EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 February 2020
EMA/PDCO/104692/2020
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes for the meeting on 25-28 February 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. 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. 22 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 3.2.1 and 3.3.18.

1.2. Adoption of agenda

PDCO agenda for 24th -28th February 2020

The agenda of the PDCO meeting 25th-28th February was adopted.

1.3. Adoption of the minutes

PDCO minutes for 28th – 31st January 2020

The minutes of the January 2020 PDCO meeting 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. Lenadogene nolparvovec (GS010) - Orphan - EMEA-001992-PIP02-16

GenSight-Biologics; Treatment of Leber hereditary optic neuropathy (LHON)

Day 120 opinion

Ophthalmology

Summary of committee discussion:

The applicant updated their PIP proposal according to the outcome of the PDCO discussion The PDCO adopted a positive opinion for this PIP for the treatment of Leber Hereditary Optic Neuropathy for the paediatric population from 6 years of age. A waiver was agreed on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset.

2.1.2. Dihomo-γ-linolenic acid - EMEA-002364-PIP03-19

DS Biopharma Ltd.; Treatment of atopic dermatitis

Day 120 opinion

Dermatology

Summary of committee discussion:

The PDCO adopted a positive opinion, including a waiver on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit or to fulfil a therapeutic need of the specified paediatric subset.

2.1.3. Lebrikizumab - EMEA-002536-PIP01-18

Dermira Inc.; Treatment of atopic dermatitis

Day 120 opinion

Dermatology

Summary of committee discussion:

The applicant's response to the D90 issues was considered acceptable and a positive opinion was adopted for lebrikizumab in the treatment of atopic dermatitis.

2.1.4. N-(3-{6-Amino-5-[2-(N-methylprop-2-enamido)ethoxy]pyrimidin-4-yl}-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide (LOU064) - EMEA-002582-PIP01-19

Novartis Europharm Limited; Treatment of chronic spontaneous urticaria

Day 120 opinion

Dermatology

Summary of committee discussion:

In conclusion, all issues have been resolved.
The Committee adopted a positive opinion, including a deferral for quality, clinical and extrapolation studies and waiver in children on the grounds that the specific medicinal product is likely to be unsafe in the concerned paediatric subset.

2.1.5. Ladarixin - EMEA-002642-PIP01-19

Dompé farmaceutici SpA; Treatment of type 1 diabetes mellitus

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

During its plenary on 28 February 2020, the PDCO adopted a positive PIP Opinion for ladarixin for the treatment of new-onset type 1 diabetes mellitus (T1D) with residual beta cell function.

2.1.6. Alpha1-proteinase inhibitor (human) (A1-PI) - EMEA-001312-PIP02-19

CSL Behring GmbH; Prevention of graft-versus-host disease (GVHD)

Day 120 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The applicant clarified all outstanding issues between Day 90 and Day 120. As all issues had been resolved the PDCO adopted a positive opinion for this PIP for prevention of graft versus host disease (GVHD). A waiver was granted on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2.1.7. Polymyxin B - EMEA-002595-PIP01-19

The GARDP Foundation; Treatment of infections due to aerobic Gram-negative bacteria

Day 120 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO further discussed the proposed plan.
In conclusion, based on the assessment of this application and the plenary discussion, the PDCO agreed a paediatric investigation plan for polymyxin B in the treatment of infections due to aerobic Gram-negative bacteria. The paediatric development includes the entire paediatric age range. The plan is not deferred and due to complete in 2026.

2.1.8. Leriglitazone - Orphan - EMEA-002106-PIP01-16

Minoryx Therapeutics S.L.; Treatment of adrenoleukodystrophy

Day 120 opinion

Neurology

Summary of committee discussion:

The PDCO adopted a positive opinion agreeing with the PIP for leriglitazone in the condition of treatment of adrenoleukodystrophy.

2.1.9. Cenobamate - EMEA-002563-PIP02-19

Arvelle Therapeutics Netherlands B.V.; Treatment of epilepsy

Neurology

Summary of committee discussion:

The PDCO adopted a favourable opinion on the paediatric investigation plan for cenobamate for the treatment of epilepsy for all the subsets of the paediatric population. No waiver was requested.
It is reminded to the Applicant that the commitments regarding the timelines and dependencies should be followed, and will be carefully considered by the PDCO.

2.1.10. 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea - Orphan - EMEA-002526-PIP02-19

Deciphera Pharmaceuticals LLC; Treatment of gastrointestinal stromal tumours

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this application in line with the outcome conclusion at D90.
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 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of gastrointestinal stromal tumours based on the ground of lack of significant therapeutic benefit since clinical studies in the proposed target population within the condition 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.

2.1.11. Bintrafusp alfa - Orphan - EMEA-002586-PIP01-19

Merck Europe B.V.; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system neoplasms, haematopoietic and lymphoid tissue neoplasms)

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the paediatric investigation plan for bintrafusp alfa.
In conclusion, the PDCO recommends granting a paediatric investigation plan for bintrafusp alfa for the entire paediatric population from birth to less than 18 years of age for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system neoplasms, haematopoietic and lymphoid tissue neoplasms).

