-PIP01-20-M02

Amgen Europe B.V.; Treatment of atopic dermatitis

Day 30 discussion

Dermatology

3.3.3. Avatrombopag maleate - EMEA-001136-PIP01-11-M02

Swedish Orphan Biovitrum AB; Treatment of chronic immune thrombocytopenia

Day 30 discussion

Haematology-Hemostaseology

3.3.4. Crovalimab - EMEA-002709-PIP01-19-M01

Roche Registration GmbH; Treatment of atypical haemolytic uremic syndrome / Treatment of paroxysmal nocturnal haemoglobinuria

Day 30 discussion

Haematology-Hemostaseology

3.3.5. Garadacimab - Orphan - EMEA-002726-PIP01-19-M03

CSL Behring GmbH; Prevention of hereditary angioedema attacks

Day 30 discussion

Haematology-Hemostaseology

3.3.6. Allogeneic bone marrow derived mesenchymal stromal cells, ex-vivo expanded - Orphan - EMEA-002706-PIP01-19-M02

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

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.7. Avibactam / ceftazidime - EMEA-001313-PIP01-12-M13

Pfizer Europe MA EEIG; Treatment of bacterial infections

Day 30 discussion

Infectious Diseases

3.3.8. Aztreonam / avibactam - EMEA-002283-PIP01-17-M04

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

Day 30 discussion

Infectious Diseases

3.3.9. Cobicistat / atazanavir sulphate - EMEA-001465-PIP01-13-M05

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

Day 30 discussion

Infectious Diseases

3.3.10. Cobicistat / darunavir - EMEA-001280-PIP01-12-M05

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

Day 30 discussion

Infectious Diseases

3.3.11. Lamivudine (3TC) / abacavir (ABC) / dolutegravir (DTG) - EMEA-001219-PIP01-11-M06

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

Day 30 discussion

Infectious Diseases

3.3.12. Tazobactam / ceftolozane - EMEA-001142-PIP02-16-M01

Merck Sharp & Dohme (Europe), Inc.; Treatment of pneumonia

Day 30 discussion

Infectious Diseases

3.3.13. Tenofovir alafenamide / emtricitabine / cobicistat / darunavir - EMEA-001825-PIP01-15-M04

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

Day 30 discussion

Infectious Diseases

3.3.14. Isoflurane - EMEA-002320-PIP01-17-M03

Sedana Medical AB; Sedation of mechanically ventilated patients

Day 30 discussion

Neonatology - Paediatric Intensive Care

3.3.15. Fordadistrogene movaparvovec - Orphan - EMEA-002741-PIP01-20-M01

Pfizer Europe MA EEIG; Treatment of Duchenne muscular dystrophy

Day 30 discussion

Neurology

3.3.16. Galcanezumab - EMEA-001860-PIP03-16-M08

Eli Lilly and Company Limited; Prevention of migraine headache

Day 30 discussion

Neurology

3.3.17. Evoncabtagene pazurgedleucel - EMEA-002881-PIP01-20-M01

CRISPR Therapeutics AG; Treatment of B-lymphoblastic leukaemia/lymphoma / Treatment of mature B cell neoplasms

Day 30 discussion

Oncology

3.3.18. Calcium chloride / aprotinin / thrombin / fibrinogen - EMEA-001079-PIP01-10-M06

Kedrion S.p.A.; Treatment of haemorrhage resulting from a surgical procedure / Prevention of haemorrhage resulting from a surgical procedure

Day 30 discussion

Other

3.3.19. Lanadelumab - Orphan - EMEA-001864-PIP03-19-M01

Takeda Pharmaceuticals International AG Ireland Branch; Prevention of attacks of idiopathic non-histaminergic angioedema (INHA)

