29 May 2020
EMA/PDCO/295795/2020
Human Medicines Division

Paediatric Committee (PDCO)

Minutes for the meeting on 26-29 May 2020

Chair: Koenraad Norga – Vice-Chair: Sabine Scherer

Disclaimers

Some of the information contained in these 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.

Further information with relevant explanatory notes can be found at the end of this document.

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

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.

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 was replaced by the Vice-Chair Sabine Scherer for the discussion on agenda topic 2.1.15, 2.3.1, 2.3.6.

1.2. Adoption of agenda

PDCO agenda for 26-29 May 2020

The agenda of the PDCO meeting 26-29 May 2020 was adopted.

1.3. Adoption of the minutes

PDCO minutes from the meeting held on 28-30 April 2020

The minutes of the PDCO meeting 28 – 30 April 2020 were adopted and will be published on the EMA website.

2. Opinions

Disclosure of some information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

2.1. Opinions on Products

2.1.1. Pegzilarginase - Orphan - EMEA-001925-PIP02-19

Aeglea BioTherapeutics, Inc.; Treatment of hyperargininaemia

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

During its plenary on 29 May 2020, the PDCO adopted a positive Opinion on the PIP application for pegzilarginase, for the treatment of hyperargininaemia.
A deferral in a subset of the patient population was now requested by the applicant and agreed.
All other minor issues regarding the PIP Opinion wordings could be addressed/clarified by the applicant as well.

2.1.2. Ravagalimab - EMEA-002617-PIP01-19

AbbVie Ltd; Treatment of ulcerative colitis

Day 120 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The applicant's response to the D90 issues was considered acceptable. A positive opinion was adopted for ravagalimab for the treatment of ulcerative colitis in a subset of paediatric patients. A waiver on the grounds lack of significant benefit was adopted.

2.1.3. Tecovirimat monohydrate - Orphan - EMEA-001205-PIP02-19

SIGA Technologies, Inc.; Treatment of orthopoxvirus disease (smallpox, monkeypox, cowpox, and vaccinia)

Day 120 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO agreed on a positive opinion.

2.1.4. Tominersen - Orphan - EMEA-002546-PIP01-19

Roche Registration GmbH; Treatment of huntington's disease

Day 120 opinion

Neurology

Summary of committee discussion:

The remaining issues after the PDCO discussion at Day 90 have been resolved satisfactorily The PDCO adopted a positive opinion, including a waiver for children from birth to less than 2 years of age and a deferral for all measures in the PIP, apart from the non-clinical studies.

2.1.5. Rozanolixizumab - Orphan - EMEA-002681-PIP01-19

UCB Pharma S.A.; Treatment of myasthenia gravis

Day 120 opinion

Neurology

Summary of committee discussion:

The PDCO in May 2020 discussed the responses received by the applicant on the issues raised at D90. Therefore, the PDCO agreed a positive opinion for a waiver for rozanolixizumab in the condition of Treatment of Myasthenia Gravis with a waiver for the subset of a paediatric population and a deferral based on the grounds that the specific medicinal product is likely to be ineffective in this age subgroup.

2.1.6. Ondansetron (hydrochloride) - EMEA-002623-PIP01-19

Adial Pharmaceuticals; Treatment of alcohol use disorder (AUD)

Day 120 opinion

Other / Neurology

Summary of committee discussion:

The additional information provided by the applicant was noted, and the key elements adapted accordingly.

Based on the assessment of this application and in line with the Day 90 discussion at the Paediatric Committee, a positive opinion was subsequently adopted by the PDCO at its plenary at Day 120. Moreover, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for ondansetron for a subset of the paediatric population in the condition of Treatment of Alcohol Use Disorder (AUD).

The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.7. Rosuvastatin / ezetimibe - EMEA-002202-PIP02-20

Krka, d.d., Novo mesto; Prevention of cardiovascular events

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

Based on the assessment of this application the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for Ezetimibe / Rosuvastatin for all subsets of the paediatric population (0 to 18 years of age) in the condition “prevention of cardiovascular events” on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.8. Icosasodium{26-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]-14,14-bis{[(3-{6-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]hexyl}amino)-3-oxopropoxy)]methyl}-8,12,19-trioxo-16-oxa-7,13,20-triazahexacosyl}2′-O-(2-methoxyethyl)-(3′→5′)-[2′-O-(2-methoxyethyl)guanylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methylcytidylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methyluridylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methylcytidylyl-(3′→5′)-2′-deoxy-5-methyl-P-sulfidocytidylyl-(3′→5′)-2′-deoxy-P-sulfidoguanylyl-(3′→5′)-P-sulfidothymidylyl-(3′→5′)-P-sulfidothymidylyl-(3′→5′)-2′-deoxy-P-sulfidoguanylyl-(3′→5′)-2′-deoxy-P-sulfidoguanylyl-(3′→5′)-P-sulfidothymidylyl-(3′→5′)-2′-deoxy-P-sulfidoguanylyl-(3′→5′)-2′-deoxy-5-methyl-P-sulfidocytidylyl-(3′→5′)-P-sulfidothymidylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methyluridylyl-(3′→5′)-2′-O-(2-methoxyethyl)guanylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methyl-P-sulfidouridylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methyl-P-sulfidouridylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methylcytidine]-5-methyl-P-sulfidouridylyl-5′-yl phosphate (TQJ230) - EMEA-002786-PIP01-20

Novartis Europharm Ltd.; Prevention of cardiovascular events due to atherosclerotic cardiovascular disease in patients with elevated lipoprotein a (Lp(a))

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

Based on the assessment of this application the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for all subsets of the paediatric population (0 to 18 years of age) in the condition of "Prevention of cardiovascular events due to atherosclerotic cardiovascular disease in patients with elevated Lp(a)" on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible due to the limited patient population and extremely low cardiovascular event rate in the targeted paediatric population.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.9. Recombinant human IgG1λ monoclonal Fab antibody - EMEA-002766-PIP01-20

PhaseBio Pharmaceuticals Inc.; Reversal of antiplatelet effects of ticagrelor in patients with uncontrolled major or life-threatening bleeding or requiring urgent surgery or invasive

procedure

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The PDCO's view expressed at D30 was re-discussed and endorsed.
Considering the current development of ticagrelor for sickle cell disease in children, the PDCO confirmed the unmet need for a reversal agent in this condition.
Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO disagrees with the applicant's request for a waiver. The Committee decided to adopt a negative opinion on this product specific waiver for this recombinant human IgG1λ monoclonal Fab antibody for the condition of reversal of antiplatelet effects of ticagrelor in patients with uncontrolled major or life-threatening bleeding or requiring urgent surgery or invasive procedure.