2.1.12. Pracinostat - Orphan - EMEA-002567-PIP01-19

Helsinn Birex Pharmaceuticals limited; Treatment of acute myeloid leukemia

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this procedure in line with the discussion outcome at Day 90. Overall the committee agreed to a waiver and a PIP for treatment of patients with AML in the last line setting.

2.1.13. Temozolomide - EMEA-002634-PIP01-19

Accord Healthcare S.L.U.; Treatment of malignant glioma

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the procedure in line with the conclusions made at D90. Overall a positive Opinion was agreed by the committee.

2.1.14. 2-[[2-ethyl-6-[4-[2-(3-hydroxyazetidin-1-yl)-2-oxoethyl]piperazin-1-yl]-8-methylimidazo[1,2-a]pyridin-3-yl](methyl)amino]-4-(4-fluorophenyl)-1,3-thiazole-5-carbonitrile (GLPG1690) - Orphan - EMEA-002333-PIP02-19

Galapagos NV; Treatment of interstitial pulmonary diseases with fibrosis

Day 120 opinion

Pneumology – Allergology

Summary of committee discussion:

The committee's views expressed on day 90 were re-discussed and endorsed. Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO adopted a positive opinion.

2.1.15. (S)-(2-(5-chloro-4-methyl-1H-benzo[d]imidazol-2-yl)-2-methylpyrrolidin-1-yl)(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone hydrochloride (daridorexant) - EMEA-002121-PIP03-19

Idorsia Pharmaceuticals Deutschland GmbH; Treatment of insomnia

Day 120 opinion

Psychiatry

Summary of committee discussion:

The PDCO reviewed and discussed the new information received since Day 90 and concluded that the justifications are adequate, and the described changes are duly implemented in the PIP. The Committee wishes to remind the applicant that while the Paediatric Investigation Plan defines the essential dataset required for licensing in Europe, it

is strongly recommended that the totality of the available and relevant data is submitted as part of the initial marketing authorisation application – including the reports of the studies conducted in the USA, which are not part of the PIP.
A positive opinion endorsing the modified Paediatric Investigation Plan has been adopted.

2.1.16. Pneumococcal polysaccharides individually biotinylated and complexed with a carrier protein (recombinant fusion construct of rhizavidin and *Streptococcus pneumoniae* derived proteins), 24-valent – EMEA-002641-PIP01-19

Astellas Pharma Europe, B.V.; Prevention disease caused by *Streptococcus pneumoniae*

Day 120 opinion

Vaccines

Summary of committee discussion:

Based on the assessment of this application, the PDCO agreed a paediatric investigation plan for this multivalent pneumococcal vaccine in the condition of prevention of disease caused by *Streptococcus pneumoniae*.
The PIP includes a waiver with a deferral granted for the study in immunocompromised children and adolescents at higher risk for invasive pneumococcal disease.

2.1.17. Pneumococcal Polyssacharide Serotype 6A conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 14 conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 3 conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 12F conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 23F conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 33F conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 5 conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 7F conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 6B conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 19A conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 19F conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 8 conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 11A conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 15B conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 1 conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 22F conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 4 conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 9V conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 10A conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 18C conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate - EMEA-002330-PIP01-18

Pfizer MA EEIG; Prevention of disease caused by *Streptococcus pneumoniae*

Day 120 opinion

Vaccines

Summary of committee discussion:

The PDCO adopted a positive opinion on the paediatric investigation plan.

2.1.18. Glycerol / urea - EMEA-002511-PIP02-19

ACO Hud Nordic AB; Treatment of dry skin

Day 60 opinion

Dermatology

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 urea / glycerol for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of treatment of dry skin on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.19. Natalizumab - EMEA-001095-PIP03-19

Biogen Limited Idec; Treatment of multiple sclerosis

Day 60 opinion

Neurology

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO recommends granting a product-specific waiver for natalizumab in all subsets of the paediatric population for the treatment of multiple sclerosis on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to the specified paediatric subset(s).
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.20. 3-(((1S,2S,3R)-2,3-difluoro-1-hydroxy-7-(methylsulfonyl)-2,3-dihydro-1H-inden-4-yl)oxy)-5-fluorobenzonitrile - EMEA-002619-PIP01-19

Merck, Sharp & Dohme (Europe) Inc; Treatment of renal neoplasms

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this procedure at Day 60 during the February 2020 plenary meeting. 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 3-(((1S,2S,3R)-2,3-difluoro-1-hydroxy-7-(methylsulfonyl)-2,3-dihydro-1H-inden-4-yl)oxy)-5-fluorobenzonitrile for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'treatment of renal neoplasms' on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.
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.

2.1.21. 4-[4-({4-[({2-[(3S)-2,6-dioxopiperidin-3-yl]-1-oxo-2,3-dihydro-1H-isoindol-4-yl}oxy)methyl]phenyl}methyl)piperazin-1-yl]-3-fluorobenzonitrile - EMEA-002714-PIP01-19

Celgene Europe B.V.; Treatment of mature B-cell neoplasms

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO's views expressed at D30 were endorsed.
The PDCO therefore agrees with the applicant's request for a waiver and recommends granting a waiver for 4-[4-({4-[({2-[(3S)-2,6-dioxopiperidin-3-yl]-1-oxo-2,3-dihydro-1H-isoindol-4-yl}oxy)methyl]phenyl}methyl)piperazin-1-yl]-3-fluorobenzonitrile for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of treatment of mature B-cell neoplasms on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).
The PDCO 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.

