17 December 2021
EMA/PDCO/687396/2021
Human Medicines Division

Paediatric Committee (PDCO)

Minutes for the meeting on 9-12 November 2021

Chair: Koenraad Norga – Vice-Chair: Sabine Scherer

Disclaimers

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

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

Note on access to documents

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

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1. Introductions

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

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

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some meeting participants in upcoming discussions as included in the pre-meeting list of participants and restrictions.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 17 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

Due to restricted involvement, the Chair Koenraad Norga deputised chairing the meeting to the Vice-Chair Sabine Scherer for the agenda topic(s) 3.1.25.

1.2. Adoption of agenda

The agenda for 9-12 November 2021 meeting was adopted with amendments.

1.3. Adoption of the minutes

The minutes for 12-15 October 2021 meeting were adopted and will be published on the EMA website.

2. Opinions

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

2.1. Opinions on Products

2.1.1. Autologous CD34+ hematopoietic stem cells with a CRISPR-edited erythroid enhancer region of the BCL11A gene - Orphan - EMEA-002730-PIP03-21

Vertex Pharmaceuticals (Ireland) Limited; 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 and adolescents from 6 months to less than 18 years of age, in the condition of treatment of sickle cell disease was adopted. The PDCO agreed on a waiver in a subset of children on the grounds of lack of significant therapeutic benefit over existing treatments. The PDCO granted a deferral for the completion of this PIP.

2.1.2. Autologous CD34+ hematopoietic stem cells with a CRISPR-edited erythroid enhancer region of the BCL11A gene - Orphan - EMEA-002730-PIP04-21

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

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 and adolescents from 6 months to less than 18 years of age, in the condition of treatment of beta-thalassemia intermedia and major was adopted. The PDCO agreed on a waiver in a subset of children on the grounds of lack of significant therapeutic benefit over existing treatments. The PDCO granted a deferral for the completion of this PIP.

2.1.3. Leniolisib - Orphan - EMEA-002989-PIP01-21

Pharming Group N.V.; Treatment of activated phosphoinositide 3-kinase delta syndrome (APDS)

Day 120 opinion

Immunology-Rheumatology-Transplantation

Summary of Committee discussion:

In the written responses, the applicant addressed the remaining issues raised by the Committee at D90. The planned oral explanation was cancelled.
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 treatment of activated

phosphoinositide 3-kinase delta syndrome, in the condition of treatment of activated phosphoinositide 3-kinase delta syndrome was adopted by majority. The PDCO agreed on a waiver in a subset of children from birth to less than 1 year of age on the ground of lack of safety. The PDCO granted a deferral for the completion of this PIP.

2.1.4. Exebacase - EMEA-002947-PIP01-20

ContraFect Corporation; Treatment of *Staphylococcus aureus* bacteraemia

Day 120 opinion

Infectious Diseases

Summary of Committee discussion:

The PDCO view expressed at Day 30 was re-discussed and endorsed.
The Committee adopted a positive opinion for the PIP, including a deferral for the paediatric, modelling & simulation and extrapolation studies.

2.1.5. Tosatoxumab - Orphan - EMEA-002506-PIP03-21

Aridis Pharmaceuticals Inc; Treatment of *Staphylococcus aureus* pneumonia

Day 120 opinion

Infectious Diseases / Pneumology - Allergology

Summary of Committee discussion:

In November 2021 the PDCO noted the clarification provided by the applicant and agreed a PIP for tosatoxumab in the condition treatment of *Staphylococcus aureus* pneumonia with a deferral.
The PIP includes one quality measure, two clinical studies a modelling and simulation study and an extrapolation study.

2.1.6. 2'-O-(2-methoxyethyl) modified antisense oligonucleotide targeting glial fibrillary acidic protein pre-mRNA (ION373) - Orphan - EMEA-002822-PIP01-20

Ionis Pharmaceuticals; Treatment of Alexander disease

Day 120 opinion

Neurology

Summary of Committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the applicant's modified proposal for a paediatric investigation plan. A positive opinion endorsing the PIP has therefore been adopted.

2.1.7. Vatiquinone - Orphan - EMEA-001238-PIP03-21

PTC Therapeutics International; Treatment of Friedreich's ataxia

Day 120 opinion

Neurology

Summary of Committee discussion:

Taking into account information submitted between Day 90 and Day 120 the PDCO adopted a positive opinion on this PIP for the condition "treatment of Friedreich's ataxia", covering all paediatric age groups.

2.1.8. Repotrectinib - EMEA-002635-PIP02-21

Premier Research SLU; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic neoplasms)

Day 120 opinion

Oncology

Summary of Committee discussion:

Based on the assessment of this application and the additional information provided by the applicant, a positive opinion for the PIP for repotrectinib for treatment of patients from birth to less than 19 years of age with advanced or metastatic malignancies harbouring NTRK1-3 fusions that have been pretreated with a TRK tyrosine kinase inhibitor, in the condition of treatment of all conditions included in the category of malignant neoplasms (except haematopoietic neoplasms). The PDCO granted a deferral for the completion of this PIP.

2.1.9. Efgartigimod alfa - EMEA-002597-PIP07-21

argenx; Treatment of pemphigus

Day 60 opinion

Dermatology

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 efgartigimod alfa for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of pemphigus on the grounds that the specific medicinal product is likely to be unsafe for the subset from birth to less than 2 years of age and on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible for the subset from 2 years to 18 years of age.