2.1.10. Bisoprolol fumarate / trimetazidine dihydrochloride - EMEA-002768-PIP01-20

Les Laboratoires Servier; Treatment of ischaemic coronary artery disorders

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

Based on the assessment of this application and in line with the Day 30 discussion at the Paediatric Committee, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for Trimetazidine dihydrochloride / Bisoprolol fumarate for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of ischaemic coronary artery disorders.

The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.11. Metformin hydrochloride / sitagliptin hydrochloride monohydrate - EMEA-002732-PIP02-20

Adamed Pharma S.A.; Improvement of glycaemic control in patients with type 2 diabetes

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Based on the assessment of this application and in line with Day 30 discussion at the Paediatric Committee, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for metformin hydrochloride / sitagliptin hydrochloride monohydrate for all subsets of the paediatric population (0 to 18 years of age) in the

condition of Treatment of type 2 diabetes mellitus.

The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.12. Ravagalimab - EMEA-002617-PIP02-19

AbbVie Ltd; Treatment of Sjögren's syndrome

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO's view expressed at D30 was re-discussed and endorsed.
Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for ravagalimab for all subsets of the paediatric population (0 to 18 years of age) in the condition of Sjögren's syndrome.

2.1.13. Sutimlimab - EMEA-002542-PIP02-19

Genzyme Europe B.V.; Treatment of immune thrombocytopenia purpura

Day 60 opinion

Immunology-Rheumatology-Transplantation / Haematology-Hemostaseology

Summary of committee discussion:

Between Day 30 and Day 60 the applicant provided additional information regarding the positioning of sutimlimab as third line treatment for patients with immune thrombocytopenia.
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 sutimlimab for all subsets of the paediatric population (0 to less than 18 years of age) in the condition "treatment of immune thrombocytopenia" on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) 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.

2.1.14. Niraparib (tosylate monohydrate) / abiraterone (acetate) - EMEA-002789-PIP01-20

Janssen Research & Development; Treatment of prostate malignant neoplasms

Day 60 opinion

Oncology

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for niraparib tosylate monohydrate / abiraterone acetate for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of prostate malignant neoplasms.

The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.15. Humanised antibody targeting the inducible T cell co-stimulatory receptor - EMEA-002781-PIP01-20

GlaxoSmithKline (Ireland) Limited; Treatment of head and neck epithelial malignant neoplasms

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO's views expressed at D30 were endorsed.
The Members reiterated that while dedicated paediatric studies in patients with 'nasopharyngeal carcinoma' within the head and neck squamous cell carcinomas are not considered feasible the applicant is highly encouraged to open adult studies also to adolescent patients with nasopharyngeal carcinoma/ head and neck squamous cell carcinomas when relevant.
The PDCO therefore agreed with the applicant's request for a waiver. The PDCO recommends granting a waiver for humanised antibody targeting the inducible T cell co-stimulatory receptor for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of treatment of head and neck epithelial malignant neoplasms based on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.16. Neratinib - EMEA-002783-PIP01-20

Pierre Fabre Médicament; Treatment of breast cancer

Day 60 opinion

Oncology

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the applicant's request for a waiver. The PDCO recommends granting a waiver for neratinib for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of breast cancer on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.17. Rucaparib (camsylate) - EMEA-002760-PIP01-19

Clovis Oncology Ireland Ltd.; Treatment of fallopian tube cancer/ Treatment of ovarian cancer/ Treatment of prostate malignant neoplasms/ Treatment of primary peritoneal cancer

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this application in line with the outcome of the D30 discussion. Again, the PDCO emphasised that it considers that the product, based on the mechanism of action has a potential to address unmet medical needs in children with cancer, taking note of the ongoing adult Phase II trial in patients with solid tumours. The committee reiterated in this respect the encouragement to include also adolescents into this trial in order to enhance robust evidence generation across all age groups.
Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for Rucaparib camsylate for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of fallopian tube cancer, treatment of ovarian cancer, treatment of prostate malignant neoplasms, treatment of primary peritoneal cancer based on the on the ground that the diseases do not occur in children for all conditions apart for a subset of paediatric population for treatment of ovarian cancer for which the agreed ground is of significant therapeutic benefit.

The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.18. Remdesivir – EMEA-002826-PIP01-20 (discussed at the extraordinary PDCO plenary meeting held on 14th May 2020)

Gilead Sciences International Ltd.; treatment of coronavirus disease 19 (COVID19)

Opinion

Infectious diseases

Summary of committee discussion:

Taking into account the D30 discussion and the applicant's responses to the request for modification, the PDCO re-discussed at its plenary meeting on 14 May 2020 the proposed PIP and adopted a positive opinion on the PIP for remdesivir for treatment of COVID-19 for all subsets of the paediatric population from birth to less than 18 years of age and a deferral for all measures.

It was agreed that the focus of development will be hospitalized children regardless of their severity status, from birth (from 32 weeks gestational age) to less than 18 years of age, with COVID-19.

The start date of the study was set at June 2020.