2.1.22. Lazertinib (mesylate) - EMEA-002725-PIP01-19

Janssen-Cilag International N.V.; Treatment of lung carcinoma (small cell and non-small cell carcinoma)

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 Lazertinib mesylate for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of Lung Carcinoma (Small Cell and Non-Small Cell Carcinoma).

Because lung cancer is indeed observed sporadically in children, the ground for the waiver granted is that the proposed product does not cover an unmet therapeutic need as studies are not feasible due to the scarcity of the disease in the 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.

2.1.23. Lanadelumab - Orphan - EMEA-001864-PIP02-19

Shire Pharmaceuticals Ireland Limited (a Takeda company); Prevention of acquired angioedema attacks

Day 60 opinion

Other

Summary of committee discussion:

During its plenary on 28 February 2020, the PDCO adopted a favourable opinion on the full waiver request for Lanadelumab for the prevention of acquired angioedema attacks (AAE). The PDCO supports the full waiver request in all paediatric age subsets on the grounds of the disease only occurring in the adult population. Acquired angioedema due to C1-INH deficiency is not a disease which occurs in the paediatric population. Symptom onset is not described in patients before 21 years of age.

2.1.24. Pegcetacoplan - Orphan - EMEA-002600-PIP01-19

Apellis Ireland Limited; Treatment of paroxysmal nocturnal haemoglobinuria

Day 120 Opinion

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO re-discussed this procedure in line with the discussion outcome at day 90.
The PDCO concluded on a positive Opinion for development of pegcetacoplan for patients with Paroxysmal Nocturnal Haemoglobinuria (PNH). The committee agreed to a waiver based on the ground of lack of safety in the concerned subset of the paediatric patient population.

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. Lubiprostone - EMEA-C-000245-PIP01-08-M06

Sucampo AG; Treatment of constipation

Day 60 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

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

EMEA-C4-000245-PIP01-08-M05

The PDCO adopted on 28 February 2020 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision P/0363/2019 of 4 November 2019.

2.2.2. Avatrombopag (maleate) - EMEA-C1-001136-PIP01-11-M01

Dova Pharmaceuticals Ireland Ltd.; Treatment of idiopathic thrombocytopenic purpura

Day 60 letter

Haematology-Hemostaseology

Summary of committee discussion:

Following the additional information received on the issues previously identified at Day 30, the PDCO reviewed the completed studies and the study initiation date and considered that these are compliant with the latest Agency's Decision P/0373/2019 of 22 November 2019. The PDCO finalised this partially completed compliance procedure on 28 February 2020.

2.2.3. Mepolizumab - EMEA-C-000069-PIP04-13-M02

GSK Trading Services Limited; Treatment of vasculitides

Day 30 opinion

Pneumology – Allergology

Summary of committee discussion:

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

- EMEA-C1-000069-PIP04-13-M01

The PDCO adopted on 28/02/2020 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0300/2018) of 12/09/2018.

2.2.4. Sitagliptin phosphate - EMEA-C-000470-PIP01-08-M11

Merck Sharp & Dohme (Europe), Inc.; Treatment of type 2 diabetes mellitus

Day 30 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO discussed the compliance check request.
The PDCO adopted on 28 February 2020 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision P/0358/2019 of 4/10/2019.

2.2.5. Ambrisentan - EMEA-C2-000434-PIP01-08-M06

Glaxo Group Limited; Treatment of pulmonary arterial hypertension

Day 30 letter

Cardiovascular Diseases

Summary of committee discussion:

The PDCO discussed the completed studies
In conclusion, the PDCO considered that the studies are compliant with the latest Agency's Decision P/0370/2019 of 08 November 2019.
The PDCO finalised this partially completed compliance procedure on 28 February 2020.

2.2.6. Cabozantinib (S)-malate - EMEA-C1-001143-PIP01-11

Ipsen Pharma; Treatment of malignant solid tumours

Day 30 letter

Oncology

Summary of committee discussion:

The PDCO discussed the partial compliance check request.

It considered the study 2 to be compliant.

The delay in completion of the study 3 was considered not having any impact on the overall objective of the trial. Hence compliance also agreed.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Tralokinumab - EMEA-001900-PIP02-17-M03

LEO Pharma A/S; Treatment of atopic dermatitis

Day 60 opinion

Dermatology

Summary of committee discussion:

The PDCO discussed the Applicant’s responses at Day.
The PIP completion delay was agreed by the members.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency’s latest decision (P/0104/2019 of 25 March 2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.2. Mirikizumab - EMEA-002208-PIP01-17-M01

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

Day 60 opinion

Dermatology / Gastroenterology-Hepatology

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/0283/2018 of 12 September 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.3. Semaglutide - EMEA-001441-PIP01-13-M03

Novo Nordisk A/S; Treatment of type 2 diabetes mellitus

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

During its plenary meeting on 28 February 2020 the PDCO adopted a favourable PIP Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0036/2019 of 29/01/2019), for semaglutide (s.c.) for the treatment of type 2 diabetes mellitus (T2D).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.4. Elafibranor - EMEA-001857-PIP01-15-M01