2.1.10. Secukinumab - EMEA-000380-PIP08-21

Novartis Europharm Limited; Treatment of vasculitides

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of Committee discussion:

Based on the assessment of this application and discussions at the Paediatric Committee the

PDCO agreed with the applicant's request for a waiver. The PDCO recommended granting a waiver for the proposed medicine for all subsets of the paediatric population from birth to less than 18 years of age for the condition of treatment of vasculitides on the grounds of lack of 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.

2.1.11. Phenylephrine / acetylcysteine / paracetamol - EMEA-003091-PIP01-21

HEXAL AG; Treatment of upper respiratory tract infections

Day 60 opinion

Infectious Diseases / Oto-rhino-laryngology

Summary of Committee discussion:

Based on the assessment of this application the PDCO agreed with the applicant's request for a waiver.
The PDCO granted a waiver for paracetamol / acetylcysteine / phenylephrine for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of upper respiratory tract infections.

2.1.12. Troriluzole - EMEA-003084-PIP01-21

Treatment of spinocerebellar ataxia

Day 60 opinion

Neurology

Note: Withdrawal request received on 29 October 2021

2.1.13. Humanised IgG2k Fc-modified bispecific antibody against CD3 and BCMA (PF-06863135) - Orphan - EMEA-003083-PIP01-21

Pfizer Europe MA EEIG; Treatment of multiple myeloma

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed at Day 60, during the November 2021 plenary meeting, an application for a waiver for humanised IgG2k Fc-modified bispecific antibody against CD3 and BCMA (PF-06863135) for the 'treatment of multiple myeloma' on the grounds that the disease does not occur in the paediatric population.
The PDCO confirmed all conclusions reached at Day 30 and adopted a positive opinion on a product specific waiver for humanised IgG2k Fc-modified bispecific antibody against CD3 and BCMA (PF-06863135) for all subsets of the paediatric population (from birth to less than

18 years of age) in the condition of treatment of multiple myeloma on the grounds that the disease does not occur in the paediatric population.
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. Milademetan tosilate - Orphan - EMEA-003093-PIP01-21

Rain Therapeutics, Inc.; Treatment of liposarcomas

Day 60 opinion

Oncology

Note: Withdrawal request received on 11 November 2021

2.1.15. Molnupiravir - EMEA-002940-PIP02-21

Prevention 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 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 birth to less than 18 years of age, in the condition of prevention of coronavirus disease 2019 (COVID-19), was adopted. The PDCO granted a deferral for the completion of this PIP.

2.1.16. Plitidepsin - Orphan - EMEA-000095-PIP02-21

Pharma Mar, S.A.; Treatment of coronavirus disease 2019 (COVID-19)

Day 60 opinion

Infectious Diseases

Summary of Committee discussion:

Based on the assessment of this application and discussions at the Paediatric Committee, the PDCO disagrees with the applicant's proposal for the paediatric investigation plan for plitidepsin. The PDCO therefore recommends granting a waiver for all subsets of the paediatric population from birth to less than 18 years of age in the condition of treatment of coronavirus disease 2019 (COVID-19) of its own motion based on the grounds that the specific medicinal product is likely to be unsafe.

2.2. Opinions on Compliance Check

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

2.2.1. Landiolol hydrochloride - EMEA-C1-001150-PIP02-13-M04

Orpha-Devel Handels und Vertriebs GmbH; Treatment of supraventricular arrythmias

Day 60 letter

Cardiovascular Diseases

Note: Withdrawal request received on 3 November 2021

2.2.2. Nivolumab - EMEA-C3-001407-PIP02-15-M05

Bristol-Myers Squibb Pharma EEIG; Treatment of malignant neoplasms of lymphoid tissue and treatment of malignant neoplasms of the central nervous system

Day 30 letter

Oncology

Summary of Committee discussion:

The PDCO took note of the conclusions on the compliance check on Study 1 (CA209070). The study was considered to have been completed in compliance with the latest Agency's Decision (P/0237/2021) of 14 June 2021.
The PDCO finalised this partially completed compliance procedure on 12 November 2021.

2.2.3. PEGylated-fibroblast growth factor 21 (BMS-986036) - EMEA-C1-002448-PIP01-18-M02

Bristol-Myers Squibb International Corporation; Treatment of non-alcoholic steatohepatitis (NASH)

Day 30 letter

Gastroenterology-Hepatology

Summary of Committee discussion:

The PDCO discussed the completed studies 3, 4 and 5, and considered that these are compliant with the latest Agency's Decision (P/0346/2021) of 18 August 2021.
The PDCO finalised this partially completed compliance procedure on 12 November 2021.

2.2.4. Selpercatinib - EMEA-C2-002544-PIP01-18-M01

Eli Lilly and Company; 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 discussed the completed study and considered that these are compliant with the latest Agency's Decision P/0398/2021 of 30 September 2021.
The PDCO finalised this partially completed compliance procedure on 12 November 2021.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Nemolizumab - EMEA-001624-PIP01-14-M04

Galderma International S.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, the PDCO considered that the proposed changes could be accepted.
The Committee adopted a favourable opinion on the modification of the agreed PIP as set in the Agency’s latest decision (P/0253/2021 of 9 July 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.2. Alirocumab - EMEA-001169-PIP01-11-M05

sanofi-aventis recherche & développement; Treatment of elevated cholesterol

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency’s latest decision (P/0047/2018 of 19 February 2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.3. Estetrol / drospirenone - EMEA-001332-PIP01-12-M05

Estetra SRL; Prevention of pregnancy

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be

accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0478/2020 of 1 December 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.4. Romosozumab - EMEA-001075-PIP04-15-M04

UCB Pharma S.A.; Treatment of osteoporosis

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

In November 2021 the PDCO discussed the replies presented by the applicant to the issues raised at D30 and presented also their views in an oral explanation.