2.2. Opinions on Compliance Check

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

2.2.1. Live, attenuated, chimeric dengue virus, serotype 1 / Live, attenuated, chimeric dengue virus, serotype 2 / Live, attenuated, chimeric dengue virus, serotype 3 / Live, attenuated, chimeric dengue virus, serotype 4 - EMEA-C-001545-PIP01-13-M02

Sanofi Pasteur; Prevention of dengue disease

Day 60 opinion

Vaccines

Summary of committee discussion:

The PDCO adopted a positive compliance opinion.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Alogliptin benzoate (as alogliptin) - EMEA-000496-PIP01-08-M08

Takeda Development Centre Europe 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/0078/2020 of 18/03/2020).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.2. Drospirenone / estetrol monohydrate - EMEA-001332-PIP01-12-M03

Estetra SPRL; Prevention of pregnancy

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The applicant's response to the D30 issues was considered acceptable.
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/0359/2016 of 21 December 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.3. FVIII Fc – von Willebrand factor – XTEN fusion protein (rFVIIIFc-VWF-XTEN) Orphan - EMEA-002501-PIP01-18-M01

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

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The Paediatric Committee discussed the clarification received from the applicant before D60 as well as their request for an oral explanation.
It was concluded that the proposed modifications could be accepted.
Finally, the PDCO noted that the applicant also requested an oral explanation at the time of the initial PIP (D120). It is flagged to the applicant that a TC with the Rapporteur and Peer Reviewer for discussion of the controversial issues is always preferred before requesting an oral explanation.

2.3.4. Recombinant human monoclonal antibody to GM-CSF (otilimab)- EMEA-001882-PIP02-16-M02

GlaxoSmithKline Trading Services Limited; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis)

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

In May 2020 the PDCO considered that the proposed changes, as discussed already in April, 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/0287/2019 of 16/8/2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.5. Doravirine - EMEA-001676-PIP01-14-M03

Merck Sharp & Dohme (Europe), Inc.; Treatment of human immunodeficiency virus type 1 (HIV-1) infection

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0115/2017 of 21/04/2017).

2.3.6. Eravacycline - EMEA-001555-PIP01-13-M04

Tetraphase Pharmaceuticals, Inc.; Treatment of complicated intra-abdominal infection

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0251/2019 of 16/07/2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.7. Fostemsavir (tromethamine) - EMEA-001687-PIP01-14-M04

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

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO discussed in May 2020 the responses provided by the applicant on the outstanding points raised in April.
The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0040/2019 of 29/1/2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.8. Doravirine / lamivudine / tenofovir disoproxil (fumarate) - EMEA-001695-PIP01-14-M03

Merck Sharp & Dohme (Europe), Inc.; Treatment of human immunodeficiency virus-1 (HIV-1) infection

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

In May 2020 the PDCO discussed the responses of the applicant received after D30 A number of simplifications were made in the text of opinion to improve accuracy and focus on requirements.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0116/2017 of 28/04/2017).

2.3.9. Vaborbactam / meropenem - EMEA-001731-PIP01-14-M02

Menarini International Operations Luxembourg S.A.; Treatment of Gram-negative bacterial infections

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

In May 2020 PDCO considered that the proposed changes could be accepted. The applicant can proceed in requesting closure of P/0230/2015 22 October 2015 (EMEA-001740-PIP01-14).
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0229/2015 of 22/10/2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.10. Alemtuzumab - EMEA-001072-PIP01-10-M04

Genzyme Europe B.V.; 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 and granting a product-specific waiver on the grounds that the specific medicinal product is likely to be unsafe.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.11. Brivaracetam - Orphan - EMEA-000332-PIP02-17-M01

UCB Pharma S.A.; Treatment of paediatric epilepsy syndromes

Day 60 opinion

Neurology

Summary of committee discussion:

Since day 30 the Applicant submitted a significant amount of information clarifying their

proposal and adjusting it to the PDCO's expectations.
With these adjustments the PDCO considered all issues resolved and adopted a positive opinion confirming the modified PIP. The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.12. Bempegaldesleukin - EMEA-002492-PIP01-18-M01

Nektar Therapeutics; Treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoetic, and lymphoid tissue neoplasms)

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this procedure at Day 60 during the May 2020 plenary meeting. 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/0298/2019 of 14 August 2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.13. Bosutinib - EMEA-000727-PIP01-09-M04

Pfizer Europe MA EEIG; Treatment of chronic myeloid leukaemia

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the request for modification considering the responses provided by the applicant after the D30 discussion.
In conclusion the PDCO considered that all the proposed changes could be accepted and a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0282/2019 of 14 August 2019) was adopted.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.14. Brentuximab vedotin - Orphan - EMEA-000980-PIP01-10-M06

Takeda Pharma A/S; Treatment of Hodgkin lymphoma / Treatment of anaplastic large cell lymphoma

Day 60 opinion

Oncology

Summary of committee discussion:

The committee's views expressed on day were re-discussed taking into account the applicant's additional clarifications, which are considered agreeable.

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/0232/2017 of 11 August 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.15. Olaparib - EMEA-002269-PIP01-17-M01

AstraZeneca AB; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic, and lymphoid tissue)

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO discussed the clarifications provided by the applicant after D30 including the applicant's comments on the draft opinion.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0262/2018 of 15 August 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.16. Tapentadol - EMEA-000325-PIP01-08-M10

Grünenthal GmbH; Chronic pain / Treatment of chronic pain

Day 60 opinion

Pain

Summary of committee discussion:

The committee's views expressed on day 30 were re-discussed, taking into account the applicant's additional clarifications which are considered acceptable.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0111/2018 of 11 April 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.17. Vortioxetine - EMEA-000455-PIP02-10-M06

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

Day 60 opinion

Psychiatry

Summary of committee discussion:

The PDCO reviewed and discussed the modification along with the assessors' comments including the additional information received after day 60. An oral explanation meeting took place at the PDCO virtual plenary meeting on 28 May 2020 with the Applicant's representatives in attendance.

A positive opinion modifying the study timelines has been adopted accordingly. The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.4. Opinions on Re-examinations

No items

2.5. Opinions on Review of Granted Waivers

No items

2.6. Finalisation and adoption of opinions

No items

2.7. Partial Compliance Checks completed by EMA

The following partial compliance checks have concluded positively without PDCO discussion. The Committee has been informed in writing.