GENFIT SA; Treatment of non-alcoholic fatty liver disease including non-alcoholic steatohepatitis

Day 60 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The applicant's responses to the D30 issues were 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/0237/2016 of 9 September 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.5. Etrolizumab - EMEA-001434-PIP01-13-M03

Roche Registration GmbH; Treatment of ulcerative colitis / Treatment of Crohn's disease

Day 60 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The applicant provided clarification to the points raised during the PDCO Day 30 discussion and provided further comments/clarifications.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0327/2019 of 11 September 2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.6. Linaclotide - EMEA-000927-PIP01-10-M05

Allergan Pharmaceuticals International Limited; Treatment of functional constipation

Day 60 opinion

Gastroenterology-Hepatology

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/0252/2016 of 26 September 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.7. Boceprevir - EMEA-000583-PIP01-09-M08

Merck Sharp & Dohme (Europe), Inc; Treatment of chronic hepatitis C

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/0097/2016 of 15 April 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.8. Tenofovir (disoproxil fumarate) - EMEA-000533-PIP01-08-M08

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

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0262/2017 of 4 September 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.9. Galcanezumab - EMEA-001860-PIP03-16-M04

Eli Lilly and Company Limited; Prevention of migraine headaches

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 agreed with the proposed changes to the PIP
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0248/2019 of 16/7/2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.10. Autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti CD19 CD28/CD3-zeta chimeric antigen receptor and cultured (KTE-X19) - Orphan - EMEA-001862-PIP01-15-M02

Kite Pharma EU B.V.; Treatment of acute lymphoblastic leukaemia

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this procedure at Day 60 during the February 2020 plenary meeting.
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/0002/2019 of 3 January 2019).

2.3.11. Axicabtagene ciloleucel - Orphan - EMEA-002010-PIP01-16-M02

Kite Pharma EU B.V.; Treatment of mature B-cell neoplasms

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this procedure at Day 60 during the February 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/0004/2019 of 3 January 2019).

2.3.12. Blinatumomab - Orphan - EMEA-000574-PIP02-12-M03

Amgen Europe B.V.; Treatment of acute lymphoblastic leukaemia

Day 60 opinion

Oncology

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, 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/0401/2017 of 19/12/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.13. Copanlisib - Orphan - EMEA-001757-PIP02-15-M01

Bayer AG; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue) / Treatment of mature B-cell neoplasms

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO's views expressed at D30 were confirmed and 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/0262/2016 of 5 October 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.14. Clostridium botulinum neurotoxin type A (150 kD), free from complexing proteins - EMEA-001039-PIP02-12-M04

Merz Pharmaceuticals GmbH; Treatment of sialorrhea

Day 60 opinion

Ophthalmology / Neurology

Summary of committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed.
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/0195/2019 of 15/05/2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.15. Palovarotene - Orphan - EMEA-001662-PIP01-14-M03

Ipsen Pharma; Treatment of fibrodysplasia ossificans progressiva

Day 60 opinion

Other

Summary of committee discussion:

The PDCO re-discussed this procedure at Day 60 during the February 2020 plenary meeting. The PDCO took into consideration the update the applicant provided on the current situation with the clinical studies carried out with palovarotene.
The PDCO agreed that this modified request for modification is now acceptable. The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0121/2018 of 11 April 2018).

2.3.16. Monovalent, live, recombinant, replication-incompetent adenoviral serotype 26 vectored vaccine expressing the full length glycoprotein of the Ebola virus Mayinga variant (Ad26.ZEBOV) - EMEA-002307-PIP01-17-M01

Janssen Cilag International NV; Prevention of Ebola virus disease

Day 60 opinion

Vaccines

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, 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/0116/2019 of 18/03/2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.17. Multivalent, live, recombinant, non-replicating in human cells, Modified Vaccinia Ankara vectored vaccine, expressing the EBOV Mayinga glycoprotein, the Sudan virus Gulu GP, the Marburg virus Musoke GP, and the Taï Forest virus nucleoprotein (MVA-BN-Filo) - EMEA-002308-PIP01-17-M01

Janssen Cilag International NV; Prevention of Ebola virus disease

Day 60 opinion

Vaccines

Summary of committee discussion:

Based on the review of the rationale submitted by the application for modifying the agreed paediatric investigation plan, 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/0117/2019 of 18/03/2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.18. Regorafenib - EMEA-001178-PIP01-11-M05

Bayer AG; Treatment of all conditions contained in the category of malignant neoplasms (except haematopoietic and lymphoid tissue)

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0158/2019 of 17/4/2019).
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. Ustekinumab - EMEA-C1-000311-PIP04-13-M01

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

Day 1 letter

Immunology-Rheumatology-Transplantation / Gastroenterology-Hepatology

2.7.2. Ticagrelor - EMEA-C3-000480-PIP01-08-M11

AstraZeneca AB; Prevention of thromboembolic events

Day 30 letter

Cardiovascular Diseases / Haematology-Hemostaseology

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. Livoletide - Orphan - EMEA-002455-PIP01-18