Based on these considerations, the PDCO agreed on removing studies 4 and 5 from the opinion and adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0255/2021 of 9 July 2021).

This PIP would no longer cover for a glucocorticoid induced osteoporosis (GIOP) indication, therefore, should the applicant reconsider development in adults they will need to liaise with the PDCO to address this aspect.

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

2.3.5. Tirzepatide - EMEA-002360-PIP01-18-M01

Eli Lilly and Company Ltd; Treatment of type 2 diabetes mellitus

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0311/2019 of 10 September 2019).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.6. Vedolizumab - EMEA-000645-PIP01-09-M08

Takeda Pharma A/S; Treatment of Crohn's disease / 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/0361/2020 of 05 October 2020).

2.3.7. Crizanlizumab - Orphan - EMEA-002141-PIP01-17-M03

Novartis Europharm Limited; Treatment of sickle cell disease

Day 60 opinion

Haematology-Hemostaseology

Summary of Committee discussion:

In the written response, the applicant addressed the remaining issues raised by the Committee. Based on the review of the rationale submitted by the 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/0379/2019 of 4 December 2019).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.8. Giroctocogene fitelparvovec - Orphan - EMEA-002724-PIP01-19-M02

Pfizer Europe MA EEIG; Treatment of haemophilia A

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, 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/0332/2021 of 05/08/2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.9. Tozinameran - EMEA-002861-PIP02-20-M03

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

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 overall 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/0179/2021 of 23 April 2021).

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

2.3.10. Fully human IgG1 RB-1 YTE anti-RSV F monoclonal antibody (MK-1654) - EMEA-002755-PIP01-19-M01

Merck Sharp & Dohme (Europe), Inc.; Prevention of lower respiratory tract infection caused by respiratory syncytial virus

Day 60 opinion

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 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/0486/2020 issued on 22 December 2020.
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.11. Fenfluramine (hydrochloride) - Orphan - EMEA-001990-PIP01-16-M04

Zogenix International Ltd; Treatment of Dravet syndrome

Day 60 opinion

Neurology

Summary of Committee discussion:

Between Day 30 and Day 60 the applicant provided further information on the outstanding issues.
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/0475/2020 of 1 December 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.12. Risdiplam - Orphan - EMEA-002070-PIP01-16-M06

Roche Registration GmbH; Treatment of spinal muscular atrophy

Day 60 opinion

Neurology

Summary of Committee discussion:

The PDCO confirmed the outcome of the Day 30 discussion and agreed with the changes to the key elements related to the design of the PIP Study 6. Completion dates of Study 6, 7 and 8 were also changed.

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the discussed and appropriately worded 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/0089/2020 issued on 18 March 2020).

2.3.13. Avelumab - EMEA-001849-PIP02-15-M04

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

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 change 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/0504/2020 of 22 December 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.14. Eribulin - EMEA-001261-PIP01-11-M07

Eisai GmbH; Treatment of soft tissue sarcoma

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed at day 60, during the November 2021 plenary meeting, a modification for eribulin for the treatment of soft tissue sarcoma.
The applicant requested to remove a clinical study from the PIP. This will result in a waiver for children less than 6 months of age and in a modification of the deferral. In addition, the applicant requested to modify some key elements of three clinical studies.
The PDCO confirmed all the conclusions reached at day 30. Therefore, the PDCO adopted a positive opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0040/2021 of 27 January 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.15. Lisocabtagene maraleucel - Orphan - EMEA-001995-PIP01-16-M03

Bristol-Myers Squibb Pharma EEIG; Treatment of mature B cell neoplasms / Treatment of B-lymphoblastic leukaemia/lymphoma

Day 60 opinion

Oncology

Summary of Committee discussion:

The PDCO re-discussed at day 60, during the November 2021 plenary meeting, a modification for lisocabtagene maraleucel for the treatment of B-lymphoblastic leukaemia/lymphoma and the treatment of mature B cell neoplasms.
The applicant requests to delay PIP completion.
The PDCO confirmed all the conclusions reached at day 30 and adopted a positive opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0198/2019 of 12 June 2019).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.16. Pembrolizumab - EMEA-001474-PIP02-16-M02

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

Day 60 opinion

Oncology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0008/2018 of 30 January 2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.17. Alpelisib - Orphan - EMEA-002016-PIP03-19-M01

Novartis Europharm Limited; Treatment of PIK3CA related overgrowth spectrum

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/0329/2020 of 17 August 2020).