2.7.1. [N-(2,4-Di-tert-butyl-5-hydroxyphenyl)-1,4-dihydro-4-oxoquinoline-3-carboxamide] - EMEA-C10-000335-PIP01-08-M14

Vertex Pharmaceuticals (Ireland) Limited; Treatment of cystic fibrosis

Letter adopted

Other

2.7.2. Nirsevimab (anti-respiratory syncytial virus human IgG1κ monoclonal antibody) - EMEA-C1-001784-PIP01-15-M02

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

Letter adopted

Infectious diseases

3. Discussion of applications

Disclosure of some information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.1. Discussions on Products D90-D60-D30

3.1.1. Lonapegsomatropin - EMEA-002692-PIP01-19

Growth hormone deficiency

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.2. Cilofexor - Orphan - EMEA-002554-PIP02-19

Gilead Sciences International Ltd.; Treatment of primary sclerosing cholangitis (PCS)

Day 90 discussion

Gastroenterology-Hepatology

3.1.3. Guselkumab - EMEA-001523-PIP05-19

Crohn's disease / Treatment of Crohn's disease

Day 90 discussion

Gastroenterology-Hepatology

3.1.4. Marstacimab - Orphan - EMEA-002285-PIP02-19

Pfizer Europe MA EEIG; Treatment of congenital haemophilia B / Treatment of congenital haemophilia A / Prophylaxis of bleeding in haemophilia B / Prophylaxis of bleeding in haemophilia A

Day 90 discussion

Haematology-Hemostaseology

3.1.5. Rilzabrutinib - Orphan - EMEA-002438-PIP02-19

Principia Biopharma, Inc.; Immune thrombocytopenia / Treatment of immune thrombocytopenia

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.6. Ritonavir / darunavir - EMEA-002537-PIP02-19

Treatment of human immunodeficiency virus (HIV-1) infection

Day 90 discussion

Infectious Diseases

3.1.7. EMEA-002566-PIP01-19

Treatment of multiple sclerosis / Treatment of secondary progressive multiple sclerosis / Treatment of primary progressive multiple sclerosis / Treatment of relapsing remitting multiple sclerosis

Day 90 discussion

Neurology

3.1.8. Soticlestat - EMEA-002572-PIP02-19

Dravet syndrome, Lennox-Gastaut syndrome / Treatment of seizures associated with Dravet syndrome / Treatment of seizures associated with Lennox-Gastaut syndrome

Day 90 discussion

Neurology

3.1.9. RAAV8-Des-hMTM1 - Orphan - EMEA-002571-PIP01-19

Audentes Therapeutics, Inc.; X-linked myotubular myopathy (XLMTM)

Day 90 discussion

Other

3.1.10. Fasinumab - EMEA-002059-PIP02-19

Chronic pain / Chronic musculoskeletal pain / Chronic non-musculoskeletal pain / Treatment of chronic cancer pain in a palliative care setting / Treatment of moderate to severe chronic pain associated with osteoarthritis (OA) of the knee or hip in patients who achieve an inadequate response to or are intolerant to currently available analgesics (adults only)

Day 90 discussion

Pain

3.1.11. EMEA-002735-PIP01-19

Cardioplegia / For induction of cardioplegia in paediatric patients of all ages undergoing cardiac surgery to correct congenital heart malformation in operations requiring cardiopulmonary bypass (CPB) support

Day 60 discussion

Cardiovascular Diseases

3.1.12. EMEA-002329-PIP02-20

Treatment of dermatitis and eczema / Treatment of chronic hand eczema / Treatment of atopic dermatitis

Day 60 discussion

Dermatology

3.1.13. Insulin 287 - EMEA-002761-PIP01-20

Type 2 diabetes mellitus / Type 1 diabetes mellitus

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.14. Venglustat - Orphan - EMEA-001716-PIP05-20

Genzyme Europe B.V.; Polycystic kidney, autosomal dominant / Long term treatment to slow the progression of cysts development in paediatric patients from 12 years to <18 years old with autosomal dominant polycystic kidney disease

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Uro-nephrology

3.1.15. Bispecific antibody binding to clotting factor IX and X - EMEA-002762-PIP02-20

Treatment of haemophilia A / Routine prophylaxis to prevent or reduce frequency of bleeding episodes in patients with haemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors / For use in all age groups

Day 60 discussion

Haematology-Hemostaseology

3.1.16. Human Fibrinogen - EMEA-002769-PIP01-20

Treatment of congenital fibrinogen deficiency / Treatment of congenital fibrinogen deficiency

Day 60 discussion

Haematology-Hemostaseology

3.1.17. Secukinumab - EMEA-000380-PIP06-19

Lupus nephritis

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.18. Fully human IgG1 RB-1 YTE anti-RSV F monoclonal antibody (mAb) - EMEA-002755-PIP01-19

Prevention of lower respiratory tract infection caused by respiratory syncytial virus

Day 60 discussion

Infectious Diseases

3.1.19. Itraconazole - Orphan - EMEA-002787-PIP01-20

Laboratoires SMB S.A.; Prevention of invasive mould disease / Prevention of invasive mould disease in adolescents with acute leukaemia and neutropaenia

Day 60 discussion

Infectious Diseases / Oncology

3.1.20. Retinol (vitamin A) - Orphan - EMEA-002790-PIP01-20

Orphanix GmbH; Prevention of bronchopulmonary dysplasia (BPD)

Day 60 discussion

Neonatology - Paediatric Intensive Care

3.1.21. Acetyl-L-leucine - Orphan - EMEA-002796-PIP01-20

IntraBio Ltd.; Niemann-Pick disease type C

Day 60 discussion

Neurology

3.1.22. Adeno-associated viral vector serotype 9 containing the human mini-dystrophin gene - Orphan - EMEA-002741-PIP01-20

Pfizer Europe MA EEIG; Treatment of Duchenne muscular dystrophy

Day 60 discussion

Neurology

3.1.23. Edaravone - Orphan - EMEA-002785-PIP01-20

Treeway B.V.; Treatment of amyotrophic lateral sclerosis

Day 60 discussion

Neurology

3.1.24. EMEA-002763-PIP01-20

Paediatric low grade glioma / Relapsed or refractory paediatric low grade glioma in adolescents and children 1 year of age and older

Day 60 discussion

Oncology

3.1.25. Autologous tumour-infiltrating lymphocytes: lifileucel - EMEA-002776-PIP01-20

Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic neoplasms)