Millendo Therapeutics SAS; Treatment of Prader-Willi syndrome

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.2. Edasalonexent [N-(2-((4Z,7Z,10Z,13Z,16Z,19Z)-docosa-4,7,10,13,16,19-hexaenamido)ethyl)-2-hydroxybenzamide] - Orphan - EMEA-001960-PIP02-16

Catabasis Pharmaceuticals Inc.; Duchenne muscular dystrophy / Treatment of Duchenne muscular dystrophy

Day 90 discussion

Neurology

3.1.3. Cyclophosphamide - EMEA-002644-PIP01-19

Treatment of all malignant neoplasms

Day 90 discussion

Oncology

3.1.4. Imatinib - EMEA-002643-PIP01-19

Treatment of newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) integrated with chemotherapy/Treatment of Chronic myelogenous leukaemia: Philadelphia chromosome (Ph1) positive with crisis of blast cells / Paediatric patients with newly diagnosed Philadelphia chromosome (bcr-abl) positive (Ph+) chronic myeloid leukaemia (CML) for whom bone marrow transplantation is not considered as the first line of treatment /Paediatric patients with Ph+ CML in chronic phase after failure of interferon-alpha therapy or in accelerated phase or blast crisis /Paediatric patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) integrated with chemotherapy

Day 90 discussion

Oncology

3.1.5. EMEA-002674-PIP01-19

Treatment of acne vulgaris

Day 60 discussion

Dermatology

3.1.6. Crinecerfont - Orphan - EMEA-002700-PIP01-19

Neurocrine Therapeutics Ltd; Treatment of congenital adrenal hyperplasia

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.7. Lerodalcibep - EMEA-002720-PIP01-19

Treatment of elevated cholesterol / Treatment of elevated low-density lipoprotein cholesterol (LDL-C) in children from 6 to less than 18 years of age with heterozygous familial hypercholesterolaemia (HeFH) or with homozygous familial hypercholesterolaemia (HoFH)

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.8. Recombinant human acid alpha-glucosidase - Orphan - EMEA-002447-PIP01-18

Amicus Therapeutics Europe Limited; Treatment of glycogen storage disease type II (Pompe's disease)

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.9. Venglustat - Orphan - EMEA-001716-PIP04-19

Genzyme Europe B.V.; E.75.0 GM2 gangliosidosis, E.75.1 Other gangliosidosis, GM1, GM3, E.77.1 Defects in glycoprotein degradation, sialidosis / Long term treatment of patients with a confirmed diagnosis of late onset GM2 gangliosidosis / Long term treatment in patients within the same biochemical pathway as GM2 gangliosidosis / Long term treatment in patients with juvenile (subacute) and adolescent (late-onset) GM2 gangliosidosis ages 2 years old and older, males/females

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Neurology

3.1.10. Garadacimab - EMEA-002726-PIP01-19

Hereditary angioedema attacks (HAE)

Day 60 discussion

Haematology-Hemostaseology

3.1.11. Recombinant adeno-associated viral vector serotype 6 encoding the B-domain-deleted human factor VIII - Orphan - EMEA-002724-PIP01-19

Pfizer Europe MA EEIG; Treatment of haemophilia A (congenital FVIII deficiency)

Day 60 discussion

Haematology-Hemostaseology

3.1.12. Alpha1-proteinase inhibitor (human) - EMEA-001312-PIP03-19

Prevention of graft-versus-host disease

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.13. Doravirine / islatravir - EMEA-002707-PIP01-19

Treatment of human immunodeficiency virus-1 (HIV-1) infection / Doravirine/islatravir is indicated alone or in combination with other antiretroviral medicinal products for the treatment of HIV-1 infection in paediatric patients from 28 days to less than 18 years of age

Day 60 discussion

Infectious Diseases

3.1.14. Vonoprazan - EMEA-002703-PIP01-19

Helicobacter Pylori / Reflux oesophagitis / Treatment of erosive reflux oesophagitis and relief of heartburn / Eradication of Helicobacter pylori (H. pylori) concurrently given with appropriate antibiotic therapy

Day 60 discussion

Infectious Diseases / Gastroenterology-Hepatology

3.1.15. Autologous CD4 and CD8 T-cells that have been transduced with a self-inactivating lentiviral vector expressing an affinity enhanced NY-ESO-1 specific T-Cell Receptor - Orphan - EMEA-002476-PIP02-19

GlaxoSmithKline Trading Services Limited; Soft tissue sarcoma

Day 60 discussion

Oncology

3.1.16. Efbemalenograstim alfa - EMEA-002507-PIP02-19

Prevention of chemotherapy-induced neutropenia and febrile neutropenia / Reduction in the duration of neutropenia and the incidence of febrile neutropenia in patients treated with cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukaemia and myelodysplastic syndromes)

Day 60 discussion

Oncology

3.1.17. Relatlimab / nivolumab - EMEA-002727-PIP01-19

Treatment of melanoma / Relatlimab/nivolumab fixed dose combination for treatment of unresectable or metastatic melanoma in patients from 12 to 18 years

Day 60 discussion

Oncology

3.1.18. Romiplostim - EMEA-000653-PIP02-19

Secondary thrombocytopenia / Treatment of chemotherapy-induced thrombocytopenia (CIT) in children <18 years of age with solid tumours