2.3.18. Human thrombin (component 2) / Human fibrinogen (component 1) - EMEA-001598-PIP01-13-M04

Instituto Grifols, S.A.; Treatment of haemorrhage resulting from a surgical procedure

Day 60 opinion

Other

Note: Withdrawal request received on 29 October 2021

2.3.19. Palovarotene - Orphan - EMEA-001662-PIP01-14-M05

Ipsen Pharma; Treatment of fibrodysplasia ossificans progressiva

Day 60 opinion

Other

Summary of Committee discussion:

The PDCO re-discussed at day 60, during the November 2021 plenary meeting, a modification for palovarotene for the treatment of fibrodysplasia ossificans progressiva. The applicant requested a waiver for younger children and to modify the wording of some key binding elements.
After further discussion, the PDCO adopted a positive opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0441/2020 of 1 December 2020).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.20. Nedosiran (DCR-PHXC) - Orphan - EMEA-002493-PIP01-18-M03

Dicerna Ireland Limited; Treatment of primary hyperoxaluria

Day 60 opinion

Uro-nephrology

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0071/2021 of 17 March 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.21. COVID-19 Vaccine (ChAdOx1-S [recombinant]) - EMEA-002862-PIP01-20-M02

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

Day 30 opinion

Vaccines

Summary of Committee discussion:

The PDCO discussed the modification request on 11 November 2021. The request refers to the start of the adolescent study (Study 4) and subsequent modifications of the timelines of the other studies.
During the previous modification it was agreed that Study 4, which is the first study in the paediatric population, would not start until the mechanism and risk factors for thrombotic-thrombocytopenic syndrome (TTS) in adults have been established to allow a decision on the initiation of the study, and a provisional date for discussion of the state of knowledge of TTS with PDCO and potential re-start of the study had been set to November 2021. Since there are no major advancements in what is known of mechanisms and risk factors of TTS, the applicant requested that this date is postponed to an undetermined time in the future.

The PDCO agreed to the request since at the moment the risk of TTS in young populations cannot be excluded. This implied re-planning the dates of all paediatric studies in the PIP, which were set at later timepoints than what proposed by the applicant in the modification, in order to maintain the age-descending time alignment between studies. The opinion with the revised date was shared with the applicant before PDCO.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0266/2021 of 7 July 2021).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.4. Opinions on Re-examinations

2.4.1. Perflubutane - EMEA-003037-PIP01-21

GE Healthcare AS; Diagnostic evaluation of focal hepatic lesions

Day 30 opinion

Diagnostic / Oncology

Summary of Committee discussion:

The applicant attended the PDCO meeting on November 10th of 2021 and gave an oral explanation followed by a discussion with the PDCO members concerning this product specific waiver request re-examination. Based on the discussions, the PDCO concluded to maintain its initial position to a negative opinion on this waiver request at the time of the re-examination.

2.4.2. CX-024414 (single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free in vitro transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2) - EMEA-002893-PIP01-20-M01

MODERNA BIOTECH SPAIN, S.L.; Prevention of coronavirus disease 2019 (COVID-19)

Day 30 opinion

Vaccines / Infectious Diseases

Summary of Committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan and the grounds for re-examination, 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/0481/2020.

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

2.5. Opinions on Review of Granted Waivers

No item

2.6. Finalisation and adoption of Opinions

No item

2.7. Partial Compliance Checks completed by EMA

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

2.7.1. Finerenone - EMEA-C2-001623-PIP01-14-M04

Bayer AG; Treatment of chronic kidney disease

Day 30 letter

Uro-nephrology

2.7.2. Sparsentan - EMEA-C1-001984-PIP02-20

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

Day 30 letter

Uro-nephrology

2.7.3. Tenofovir alafenamide - EMEA-C1-001584-PIP01-13-M06

Gilead Sciences International Ltd.; Treatment of chronic viral hepatitis B

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. EMEA-002958-PIP01-21

Treatment of hypertrophic cardiomyopathy

Day 90 discussion

Cardiovascular Diseases

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

Gossamer Bio 002 Limited; Treatment of pulmonary arterial hypertension

Day 90 discussion

Cardiovascular Diseases

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

Treatment of psoriasis

Day 90 discussion

Dermatology

3.1.4. EMEA-002992-PIP01-21

Treatment of fibrodysplasia ossificans progressiva (FOP)

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.5. Ethinyl estradiol / dienogest - EMEA-002229-PIP02-21

Treatment of polycystic ovary syndrome

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

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

Ascendis Pharma Bone Diseases A/S; Treatment of hypoparathyroidism

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

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

Spruce Biosciences, Inc.; Treatment of congenital adrenal hyperplasia

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.8. Benralizumab - EMEA-001214-PIP07-21

Treatment of eosinophilic gastritis/eosinophilic gastroenteritis

Day 90 discussion

Gastroenterology-Hepatology

3.1.9. Izencitinib - EMEA-002757-PIP02-21

Treatment of Crohn's disease

Day 90 discussion

Gastroenterology-Hepatology

3.1.10. 6-[(3S,4S)-4-methyl-1-(pyrimidin-2-ylmethyl)pyrrolidin-3-yl]-3-tetrahydropyran-4-yl-7H-imidazo[1,5-a]pyrazin-8-one - Orphan - EMEA-002991-PIP01-21

IMARA Inc; Treatment of sickle cell disease

Day 90 discussion

Haematology-Hemostaseology

3.1.11. Benralizumab - EMEA-001214-PIP04-19

Treatment of hypereosinophilic syndrome (HES)

Day 90 discussion

Haematology-Hemostaseology

3.1.12. Alectinib - EMEA-002431-PIP02-21

Treatment of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms)