Day 60 discussion

Oncology

3.1.26. Tabelecleucel - Orphan - EMEA-002025-PIP04-19

Atara Biotherapeutics, Inc.; Treatment of Epstein-Barr virus associated post-transplant lymphoproliferative disorder / Treatment of allogeneic haematopoietic cell transplant patients with Epstein-Barr virus associated post-transplant lymphoproliferative disease who have received one prior therapy / Treatment of solid organ transplant patients with Epstein-Barr virus associated post-transplant lymphoproliferative disease who have received one prior therapy

Day 60 discussion

Oncology

3.1.27. Adrenaline (epinephrine) - EMEA-002749-PIP01-19

Treatment of allergic reactions / The emergency treatment of allergic reactions, including anaphylaxis

Day 60 discussion

Pneumology – Allergology

3.1.28. Codon-optimised human cystic fibrosis transmembrane conductance regulator messenger ribonucleic acid complexed with lipid-based nanoparticles - Orphan - EMEA-002733-PIP01-19

Real Regulatory Limited; Cystic fibrosis / Treatment of cystic fibrosis

Day 60 discussion

Pneumology – Allergology

3.1.29. Timapiprant - EMEA-002788-PIP01-20

Treatment of asthma / Add-on maintenance treatment for severe eosinophilic asthmatic patients, aged 6-17 years, inadequately controlled on ICS plus other controller medication

Day 60 discussion

Pneumology – Allergology

3.1.30. Esketamine - EMEA-002772-PIP01-20

Bipolar depression / Major depressive disorder / Treatment-resistant bipolar depression /

Treatment-resistant depression in the course of major depressive disorder

Day 60 discussion

Psychiatry

3.1.31. Ezetimibe / pravastatin - EMEA-002805-PIP01-20

Hypercholesterolaemia / Cardiovascular events

Day 30 discussion

Cardiovascular Diseases

3.1.32. Sacubitril / valsartan - EMEA-000316-PIP03-20

Prevention of heart failure

Day 30 discussion

Cardiovascular Diseases

3.1.33. Benralizumab - EMEA-001214-PIP06-20

Bullous pemphigoid

Day 30 discussion

Dermatology

3.1.34. Dupilumab - EMEA-001501-PIP05-20

Treatment of bullous pemphigoid

Day 30 discussion

Dermatology

3.1.35. Cotadutide - EMEA-002712-PIP02-20

Treatment of chronic kidney disease (CKD) in patients with type 2 diabetes mellitus (T2DM)

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.36. Levonorgestrel - EMEA-002767-PIP01-20

Prevention of pregnancy

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

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

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

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.38. EMEA-002757-PIP01-19

Treatment of ulcerative colitis

Day 30 discussion

Gastroenterology-Hepatology

3.1.39. Elafibranor - Orphan - EMEA-001857-PIP02-20

Genfit SA; Treatment of primary biliary cholangitis

Day 30 discussion

Gastroenterology-Hepatology

3.1.40. EMEA-002773-PIP01-20

Treatment of non-alcoholic steatohepatitis (NASH)

Day 30 discussion

Gastroenterology-Hepatology

3.1.41. Crovalimab - EMEA-002709-PIP01-19

Treatment of paroxysmal nocturnal hemoglobinuria (PNH)

Day 30 discussion

Haematology-Hemostaseology

3.1.42. Olinciguat - EMEA-002759-PIP01-19

Treatment of sickle cell disease (SCD)

Day 30 discussion

Haematology-Hemostaseology

3.1.43. Voxelotor - Orphan - EMEA-002356-PIP02-20

Synteract GmbH; Sickle cell disease

Day 30 discussion

Haematology-Hemostaseology

3.1.44. Tacrolimus - EMEA-001642-PIP02-20

Solid organ transplant rejection / Prophylaxis of transplant rejection in liver, kidney or heart allograft recipients (children aged from birth to less than 18 years) / Treatment of allograft rejection resistant to treatment with other immunosupressive medical products in children aged from birth to less than 18 years

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.45. Human anti-interleukin-15 (IL-15) monoclonal antibody - EMEA-002775-PIP01-20

Non-responsive coeliac disease (NRCD) with symptoms despite 12 months of following a gluten-free diet (GFD)

Day 30 discussion

Immunology-Rheumatology-Transplantation / Gastroenterology-Hepatology

3.1.46. EMEA-002740-PIP01-19

Treatment of human immunodeficiency virus (HIV-1) infection

Day 30 discussion

Infectious Diseases

3.1.47. Sulbactam / durlobactam - EMEA-002807-PIP01-20

Treatment of bacterial infections / Treatment of infections caused by *acinetobacter baumannii-calcoaceticus* complex

Day 30 discussion

Infectious Diseases

3.1.48. Rimegepant - EMEA-002812-PIP01-20

Prevention of migraine

Day 30 discussion

Neurology

3.1.49. EMEA-002779-PIP01-20

Treatment of Canavan disease / Treatment of Canavan disease in patients from birth to less than 18 years of age

Day 30 discussion

Neurology

3.1.50. 2-(Isopropylamino)-3-methyl-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one - Orphan - EMEA-002802-PIP01-20

Deciphera Pharmaceuticals; Benign soft tissue neoplasms

Day 30 discussion

Oncology

3.1.51. Balixafortide - EMEA-002718-PIP02-20

Treatment of breast cancer

Day 30 discussion

Oncology

3.1.52. EMEA-002655-PIP02-20

Treatment of prostate cancer

Day 30 discussion

Oncology

3.1.53. Nivolumab - EMEA-001407-PIP03-20

Treatment of all conditions in the category of malignant neoplasms (except haematopoietic and lymphoid tissue other than Hodgkin lymphoma)

Day 30 discussion

Oncology

3.1.54. Oportuzumab monatox - EMEA-002797-PIP01-20

Treatment, including prevention of recurrence, of urothelial carcinoma

Day 30 discussion

Oncology

3.1.55. Sasanlimab - EMEA-002777-PIP01-20

Non-muscle invasive bladder cancer (NMIBC)

Day 30 discussion

Oncology

3.1.56. 2-(hydroxymethyl)-2-(methoxymethyl)-1-azabicyclo[2,2,2]octan-3-one - Orphan - EMEA-002621-PIP01-19

Aprea Therapeutics Inc; Treatment of malignant neoplasms of the haematopoietic and lymphoid tissue / Treatment of solid malignant tumours

Day 30 discussion

Oncology / Haematology-Hemostaseology

3.1.57. Benzimidazole - EMEA-002394-PIP02-20

Treatment of cystic fibrosis / To improve lung function and reduce pulmonary exacerbations for patients with CF in conjunction with standard therapies

Day 30 discussion

Pneumology – Allergology

Summary of committee discussion:

In relation to the planned formulation strategy, it is at present not clear whether a lower dose will be needed in younger age subsets; it was therefore discussed that one option could be to include a placeholder quality measure in the opinion.