Day 60 discussion

Oncology / Haematology-Hemostaseology

3.1.19. 4-{(2S,4S)-4-Ethoxy-1-[(5-methoxy-7-methyl-1H-indol-4-yl)methyl]piperidin-2-yl}benzoic acid hydrochloride(1/1) - Orphan - EMEA-002705-PIP01-19

Novartis Europharm Limited; C3 glomerulopathy

Day 60 discussion

Other

3.1.20. EMEA-002705-PIP02-19

IgA nephropathy

Day 60 discussion

Other

3.1.21. Alpelisib - EMEA-002016-PIP03-19

PIK3CA related overgrowth spectrum (PROS)

Day 60 discussion

Other

3.1.22. Lanadelumab - Orphan - EMEA-001864-PIP03-19

Shire Pharmaceuticals Ireland Limited (a Takeda company); Prevention of attacks of idiopathic non-histaminergic angioedema (INHA)

Day 60 discussion

Other

3.1.23. Macitentan - Orphan - EMEA-001032-PIP03-19

Janssen-Cilag International N.V.; Fontan-palliated patients

Day 30 discussion

Cardiovascular Diseases

3.1.24. Spesolimab - EMEA-002475-PIP02-19

Prevention of generalized pustular psoriasis (GPP) / Treatment of GPP / Treatment of patients with acute or chronic GPP and for the prevention of flares

Day 30 discussion

Dermatology

3.1.25. Cotadutide - EMEA-002712-PIP01-19

Treatment of non-cirrhotic non-alcoholic steatohepatitis (NASH) or non-alcoholic fatty liver disease (NAFLD) / For the resolution of steatohepatitis with no worsening of fibrosis in obese children and adolescents with non-cirrhotic non-alcoholic steatohepatitis (NASH) and non-alcoholic fatty liver disease (NAFLD)

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.26. Fenofibrate / rosuvastatin - EMEA-002743-PIP01-19

Cardiovascular risk with mixed dyslipidaemia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Cardiovascular Diseases

3.1.27. DTX401 - Orphan - EMEA-002734-PIP01-19

Ultragenyx Germany GmbH; Treatment of glycogen storage disease type Ia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.28. Benzocaine / hydrocortisone - EMEA-002739-PIP01-19

Grade II hemorrhoids / Grade I hemorrhoids / Local relief of pain, itching, burning and inflammation associated with hemorrhoids

Day 30 discussion

Gastroenterology-Hepatology

3.1.29. Etrasimod L-arginine - EMEA-002713-PIP01-19

Treatment of ulcerative colitis / Treatment of moderately or severely active ulcerative colitis

Day 30 discussion

Gastroenterology-Hepatology

3.1.30. Autologous CD34+ hematopoietic stem cells with a CRISPR-edited erythroid enhancer region of the BCL11A gene - Orphan - EMEA-002730-PIP01-19

Vertex Pharmaceuticals (Ireland) Limited; Treatment of beta-thalassemia / Treatment of transfusion-dependent beta-thalassemia

Day 30 discussion

Haematology-Hemostaseology

3.1.31. Etranacogene dezaparvovec - Orphan - EMEA-002722-PIP01-19

uniQure biopharma B.V.; Treatment of haemophilia B

Day 30 discussion

Haematology-Hemostaseology

3.1.32. Plasma kallikrein inhibitor - EMEA-002723-PIP01-19

Treatment of hereditary angioedema

Day 30 discussion

Haematology-Hemostaseology

3.1.33. Ibrexafungerp - EMEA-002535-PIP03-19

Vulvovaginal candidiasis

Day 30 discussion

Infectious Diseases

3.1.34. Adeno-associated virus serotype rh74 containing a human micro-dystrophin gene - EMEA-002677-PIP01-19

Duchenne muscular dystrophy

Day 30 discussion

Neurology

3.1.35. Diroximel - EMEA-002685-PIP02-19

Treatment of multiple sclerosis

Day 30 discussion

Neurology

3.1.36. 18-(p-[131I]-iodophenyl)octadecyl phosphocholine - Orphan - EMEA-002745-PIP01-19

Cellectar Biosciences, Inc.; Multiple myeloma / Mature B-cell lymphomas

Day 30 discussion

Oncology

3.1.37. Padsevonil - EMEA-002466-PIP02-19

Treatment of fixation off sensitivity (FOS) in patients with epilepsy / Adjunctive treatment of FOS in paediatric patients with epilepsy

Day 30 discussion

Neurology

3.1.38. Arfolitixorin - EMEA-002223-PIP01-19

Treatment of colorectal cancer

Day 30 discussion

Oncology

3.1.39. Idasanutlin - Orphan - EMEA-001489-PIP02-19

Roche Registration GmbH; Treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue) / Treatment of children with a solid malignant tumour and which is newly-diagnosed and metastatic, or refractory to first-line treatment

Day 30 discussion

Oncology

3.1.40. EMEA-002716-PIP01-19

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

Day 30 discussion

Oncology

3.1.41. Tiragolumab - EMEA-002721-PIP01-19

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

Day 30 discussion

Oncology

3.1.42. 17-mer, 2'-O-methyl modified phosphorothioate RNA oligonucleotide - Orphan - EMEA-002717-PIP01-19