Day 90 discussion

Oncology

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

SpringWorks Therapeutics, Inc; Treatment of desmoid tumours

Day 90 discussion

Oncology

3.1.14. Ribociclib - EMEA-002765-PIP02-21

Treatment of neuroblastoma

Day 90 discussion

Oncology

3.1.15. Vorasidenib - EMEA-002932-PIP02-21

Treatment of glioma

Day 90 discussion

Oncology

3.1.16. EMEA-003002-PIP01-21

Treatment of proteinuric chronic kidney disease

Day 90 discussion

Uro-nephrology

3.1.17. ExPEC9V - EMEA-002996-PIP01-21

Prevention of *E.coli* infections / Prevention of infections caused by extraintestinal pathogenic *Escherichia coli* (ExPEC)

Day 90 discussion

Vaccines

3.1.18. Venglustat - Orphan - EMEA-001716-PIP06-21

Genzyme Europe B.V.; Treatment of Fabry disease

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.19. Resmetirom - EMEA-003087-PIP01-21

Treatment of non-alcoholic steatohepatitis (NASH)

Day 60 discussion

Gastroenterology-Hepatology

3.1.20. Ritlecitinib - EMEA-002451-PIP02-21

Treatment of ulcerative colitis

Day 60 discussion

Gastroenterology-Hepatology

3.1.21. EMEA-003090-PIP01-21

Hereditary angioedema

Day 60 discussion

Haematology-Hemostaseology

3.1.22. Deucravacitinib - EMEA-002350-PIP04-21

Treatment of ulcerative colitis

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.23. Humanised IgG1K monoclonal antibody against interferon beta - Orphan - EMEA-003089-PIP01-21

Pfizer Europe MA EEIG; Treatment of dermatomyositis

Day 60 discussion

Immunology-Rheumatology-Transplantation / Dermatology

3.1.24. EMEA-003081-PIP01-21

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

Day 60 discussion

Infectious Diseases

3.1.25. Bepirovirsen - EMEA-003082-PIP01-21

Treatment of chronic hepatitis B infection

Day 60 discussion

Infectious Diseases

3.1.26. Emvododstat - EMEA-003088-PIP01-21

Treatment of coronavirus disease 2019 (COVID-19)

Day 60 discussion

Infectious Diseases

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

EigerBio Europe Limited; Treatment of hepatitis D virus infection

Day 60 discussion

Infectious Diseases

3.1.28. *Ex vivo* fused normal allogeneic human myoblast (MBN) with autologous human myoblast derived from Duchenne muscular dystrophy affected donor (MBDMD) - Orphan - EMEA-003078-PIP01-21

Dystrogen Therapeutics S.A.; Treatment of Duchenne muscular dystrophy

Day 60 discussion

Neurology

Note: Withdrawal request received on 20 October 2021

3.1.29. CD30-directed genetically modified autologous T cells (CD30.CAR-T) - EMEA-003092-PIP01-21

Treatment of Hodgkin lymphoma

Day 60 discussion

Oncology

3.1.30. Derivative of pyrazolo [1,5-a] pyrimidine - EMEA-003086-PIP01-21

Treatment of solid tumours

Day 60 discussion

Oncology

3.1.31. Benralizumab - EMEA-001214-PIP09-21

Treatment of eosinophilic granulomatosis with polyangiitis (EGPA)

Day 60 discussion

Pneumology - Allergology

3.1.32. Humanised IgG2 monoclonal antibody against APRIL - Orphan - EMEA-003085-PIP01-21

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

Day 60 discussion

Uro-nephrology

3.1.33. SARS-CoV-2 virus, beta-propiolactone inactivated - EMEA-003077-PIP01-21

Prevention of coronavirus disease 2019 (COVID-19)

Day 60 discussion

Vaccines

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

Prevention of cardiovascular events

Day 30 discussion

Cardiovascular Diseases

3.1.35. Colchicine - EMEA-003101-PIP01-21

Reduction of atherothrombic events in patients with coronary artery disease

Day 30 discussion

Cardiovascular Diseases

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

Heart failure with LVEF > 40% / Prevention of CV outcome events in patients with HF with LVEF > 40%

Day 30 discussion

Cardiovascular Diseases

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

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

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.38. Pudexacianinium chloride - EMEA-003099-PIP01-21

Ureter visualization

Day 30 discussion

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

3.1.39. Efruxifermin - EMEA-003114-PIP01-21

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

Day 30 discussion

Gastroenterology-Hepatology

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

Control and prevention of bleeding / Perioperative management

Day 30 discussion

Haematology-Hemostaseology

3.1.41. Cenerimod - EMEA-003108-PIP01-21

Treatment of systemic lupus erythematosus (SLE)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.42. Fostamatinib - EMEA-001196-PIP03-21