No issues were raised for action in relation to the non-clinical development. Regarding the proposed clinical plans, the proposals of the applicant would appear overall acceptable. It was acknowledged that the data on the use of the Respimat device in children below the age of one are still limited but the revised PIP, with efficacy data collection down to young age and more complete determination of exposures is expected to suffice to justify dosing approaches and the use of the formulation/device combination proposed by the applicant.

Some divergent views were expressed on the clinical development below 12 years of age, the Committee however considered that being the product a first-in class, randomized controlled trials even in young age groups are warranted, and they could be reconsidered at later stage. Few details from the clinical studies will need clarification.

3.1.58. Seltorexant - EMEA-002746-PIP01-20

Major depressive disorder (MDD)

Day 30 discussion

Psychiatry

3.1.59. Sparsentan - Orphan - EMEA-001984-PIP02-20

Retrophin Europe Ltd.; Treatment of focal segmental glomerular sclerosis (FSGS)

Day 30 discussion

Uro-nephrology

3.1.60. EMEA-002814-PIP01-20

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

Day 30 discussion

Vaccines

3.1.61. EMEA-002795-PIP01-20

Prevention of respiratory syncytial virus (RSV)-associated medically attended lower respiratory tract illness (MA-LRTI) and/or RSV-associated severe MA LRTI in neonates and infants by maternal immunisation / Prevention of RSV-associated medically attended lower respiratory tract illness (MA-LRTI) and/or RSV associated severe MA-LRTI in neonates and infants by active immunisation of pregnant adolescents

Day 30 discussion

Vaccines

3.1.62. EMEA-002771-PIP01-20

Prevention of influenza disease

Day 30 discussion

Vaccines / Infectious Diseases

3.2. Discussions on Compliance Check

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

3.2.1. Secukinumab - EMEA-C2-000380-PIP01-08-M04

Novartis Europharm Ltd; Treatment of psoriasis

Day 30 discussion

Dermatology

3.2.2. Eptinezumab - EMEA-C1-002243-PIP01-17

H. Lundbeck A/S; Prevention of migraine headaches

Day 30 discussion

Neurology

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Crisaborole - EMEA-002065-PIP01-16-M03

Pfizer Europe MA EEIG; Mild to moderate atopic dermatitis

Day 30 discussion

Dermatology

3.3.2. Efpeglenatide - EMEA-001903-PIP01-15-M01

Sanofi-aventis recherche et développement; Type 2 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.3. Glucagon - EMEA-001657-PIP01-14-M01

Eli Lilly and Company; Treatment of severe hypoglycaemia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.4. Ladarixin - EMEA-002642-PIP01-19-M01

Dompé farmaceutici S.p.A; Treatment of type 1 diabetes / Treatment of new-onset type 1 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.5. Pegvaliase - Orphan - EMEA-001951-PIP01-16-M01

BioMarin International Limited; Treatment of hyperphenylalaninaemia in paediatric patients with phenylketonuria

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.6. Recombinant human glutamic acid decarboxylase (rhGAD65) - EMEA-000609-PIP01-09-M02

Diamyd Medical AB; Treatment of type 1 diabetes

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.7. Ozanimod hydrochloride - EMEA-001710-PIP04-17-M01

Celgene Europe B.V.; Treatment of Crohn's disease

Day 30 discussion

Gastroenterology-Hepatology

3.3.8. Ustekinumab - EMEA-000311-PIP04-13-M03

Janssen-Cilag International NV; Treatment of Crohn’s Disease

Day 30 discussion

Gastroenterology-Hepatology

3.3.9. Ustekinumab - EMEA-000311-PIP05-17-M01

Janssen-Cilag International NV; Treatment of ulcerative colitis

Day 30 discussion

Gastroenterology-Hepatology

3.3.10. Synthetic double-stranded siRNA oligonucleotide directed against antithrombin mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues - Orphan - EMEA-001855-PIP01-15-M02

Genzyme Europe B.V.; Treatment of Haemophilia B / Treatment of Heamophilia A / Fitusiran is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in children aged ≥ 1 year with severe Haemophilia B, including patients who express neutralizing antibodies to exogenous factor IX substitution, Fitusiran is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in children aged ≥ 1 year with severe Haemophilia A, including patients who express neutralizing antibodies to exogenous factor VIII substitution

Day 30 discussion

Haematology-Hemostaseology

3.3.11. Anifrolumab - EMEA-001435-PIP02-16-M01

AstraZeneca AB; Treatment of systemic lupus erythematosus

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.12. Belatacept - EMEA-000157-PIP01-07-M05

Bristol-Myers Squibb Pharma EEIG; Prevention of rejection of transplanted kidney / In combination with corticosteroids and a mycophenolic acid (MPA), for prophylaxis of graft rejection in pediatric patients at least 12 years of age and with a stable renal transplant for

at least 6 months, who convert to a CNI-free maintenance immunosuppressive regimen

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.13. Brincidofovir - Orphan - EMEA-001904-PIP03-18-M01

Chimerix IRL Limited; Treatment of smallpox

Day 30 discussion

Infectious Diseases

3.3.14. Ceftobiprole medocaril sodium - EMEA-000205-PIP02-11-M04

Basilea Pharmaceutica International Ltd.; Bacterial pneumoniae no elsewhere classified / Pneumonia due to Streptococcus pneumoniae / Pneumonia due to Hemphilus influenzae / Treatment of nosocomial pneumonia / Treatment of community acquired pneumonia

Day 30 discussion

Infectious Diseases

3.3.15. Dasabuvir sodium - EMEA-001439-PIP01-13-M03

AbbVie Ltd; Treatment of chronic hepatitis C / Treatment of children and adolescents aged from 3 years to less than 18 years of age with genotype I chronic HCV infection and without liver decompensation, in combination with ombitasvir/paritaprevir/ritonavir