ProQR Therapeutics; Treatment of inherited retinal disorders / Treatment of Leber's congenital amaurosis due to the p.Cys998X mutation (C2991 +1655A>G) in the CEP290 gene

Day 30 discussion

Ophthalmology

3.1.43. Difelikefalin - EMEA-002565-PIP02-19

Chronic kidney disease (CKD)-associated pruritus

Day 30 discussion

Other

3.1.44. Recifercept - Orphan - EMEA-002715-PIP01-19

Pfizer Europe MA EEIG; Treatment of achondroplasia

Day 30 discussion

Other

3.1.45. EMEA-002731-PIP01-19

Treatment of schizophrenia

Day 30 discussion

Psychiatry

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.

No items

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Crisaborole - EMEA-002065-PIP01-16-M02

Pfizer Europe MA EEIG; Mild to moderate atopic dermatitis

Day 30 discussion

Dermatology

3.3.2. Avalglucosidase alfa - Orphan - EMEA-001945-PIP01-16-M02

Genzyme Europe B.V.; ICD-10: E74.0; Glycogen storage disease (Pompe disease) / Long-term use as an enzyme replacement therapy (ERT) for the treatment of patients with a confirmed diagnosis of Pompe disease (acid α-glucosidase deficiency)

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.3. Dulaglutide - EMEA-000783-PIP01-09-M05

Eli Lilly and Company; Treatment of type 2 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.4. Romosozumab - EMEA-001075-PIP04-15-M02

UCB Pharma S.A.; Treatment of osteoporosis / Treatment of osteogenesis imperfecta / Treatment of glucocorticoid-induced osteoporosis

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.5. Teplizumab - EMEA-000524-PIP01-08-M02

Provention Bio, Inc.; Recent-onset type I diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.6. Volanesorsen - Orphan - EMEA-001915-PIP01-15-M02

Akcea Therapeutics; Familial chylomicronemia syndrome

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.7. Alicaforsen (as sodium salt) - Orphan - EMEA-002060-PIP02-17-M01

Atlantic Healthcare Europe B.V.; Treatment of gastrointestinal procedural complications / Treatment of active episodes of antibiotic refractory pouchitis

Day 30 discussion

Gastroenterology-Hepatology

3.3.8. Tofacitinib - EMEA-000576-PIP03-12-M03

Pfizer Europe MA EEIG; Treatment of ulcerative colitis

Day 30 discussion

Gastroenterology-Hepatology

3.3.9. 2-iminobiotin - Orphan - EMEA-001070-PIP01-10-M02

Neurophyxia BV; Perinatal asphyxia / Treatment of perinatal asphyxia

Day 30 discussion

Neonatology - Paediatric Intensive Care

3.3.10. Isoflurane - EMEA-002320-PIP01-17-M01

Sedana Medical AB; Sedation of mechanically ventilated patients

Day 30 discussion

Neonatology - Paediatric Intensive Care

3.3.11. Dimethyl fumarate - EMEA-000832-PIP01-10-M05

Biogen Idec Ltd.; Multiple Sclerosis / Treatment of relapsing remitting forms of multiple sclerosis

Day 30 discussion

Neurology

3.3.12. Pitolisant - Orphan - EMEA-001176-PIP01-11-M04

BIOPROJET PHARMA; Narcolepsy / Narcolepsy with or without cataplexy

Day 30 discussion

Neurology

3.3.13. Setmelanotide - Orphan - EMEA-002209-PIP01-17-M01

Rhythm Pharmaceuticals, Inc; Treatment of appetite and general nutrition disorders / Treatment of obesity and/or hyperphagia associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway

Day 30 discussion

Nutrition

3.3.14. Afatinib - EMEA-001596-PIP02-17-M02

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

Day 30 discussion

Oncology

3.3.15. Talimogene laherparepvec - EMEA-001251-PIP01-11-M04

Amgen Europe B.V.; Melanoma / Treatment of adolescent patients with unresectable stage IIIB/C/IVM1a melanoma

Day 30 discussion

Oncology

3.3.16. Gilteritinib (as fumarate) - Orphan - EMEA-002064-PIP01-16-M02

Astellas Pharma Europe B.V.; Treatment of acute myeloid leukemia / Treatment of patients from 6 months to less than 18 years of age with relapsed or refractory FLT3/ITD positive acute myeloid leukaemia or newly-diagnosed FLT3/ITD positive acute myeloid leukaemia

Day 30 discussion

Oncology / Haematology-Hemostaseology

3.3.17. Ivacaftor - Orphan - EMEA-000335-PIP01-08-M14

Vertex Pharmaceuticals (Ireland) Ltd; Cystic fibrosis (E84 of ICD10) / Treatment of cystic fibrosis

Day 30 discussion

Other

3.3.18. Rolapitant - EMEA-001768-PIP02-15-M03

Chemotherapy-induced nausea and vomiting (CINV) in subjects receiving highly emetogenic chemotherapy (HEC)