Treatment of autoimmune haemolytic anaemia

Day 30 discussion

Immunology-Rheumatology-Transplantation / Haematology-Hemostaseology

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

Passage Bio, Inc.; Treatment of GM1 gangliosidosis

Day 30 discussion

Neurology

3.1.44. Corticotropin - EMEA-003097-PIP01-21

Treatment of infantile spasms

Day 30 discussion

Neurology

3.1.45. Gantenerumab - EMEA-003107-PIP01-21

Alzheimer's disease

Day 30 discussion

Neurology

3.1.46. Humanized monoclonal IgG1-based antibody - EMEA-003100-PIP01-21

Treatment of spinal muscular atrophy

Day 30 discussion

Neurology

3.1.47. Aumolertinib - EMEA-003106-PIP01-21

Treatment of lung cancer

Day 30 discussion

Oncology

3.1.48. Pembrolizumab / favezelimab - EMEA-003104-PIP01-21

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

Day 30 discussion

Oncology

3.1.49. Triazolopyrimidine derivative - EMEA-003095-PIP01-21

Diabetic retinopathy / Treatment of diabetic retinopathy

Day 30 discussion

Ophthalmology

3.1.50. Amifampridine - EMEA-003103-PIP01-21

Lambert-Eaton myasthenic syndrome

Day 30 discussion

Other

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

Hereditary angioedema / Prevention of hereditary angioedema

Day 30 discussion

Pneumology - Allergology / Haematology-Hemostaseology

3.1.52. Troriluzole - EMEA-003084-PIP02-21

Treatment of obsessive-compulsive disorder

Day 30 discussion

Psychiatry

3.1.53. EMEA-003098-PIP01-21

Treatment of proteinuric chronic kidney disease

Day 30 discussion

Uro-nephrology

3.1.54. Bardoxolone - EMEA-002488-PIP02-21

Treatment of autosomal dominant polycystic kidney disease (ADPKD)

Day 30 discussion

Uro-nephrology

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

Apellis Ireland Limited; Treatment of glomerulonephritis and nephrotic syndrome

Day 30 discussion

Uro-nephrology

3.1.56. Vibegron - EMEA-001415-PIP02-21

Treatment of myoneurogenic bladder disorders

Day 30 discussion

Uro-nephrology

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

Prevention of RSV-associated lower respiratory tract illness

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

LEO Pharma A/S; Treatment of atopic dermatitis

Day 30 discussion

Dermatology

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

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

Day 30 discussion

Gastroenterology-Hepatology

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

BioCryst Ireland Limited; Treatment of influenza

Day 30 discussion

Infectious Diseases

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

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

Day 30 discussion

Vaccines

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

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

sanofi-aventis groupe; Treatment of asthma

Day 30 discussion

Dermatology

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

Agios Netherlands B.V.; Pyruvate kinase deficiency

Day 30 discussion

Haematology-Hemostaseology

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

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

Day 30 discussion

Haematology-Hemostaseology

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

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

Day 30 discussion

Immunology-Rheumatology-Transplantation

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

Amgen Europe B.V.; Treatment of psoriasis

Day 30 discussion

Immunology-Rheumatology-Transplantation

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

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

Day 30 discussion

Immunology-Rheumatology-Transplantation

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

Pfizer Europe MA EEIG; Treatment of bacterial infections

Day 30 discussion

Infectious Diseases

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

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

Day 30 discussion

Infectious Diseases

3.3.9. Cobicistat / atazanavir sulphate - EMEA-001465-PIP01-13-M04

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

Day 30 discussion

Infectious Diseases

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

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

Day 30 discussion

Infectious Diseases

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

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

Day 30 discussion

Neurology

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

Novartis Gene Therapy EU Limited; Treatment of spinal muscular atrophy

Day 30 discussion

Neurology

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

Proveca Pharma Limited; Treatment of epilepsy

Day 30 discussion

Neurology

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

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

Day 30 discussion

Oncology

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

Pfizer Europe MA EEIG; Treatment of acute myeloid leukaemia

Day 30 discussion

Oncology

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

Amgen Europe B.V.; Treatment of solid malignant non-CNS tumours

Day 30 discussion

Oncology

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

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

Day 30 discussion

Ophthalmology

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

Takeda Pharmaceuticals International AG Ireland Branch; Hereditary angioedema

Day 30 discussion

Other

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

AstraZeneca AB; Treatment of asthma

Day 30 discussion

Pneumology - Allergology

3.3.20. Dexmedetomidine hydrochloride - EMEA-002758-PIP01-19-M01

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

Day 30 discussion

Psychiatry

4. Nominations

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

4.1. List of letters of intent received for submission of applications with start of procedure 22 November 2021 for Nomination of Rapporteur and Peer reviewer

Summary of Committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

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

Summary of Committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

4.3. Nominations for other activities

Summary of Committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

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

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

5.1. New Scientific Advice

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

No item

6. Discussion on the applicability of class waivers

6.1. Discussions on the applicability of class waiver for products

6.1.1. Tramadol hydrochloride / magnesium lactate dihydrate- EMEA-12-2021

SciencePharma spółka z ograniczoną odpowiedzialnością spółka jawna; All classes of medicinal products for treatment of primary and secondary osteoarthrosis; Management of chronic pain in adults with osteoarthritis of the hip and/or knee.

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.

Other potential paediatric interests of this medicine suggested by PDCO: treatment of pain.

6.1.2. Tozorakimab - EMEA-14-2021

AstraZeneca AB; All classes of medicinal products for the 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 symptomatic COPD in patients 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: treatment of asthma, treatment of atopic dermatitis and treatment of COVID-19.

7. Discussion on the inclusion of an indication within a condition in an agreed PIP/waiver

7.1. Discussion on the possibility to include an indication within a condition in an agreed PIP/waiver

7.1.1. Finerenone - EMEA-001623-PIP01-14-M04

Bayer AG; Treatment of chronic kidney disease

Proposed indication: Treatment of chronic kidney disease in adults with type 2 diabetes mellitus / Treatment of non-diabetic chronic kidney disease in adults

Summary of Committee discussion:

It was confirmed that the indications "treatment of chronic kidney disease in adults with type 2 diabetes mellitus" and "treatment of non-diabetic chronic kidney disease in adults" fall under the condition "treatment of chronic kidney disease" listed in the Agency Decision.