Day 30 discussion

Other

3.3.20. Azelastine hydrochloride / mometasone furoate - EMEA-003122-PIP01-21-M01

Lek Pharmaceuticals d.d.; Treatment of seasonal allergic rhinitis

Day 30 discussion

Oto-rhino-laryngology

3.3.21. Zuranolone - EMEA-003119-PIP01-21-M01

Biogen Netherlands B.V.; Treatment of postpartum depression

Day 30 discussion

Psychiatry

3.3.22. Mirabegron - EMEA-000597-PIP02-10-M09

Astellas Pharma Europe B.V.; Treatment of idiopathic overactive bladder

Day 30 discussion

Uro-nephrology

3.3.23. Synthetic double-stranded siRNA oligonucleotide directed against lactate dehydrogenase A mRNA and containing four modified nucleosides which form a ligand cluster of four N-acetylgalactosamine residues (DCR-PHXC, nedosiran) - Orphan - EMEA-002493-PIP01-18-M05

Dicerna Ireland Limited; Treatment of primary hyperoxaluria

Day 30 discussion

Uro-nephrology

3.3.24. *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-M01

Pfizer Europe MA EEIG; Invasive disease caused by *Neisseria meningitidis* group A, B, C, W and Y from 12 months of age to less than 18 years of age.

Day 30 discussion

Vaccines

3.3.25. SARS-CoV-2 virus, beta-propiolactone inactivated adjuvanted with CpG 1018 (VLA2001) - EMEA-003077-PIP01-21-M01

Valneva Austria GmbH; Prevention of coronavirus disease 2019 (COVID-19)

Day 30 discussion

Vaccines

4. Nominations

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

4.1. List of submissions of applications with start of procedure 21 November 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:

No item

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. Follow up Scientific Advice

6. Discussion on the applicability of class waivers

6.1. Discussions on the applicability of class waiver for products

6.1.1. Humanised recombinant IgG1 monoclonal antibody (ABBV-916) – EMEA-05-2022

AbbVie Ltd.; All classes of medicinal products for treatment of Alzheimer’s disease; Treatment of early 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

No item

9.1.2. Vote by Proxy

None

9.2. Coordination with EMA Scientific Committees or CMDh-v

9.2.1. Committee for Medicinal Products for Human Use (CHMP)

Summary of Committee discussion:

The list of PIP-related CHMP procedures starting in October 2022, was presented to the PDCO members.

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 interim*)

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. EMA Emergency task force (ETF) – Endorsement PDCO nomination

PDCO member: Brian Aylward

Summary of Committee discussion:

The Chair informed the Committee that Nanna Borup Johansen has become member of the Task Force.

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 October and November 2022 agenda and October 2022 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. Draft Workplan for 2023

PDCO Chair: Brian Aylward

Summary of Committee discussion:

The Committee discussed the draft PDCO workplan for 2023.

9.8. Planning and reporting

No item

10. Any other business

10.1. Conditions for orphan designation in inherited retinal diseases

Summary of Committee discussion:

The PDCO was updated on the outcome of the Committee on Orphan Medicine Products (COMP) review on the policy on Orphan Designations (OD) for inherited retinal dystrophies (IRD). This included the scientific and regulatory rationale for this change, details of the expert consultation, then amended policy, and the potential next steps for communications.

10.2. COVID-19 update

Summary of Committee discussion:

The update was cancelled.

10.3. Evolutionary PIP

Summary of Committee discussion:

The evolutionary PIP and the plan for the next steps was discussed.

10.4. Reflection paper on Digital Support to Risk Minimisation

Summary of Committee discussion:

The PDCO was informed about the recently started development of a reflection paper on digital support to risk minimisation measures and the evaluation of effectiveness of such measures and invited to participate with one or two PDCO representatives. The reflection paper is being developed by a multi-stakeholder drafting group under the oversight of PRAC in 2023 and public consultation is foreseen in 2023. The reflection paper will describe potential options of digital support tools, their opportunities and challenges alongside possible solutions with reference to broader EU initiatives on digitalisation of healthcare. This presentation will be followed about by a written call for interest to PDCO.

10.5. Revision of Paediatric Addendum on venous thromboembolism (VTE) treatment and prevention

Summary of Committee discussion:

The Paediatric Addendum on venous thromboembolism was adopted.

10.6. Upcoming Innovation Task Force (ITF) meetings

Summary of Committee discussion:

Three ITF meetings taking place in November 2022 were presented for information.