Day 30 discussion

Infectious Diseases

3.3.16. Relebactam monohydrate / cilastatin sodium / imipenem monohydrate - EMEA-001809-PIP01-15-M02

Merck Sharp & Dohme (Europe), Inc.; Treatment of Gram-negative bacterial infections / Treatment of hospital-acquired bacterial pneumonia (HABP) and ventilator-associated bacterial pneumonia (VABP) / Treatment of serious bacterial infections including HABP, VABP, complicated intra-abdominal infections (cIAI) and complicated urinary tract infections (cUTI) caused by aerobic Gram-negative organisms in patients with limited treatment options

Day 30 discussion

Infectious Diseases

3.3.17. Rilpivirine (hydrochloride) - EMEA-000317-PIP01-08-M12

Janssen-Cilag International NV; Treatment of human immunodeficiency virus (HIV-1) infection / Rilpivirine is indicated in combination with other antiretroviral (ARV) medicinal products, for the treatment of human immunodeficiency virus (HIV-1) infection in ARV-

naïve paediatric patients from 2 to less than 18 years with a baseline viral load below 100,000 HIV-1 RNA copies/mL

Day 30 discussion

Infectious Diseases

3.3.18. Ritonavir / paritaprevir / ombitasvir - EMEA-001440-PIP01-13-M03

AbbVie Ltd; Treatment of chronic Hepatitis C (HCV) infection / Treatment of children and adolescents from ≥3 years to < 18 years of age with chronic HCV infection with compensated cirrhosis or without compensated cirrhosis in combination with other medicinal products

Day 30 discussion

Infectious Diseases

3.3.19. Lasmiditan - EMEA-002166-PIP01-17-M04

Eli Lilly and Company Limited; Migraine with and without aura

Day 30 discussion

Neurology

3.3.20. Olenasufligene relduparvovec - Orphan - EMEA-002122-PIP02-17-M01

LYSOGENE; Mucopolysaccharidosis type IIIA / Treatment of children with Sanfilippo type A syndrome

Day 30 discussion

Neurology

3.3.21. Perampanel - EMEA-000467-PIP01-08-M14

Eisai Europe Limited; Treatment of treatment-resistant epilepsies / Adjunctive therapy in patients with other paediatric epilepsies / Adjunctive therapy in patients with refractory partial onset seizures including secondarily generalised seizures

Day 30 discussion

Neurology

3.3.22. Pitolisant - Orphan - EMEA-001176-PIP01-11-M05

BIOPROJET PHARMA; Narcolepsy / Narcolepsy with or without cataplexy

Day 30 discussion

Neurology

3.3.23. Concentrate of proteolytic enzyme enriched in bromelain - Orphan - EMEA-000142-PIP02-09-M09

MediWound Germany GmbH; Treatment of burns of external body surfaces / Removal of eschar in deep partial and/or full thickness burns

Day 30 discussion

Other

3.3.24. Palonosetron / fosnetupitant - EMEA-001198-PIP03-17-M04

Helsinn Birex Pharmaceuticals Limited; Prevention of chemotherapy-induced nausea and vomiting

Day 30 discussion

Other

3.3.25. *Dermatophagoides pteronyssinus* / *Dermatophagoides farinae* - EMEA-001258-PIP01-11-M06

ALK-Abelló A/S; Treatment of allergic rhinitis / Treatment of asthma / In house dust mite allergic asthma / In house dust mite allergic rhinitis

Day 30 discussion

Pneumology – Allergology

3.3.26. Glycopyrronium bromide / Formoterol fumarate dihydrate / Beclometasone dipropionate - EMEA-001875-PIP02-18-M02

Chiesi Farmaceutici S.p.A.; Treatment of asthma

Day 30 discussion

Pneumology – Allergology

3.3.27. Reslizumab - EMEA-001202-PIP02-13-M04

Teva Pharmaceuticals Europe; Treatment of asthma / Add on treatment to reduce exacerbations, relieve symptoms and improve lung function in paediatric patients from 6 to less than 18 years of age with inadequately controlled severe asthma who have a blood eosinophil count greater than equal to 300 microlitre

Day 30 discussion

Pneumology – Allergology

3.3.28. Derivative of 4H-pyrazolo[3,4-d]pyrimidin-4-one - EMEA-001742-PIP01-14-M01

Boehringer Ingelheim International GmbH; Treatment of schizophrenia / Adjunctive therapy to antipsychotic treatment for the prevention of relapse in patients with schizophrenia 13 to

<18 years of age

Day 30 discussion

Psychiatry

3.3.29. Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live) - EMEA-001786-PIP01-15-M01

Merck Sharp & Dohme (Europe), Inc.; Prevention of Ebola disease / Active immunization of individuals from 1 year of age to less than 18 years of age to protect against Ebola virus disease (EVD) caused by Zaire Ebola virus

Day 30 discussion

Vaccines

3.3.30. Purified rabies virus, WISTAR PM/WI 38-1503-3M strain (inactivated) - EMEA-002234-PIP01-17-M01

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

Day 30 discussion

Vaccines

4. Nominations

Disclosure of information related to this section cannot be released 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 26th May 2020 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

No item

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

Disclosure of information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

5.1. New Scientific Advice

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

5.2. Ongoing Scientific Advice

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

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

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

6. Discussion on the applicability of class waivers

Disclosure of some information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

6.1. Discussions on the applicability of class waiver for products

6.1.1. Inhaled long-acting dual muscarinic antagonist and long-acting β2-agonist - EMEA-05-2020

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

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 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 items

8. Annual reports on deferrals

No items

9. Organisational, regulatory and methodological matters

9.1. Mandate and organisation of the PDCO

No items

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 PDCO members were informed about the final CHMP Opinions on 4 medicinal products with recommended paediatric indications adopted in April 2020 by CHMP. These include ECALTA (anidulafungin), Harvoni (ledipasvir / sofosbuvir), Kalydeco (ivacaftor), Sovaldi (sofosbuvir).