7.1.2. Cosentyx - EMEA-000380-PIP02-09-M04

Novartis Europharm Ltd; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, spondyloarthritis, psoriatic arthritis and juvenile idiopathic arthritis)

Proposed indication: Treatment of peripheral spondyloarthritis (pSpA): concerning the subtypes of undifferentiated pSpA and reactive arthritis (ReA)

Summary of Committee discussion:

It was confirmed that the indication "Treatment of peripheral spondyloarthritis (pSpA): concerning the subtypes of undifferentiated pSpA and reactive arthritis (ReA)" falls under the condition "Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, spondyloarthritis, psoriatic arthritis and juvenile idiopathic arthritis)" listed in the Agency Decision.

8. Annual reports on deferrals

The members of the PDCO took note of the products listed in the Annex B.

9. Organisational, regulatory and methodological matters

9.1. Mandate and organisation of the PDCO

9.1.1. Update on PDCO member(s)/alternate(s) mandate status

The PDCO Chair welcomed Dr. Vlasta Zavadova representing Liechtenstein as the nominated Member.

9.1.2. Vote by proxy

No item

9.2. Coordination with EMA Scientific Committees or CMDh-v

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

Summary of Committee discussion:

The list of procedures with paediatric indications, starting in October 2021, to be evaluated by the CHMP, was presented to the PDCO members.

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

9.3.1. Non-clinical Working Group: D30 Products identified

PDCO member: Karen van Malderen

Summary of Committee discussion:

The Chair of the Non-clinical Working Group (NcWG) identified the products which will require NcWG evaluation and discussion.

9.3.2. Formulation Working Group

PDCO member: Brian Aylward

Summary of Committee discussion:

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

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

The meeting summary PCWP/HCPWP joint meeting on 21 and 22 September 2021 and the draft agenda - Annual PCWP/HCPWP joint meeting with all eligible organisations on 24 November 2021 were presented for information.

9.4. Cooperation within the EU regulatory network

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

Summary of Committee discussion:

No item

9.5. Cooperation with International Regulators

No item

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

No item

9.7. PDCO work plan

No item

9.8. Planning and reporting

No item

10. Any other business

10.1. COVID-19 update

Summary of Committee discussion:

The PDCO was updated on COVID-19 treatments and vaccines of specific relevance to the paediatric population.

10.2. International Council for Harmonisation – ICH E11A – Pediatric Extrapolation

Summary of Committee discussion:

ICH E11A is heading towards step 1 sign off (PDCO to agree this). Final version to be circulated ahead of December 2021 PDCO meeting with sign-off envisaged in January 2022.

10.3. Real World Evidence pilot with PDCO

Summary of Committee discussion:

The ongoing initiative in Real World Evidence (RWE) can be grouped into two categories: i) to study and characterise Real World Data/Evidence included in applications with the aim to provide guidance to applicants; ii) for the network to be able to generate RWE to support the committee's decision making. The presentation focused on the latter.

A catalogue of data sources that will help identify data sources when performing a study is currently under development (Q4 2022). The network could generate RWE through studies performed on the data sources accessible in-house through the EMA framework contract, and from 2022 onwards, through DARWIN EU.

Proof of concept with PDCO has started and some details were presented. The objectives are:

- to collect as many examples as possible where RWE could be useful to support decision-making,
- to provide at least two RWE analyses and evaluate their added value,
- to determine feasibility and an optimal approach for processes and selection of data sources.

Furthermore, there are 2 moments identified, when to request analysis:

1. During a procedure: identified preparing and commenting the assessment reports, or during the discussions.

2. Outside the context of a specific regulatory procedure: for some diseases of interest, when information is lacking.

Steps for proof of concept with PDCO are the following:

1. Send email proposing a research question
2. TDA-DAT will quickly look at the databases available in-house
3. A short teleconference is organised to review preliminary results
4. TDA-DAT will prepare the draft results ready
5. The report is delivered to the requesters
6. The report is published on the EU PAS Register for transparency

As an example, the study on glucocorticoids in paediatric patients was presented to show how to request an analysis and to show the results that can be produced.

10.4. R&D focus group 'evolutionary PIP'

Summary of Committee discussion:

The committee was informed about recent discussions in the designated EMA/industry focus group on a PIP model that allows the paediatric development programme to become more defined over time as more evidence becomes available, i.e. along with the evolution of scientific knowledge. It was agreed that a PDCO working group would be created to further progress this initiative.

10.5. New operational model on Working Parties - update

Summary of Committee discussion:

The new operational model for the working parties was presented at the PDCO plenary meeting. The new model was noted and clarifications were discussed on the functioning of the new operational expert groups and working parties, especially for the non-clinical domain.

11. Breakout sessions

11.1. Internal PDCO Operations

Summary of Committee discussion:

PDCO members discussed matters relating to committee internal operations.

11.2. Neonatology

Summary of Committee discussion:

Feedback from the recent annual workshop of the International Neonatal Consortium (INC) was provided.

11.3. Paediatric oncology

Summary of Committee discussion:

The group discussed how scientific meetings involving all interested stakeholders can help promoting development of the best products to fight certain types of paediatric cancer.