10.7. Upcoming Multi-regional Clinical Trials (MRCT) webinar

Summary of Committee discussion:

The PDCO was informed about an upcoming webinar series organised by the MRCT centre on models of global cooperation to facilitate paediatric medicines development.

11. Breakout sessions

11.1. Internal PDCO Operations

Summary of Committee discussion:

The PDCO discussed matters relating to internal operations.

11.2. Paediatric oncology

Summary of Committee discussion:

The group discussed procedures under assessment of the CHMP relevant to paediatrics as well as issues related to PIPs under PDCO assessment.

11.3. Vaccines

Summary of Committee discussion:

The group discussed developments in respiratory syncytial virus (RSV) vaccines.

The Chair thanked all participants and closed the meeting.

12. List of participants

List of participants including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 08-11 November 2022 meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Brian Aylward	Chair	Ireland	No interests declared	
Karl-Heinz Huemer	Member	Austria	No interests declared	
Marleen Renard	Member	Belgium	No participation in final deliberations and voting on:	2.2.5. Dabrafenib - EMEA-C-001147-PIP01-11-M07 2.2.3. Trametinib - EMEA-C-001177-PIP01-11-M06
Karen Van Malderen	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Zena Gunther	Member	Cyprus	No interests declared	
Tereza Bazantova	Alternate	Czechia	No interests declared	
Nanna Borup Johansen	Member	Denmark	No interests declared	
Louisa Braun Exner	Alternate	Denmark	No interests declared	
Jana Lass	Alternate	Estonia	No interests declared	
Pauliina Lehtolainen-Dalkilic	Member	Finland	No interests declared	
Anne Paavola	Alternate	Finland	No interests declared	
Sylvie Benchetrit	Member (Vice-Chair)	France	No interests declared	
Dominique Ploin	Alternate	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	
Ágnes Gyurasics	Member (CHMP alternate)	Hungary	No interests declared	
Sara Galluzzo	Member	Italy	No interests declared	
Dina Apele-Freimane	Member	Latvia	No participation in discussion, final	2.7.4. Nirsevimab - EMEA-C3-001784-

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			deliberations and voting on:	PIP01-15-M04
Dovile Zacharkiene	Member	Lithuania	No interests declared	
Carola de Beaufort	Member	Luxembourg	No restrictions applicable to this meeting	
Olivier Moes	Alternate	Luxembourg	No interests declared	
Herbert Lenicker	Alternate	Malta	No interests declared	
Roderick Houwen	Member	Netherlands	No participation in final deliberations and voting on:	2.3.4. Odevixibat - Orphan - EMEA-002054-PIP03-20-M02
Maaike van Dartel	Alternate	Netherlands	No interests declared	
Siri Wang	Member	Norway	No interests declared	
Anette Solli Karlsen	Alternate	Norway	No interests declared	
Marek Migdal	Member	Poland	No restrictions applicable to this meeting	
Helena Fonseca	Member	Portugal	No interests declared	
Hugo Tavares	Alternate	Portugal	No interests declared	
Dana Gabriela Marin	Member (CHMP alternate)	Romania	No interests declared	
Peter Sisovsky	Member	Slovakia	No interests declared	
Peter Szitanyi	Alternate	Slovakia	No interests declared	
Stefan Grosek	Member	Slovenia	No interests declared	
Fernando de Andrés Trelles	Member	Spain	No interests declared	
Maria Jesus Fernández Cortizo	Alternate	Spain	No interests declared	
Kristin Karlsson	Member	Sweden	No restrictions applicable to this meeting	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Fernando Cabanas	Member	Healthcare Professionals' Representative	No participation in final deliberations and voting on:	2.7.4. Nirsevimab - EMEA-C3-001784-PIP01-15-M04
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	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jaroslav Sterba	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Tomasz Grybek	Alternate	Patients' Organisation Representative	No interests declared	
María Estela Moreno Martín	Expert - via telephone*	Spain	No interests declared	
Katarina Lindahl	Expert - via telephone*	Sweden	No restrictions applicable to this meeting	
Lisbeth Barkholt	Expert - via telephone*	Sweden	No interests declared	
Elina Rönnemaa	Expert - via telephone*	Sweden	No interests declared	
Janet Koenig	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/