The CHMP also recommended approval of a new pharmaceutical form for Harvoni with new strength (45/200 mg film-coated tablets) and a new pharmaceutical form (coated granules) associated with new strengths (33.75/150 mg and 45/200 mg), for Sovaldi with new strength (200 mg film-coated tablets) and a new pharmaceutical form (coated granules) associated with new strengths (150 and 200 mg).

The list of procedures with paediatric indications to be evaluated by the CHMP, starting in April 2020, 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 identified the products which will require Non-

clinical Working Group evaluation and discussion.

9.3.2. Formulation Working Group

PDCO member: Brian Aylward

Summary of committee discussion:

Relevant products for FWG discussion were identified.

9.4. Cooperation within the EU regulatory network

9.4.1. European Network of Paediatric Research (Enpr) - European Medicines Agency (EMA): Severe Paediatric Asthma Collaborative in Europe (SPACE)

Summary of committee discussion:

The Severe Paediatric Asthma Collaborative in Europe (SPACE) was presented. The collaborative was initiated in cooperation with the European network of paediatric research at the EMA (Enpr-EMA) in 2016 with the objective to bring together paediatricians from across Europe who are active in the respiratory field in a Clinical Research Collaboration (CRC) to develop an infrastructure to enhance the participation of children with severe asthma in clinical trials. SPACE has received funding from the European Respiratory Society and has created a prospective non-interventional, pan-European observational registry of paediatric patients with severe asthma. Data entry was started in 2019, the year when SPACE also became an Enpr-EMA member network. Currently 10 centres across Europe participate in the registry and further centres have expressed their interest in taking part. Preliminary registry data in terms of epidemiology and response to biological treatment options were presented and discussed. It was mentioned that the initiative should be scaled up to increase its pan-European outreach and to also create an effective network of centres that not only are able to provide sponsors developing paediatric asthma treatments with registry data but also to conduct paediatric asthma trials in a collaborative manner. Enpr-EMA (Secretariat) offered support to this end.

9.5. Cooperation with International Regulators

No items

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

9.6.1. PCWP/HCPWP Joint meeting

Meeting Summary from the PCWP/HCPWP Joint meeting on 3-4 March 2020

Summary of committee discussion:

The Committee noted the meeting summary.

9.7. PDCO work plan

No items

9.8. Planning and reporting

No items

10. Any other business

10.1. Covid-19 update

Summary of committee discussion:

Updates were given on the current state of knowledge of COVID-19 and on the therapeutics currently under development for the condition.

11. Breakout sessions

11.1. Paediatric oncology

Summary of committee discussion:

Upcoming oncology meetings and regulatory aspects related to waivers were discussed.

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 26-29 May 2020 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:	**2.1.15.** Humanised antibody targeting the inducible T cell co-stimulatory receptor - EMEA-002781-PIP01-20 **2.3.1.** Ambrisentan - Orphan - EMEA-000434-PIP01-08-M07 **2.3.6.** Otilimab - EMEA-001882-PIP02-16-M02
Karl-Heinz Huemer	Member	Austria	No interests declared	
Johanna	Alternate	Austria	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Wernsperger				
Karen Van Malderen	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	N/A
Georgios Savva	Member	Cyprus	No interests declared	
Lucie Kravackova	Member	Czech Republic	No interests declared	
Kirstine Moll Harboe	Member	Denmark	No interests declared	
Irja Lutsar	Member	Estonia	No interests declared	
Jana Lass	Alternate	Estonia	No interests declared	
Ann Marie Totterman	Member	Finland	No interests declared	
Sylvie Benchetrit	Member	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	
Anastastia Mountaki	Alternate	Greece	No interests declared	
Ágnes Gyurasics	Member (CHMP member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	
Sara Galluzzo	Member	Italy	No interests declared	
Dina Apele-Freimane	Member	Latvia	No restrictions applicable to this meeting	N/A
Sigita Burokiene	Member	Lithuania	No interests declared	
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No interests declared	
Herbert Lenicker	Alternate	Malta	No interests declared	
Roel Bolt	Member	Netherlands	No interests declared	
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 interests declared	
Helena Fonseca	Member	Portugal	No interests declared	
Hugo Tavares	Alternate	Portugal	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
Ninna Gullberg	Member	Sweden	No interests declared	
Eva Agurell	Alternate	Sweden	No interests declared	
Fernando Cabanas	Member	Healthcare Professionals' Representative	No participation in final deliberations and voting on:	**2.7.2.** Nirsevimab (anti-respiratory syncytial virus human IgG1κ monoclonal antibody)-EMEA-C1-001784-PIP01-15-M02 **3.2.2.** Nirsevimab (anti-respiratory syncytial virus human IgG1κ monoclonal antibody)
Jorrit Gerritsen	Alternate	Healthcare Professionals' Representative	No interests declared	
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	N/A
Catherine Cornu	Alternate	Healthcare Professionals' Representative	No participation in final deliberations and voting on:	**2.7.2.** Nirsevimab (anti-respiratory syncytial virus human IgG1κ monoclonal antibody)-EMEA-C1-001784-PIP01-15-M02 **3.2.2.** Nirsevimab (anti-respiratory syncytial virus human IgG1κ monoclonal antibody) **3.3.22.** Pitolisant
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Doina Plesca	Alternate	Healthcare Professionals' Representative	No interests declared	
Günter Karl-	Member	Patients'	No restrictions	N/A

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Heinz Auerswald		Organisation Representative	applicable to this meeting	
Paola Baiardi	Alternate	Patients' Organisation Representative	No restrictions applicable to this meeting	N/A
Michal Odermarsky	Member	Patients' Organisation Representative	No participation in final deliberations and voting on:	**3.1.32.** Sacubitril / valsartan
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Viviana Giannuzzi	Alternate	Patients' Organisation Representative	No participation in final deliberations and voting on:	**2.1.14**. Atropine sulphate - EMEA-002545-PIP01-19 (as informed during last meeting)
Maria Estela Moreno Martin	Expert – via telephone*	Spain	No interests declared	
Jonathan Grigg	Expert– via telephone*	UK	No interests declared	
Norrice Liu	Expert– via telephone*	UK	No interests declared	
Meeting run with support from relevant EMA staff				

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/