11.4. Vaccines

Summary of Committee discussion:

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

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 9-12 November 2021 meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Koenraad Norga	Chair	Belgium	When chairing the meeting: To be replaced for discussions, final deliberations and voting on: When not chairing the meeting: No participation in final deliberations and voting on:	3.1.25. Bepirovirsen - EMEA-003082-PIP01-21
Karl-Heinz Huemer	Member	Austria	No interests declared	
Marleen Renard	Member	Belgium	No participation in final deliberations and voting on:	2.3.13. Avelumab - EMEA-001849-PIP02-15-M04
Karen Van Malderen	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable for the meeting	
Georgios Savva	Member	Cyprus	No interests declared	
Tereza Bazantova	Alternate	Czechia	No interests declared	
Nanna Borup Johansen	Member	Denmark	No interests declared	
Irja Lutsar	Member	Estonia	No interests declared	
Jana Lass	Alternate	Estonia	No interests declared	
Pauliina Lehtolainen-Dalkilic	Member	Finland	No interests declared	
Anne Paavola	Alternate	Finland	No interests declared	
Sylvie Benchetrit	Member	France	No interests declared	
Dominique Ploin	Alternate	France	No interests declared	
Sabine Scherer	Member (Vice-Chair)	Germany	No interests declared	
Yuansheng Sun	Alternate	Germany	No interests declared	
Eleni Katsomiti	Member	Greece	No interests declared	
Ágnes Gyurasics	Member (CHMP member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Sara Galluzzo	Member	Italy	No interests declared	
Dina Apele-Freimane	Member	Latvia	No restrictions applicable for the meeting	
Silvijus Abramavicius	Alternate	Lithuania	No restrictions applicable for the meeting	
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No interests declared	
John-Joseph Borg	Member	Malta	No interests declared	
Herbert Lenicker	Alternate	Malta	No interests declared	
Roderick Houwen	Member	Netherlands	No restrictions applicable for the 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 for the meeting	
Helena Fonseca	Member	Portugal	No interests declared	
Hugo Tavares	Alternate	Portugal	No interests declared	
Dana Gabriela Marin	Member (CHMP alternate)	Romania	No interests declared	
Peter Sisovsky	Member	Slovakia	No interests declared	
Peter Szitanyi	Alternate	Slovakia	No interests declared	
Stefan Grosek	Member	Slovenia	No interests declared	
Fernando de Andrés Trelles	Member	Spain	No interests declared	
Maria Jesus Fernández Cortizo	Alternate	Spain	No interests declared	
Eva Agurell	Member	Sweden	No interests declared	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Fernando Cabanas	Member	Healthcare Professionals' Representative	No restrictions applicable for the meeting	
Doina Plesca	Alternate	Healthcare Professionals' Representative	No interests declared	
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable for the meeting	
Catherine Cornu	Alternate	Healthcare Professionals' Representative	No participation in final deliberations and voting on:	3.3.21. COVID-19 Vaccine (ChAdOx1-S [recombinant]) - EMEA-002862-PIP01-20-M02

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 interests declared	
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Tomasz Grybek	Alternate	Patients' Organisation Representative	No interests declared	
Michal Odermarsky	Alternate	Patients' Organisation Representative	No restrictions applicable for the meeting	
María Estela Moreno Martín	Expert - via telephone*	Spain	No interests declared	
Lutz Wiesner	Expert - via telephone*	Germany	No interests declared	
Helle Christiansen	Expert - via telephone*	Denmark	No restrictions applicable to this meeting	
Eeva Sofia Leinonen	Expert - via telephone*	Finland	No interests declared	
Kristin Karlsson	Expert - via telephone*	Sweden	No restrictions applicable to this meeting	
A representative from the European Commission attended the meeting Meeting run with support from relevant EMA staff				
* Experts were evaluated against the agenda topics or activities they participated in				

13. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

Paediatric investigation plan (PIP) (section 2.1 Opinion on PIPs and section 3.1 Discussions on PIPs)
A paediatric investigation plan (PIP) is a development plan aimed at ensuring that the necessary data are obtained through studies in children, when it is safe to do so, to support the authorisation of a medicine for children. Pharmaceutical companies submit proposals for PIPs to the European Medicines Agency's Paediatric Committee (PDCO). This Committee is responsible for agreeing or refusing the plan.

Compliance checks (section 2.2 Opinions on Compliance check, section 3.2 Discussions on Compliance check)
A compliance check may be necessary before any application for marketing authorisation (even for an adult indication) can be considered valid, if there was no deferral for at least one of the studies agreed in the PIP, or after the due date of initiation or completion of a study/measure. The same applies to some regulatory applications for authorised products, as described above.

Modification of an Agreed Paediatric Investigation Plan (section 2.3 Opinions on Modification of an agreed PIP, section 3.3 Discussions on Modification of an agreed PIP)
The development plan for a medicine can be modified at a later stage as knowledge increases. Modifications can also be made if the applicant encounters such difficulties with the implementation of a PIP, which render it unworkable or no longer appropriate.
In some cases, studies can be deferred until after the studies in adults have been conducted. This ensures that research in children is done only when it is safe and ethical to do so. Even when studies are deferred, the PIP will include details of the paediatric studies and their timelines.

Class waiver (section 6 Discussion on the applicability of class waiver)
As some diseases do not affect children (for example Parkinson's disease), the development of medicines for these diseases should not be performed in children. In these cases, a PIP is not required and it will be waived**.** For more information on the classes of diseases subject to waivers, see class waivers.

Annual reports on deferrals (section 8)
If the medicinal product is approved in the EU, annual reports on the deferred measures in the PIP must be submitted to the Agency.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/