Day 30 discussion

Other

3.3.19. Methoxyflurane - EMEA-000334-PIP01-08-M09

Medical Developments UK Ltd; Treatment of acute pain / Self administration to conscious patients with minor trauma and associated pain, under supervision of personnel trained in its use / For the management of acute pain associated with short surgical procedures, such as the change of dressings, dislocations and injections

Day 30 discussion

Pain

3.3.20. Dupilumab - EMEA-001501-PIP02-13-M05

sanofi-aventis recherche & développement; Treatment of asthma

Day 30 discussion

Pneumology – Allergology

3.3.21. Ivacaftor / tezacaftor - Orphan - EMEA-001640-PIP01-14-M06

Vertex Pharmaceuticals (Europe) Ltd.; Cystic fibrosis / Treatment of cystic fibrosis

Day 30 discussion

Pneumology – Allergology

3.3.22. Influenza virus surface antigens - A/turkey/turkey/1/05 (H5N1) - EMEA-000599-PIP01-09-M07

Seqirus S.r.l.; Prevention of influenza / Active immunisation against H5N1 subtype of influenza A virus

Day 30 discussion

Vaccines

3.3.23. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - EMEA-001830-PIP01-15-M02

Seqirus S.r.l.; Prevention of influenza / Prophylaxis of influenza in an officially declared pandemic situation

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 31 March 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.

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

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. Estradiol/ Progesterone - EMEA-21-2019

Theramex Ireland Ltd; All classes of medicinal products for treatment of climacteric symptoms associated with decreased oestrogen levels, as occurring at menopause/ Hormone replacement therapy for oestrogen deficiency symptoms in postmenopausal women

Summary of committee discussion:

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

Other potential paediatric interests of this medicine suggested by PDCO: None identified at this stage.

6.1.2. Selective estrogen receptor degrader/downregulator - EMEA-22-2019

Roche Registration GmbH; The classes of oestrogen receptor modulator medicinal products for treatment of breast malignant neoplasms / In combination with palbociclib, for the treatment of women with oestrogen receptor-positive (ER +) HER2-negative (HER2 -) previously untreated locally advanced or metastatic breast cancer (MBC)

Summary of committee discussion:

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

Other potential paediatric interests of this medicine suggested by PDCO: None identified at this stage.

6.1.3. Selective estrogen receptor covalent antagonist - EMEA-01-2020

Eisai GmbH; The classes of oestrogen receptor modulator medicinal products for treatment of breast malignant neoplasms / Treatment of locally advanced or metastatic oestrogen receptor-positive, HER2 (human epidermal growth factor receptor 2)-negative breast cancer

Summary of committee discussion:

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

Other potential paediatric interests of this medicine suggested by PDCO: None identified at this stage.

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

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

No 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 January 2020. These included Staquis (crisaborole), GIVLAARI (givosiran), Rezolsta (darunavir / cobicistat) and Vaxchora (Oral cholera live-vaccine).

The CHMP also recommended approval of a new pharmaceutical form: Rezolsta (darunavir / cobicistat), of an age-appropriate oral dosage form for children above 3 years of age and weighing 15 – 25 kg.

The list of procedures with paediatric indications to be evaluated by the CHMP, starting in January 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.

9.3.3. Extrapolation - update on the guidance template

Summary of committee discussion:

The PDCO was informed about the progress of implementing a structured approach to the use of extrapolation in paediatric developments.

9.3.4. Meeting Summary from the Annual Patients and Consumers Working Party (PCWP)/ Healthcare Professionals Working Party (HCPWP) with all eligible organisations - 20 November 2019

Summary of committee discussion:

The meeting summary of the PCWP/HCPWP was noted.

9.3.5. Agenda for the Patients and Consumers Working Party (PCWP)/ Healthcare Professionals Working Party (HCPWP) on 03-04 March 2020

Summary of committee discussion:

The Agenda for the PCWP/HCPWP was noted.

9.3.6. PDCO-SAWP interaction

Summary of committee discussion:

A presentation was delivered on the PDCO-SAWP interaction and the re-examination of the composition of the SAWP. The PDCO was invited to nominate new members as representatives of the PDCO at SAWP.

9.4. Cooperation within the EU regulatory network

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

PDCO representation in Enpr-EMA's Coordinating Group

Summary of committee discussion:

The committee was informed that there was a need to appoint a new PDCO representative to become a member of the Coordinating Group of the European Network of Paediatric Research at the EMA (Enpr-EMA). Members were asked to express their interest via e-mail to the Chair within the following two weeks.

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. Fifth Accelerate Paediatric Strategy Forum for Medicinal Product Development of Epigenetic Modifiers in Children – feedback from the meeting

Summary of committee discussion:

The main conclusions of the Fifth Accelerate Paediatric Strategy Forum for Medicinal Product Development of Epigenetic Modifiers in Children were presented to the Committee.

9.7. PDCO work plan

No items

9.8. Planning and reporting

No items

10. Any other business

10.1.1. Introduction to the new H-Division

Summary of committee discussion:

A presentation of the new Human division was provided to inform the members on how the new organisational structured would impact the PDCO.

10.1.2. UK withdrawal from the EU - update

Summary of committee discussion:

An update on the UK withdrawal from the EU was presented.

10.1.3. PDCO meeting

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

The group discussed paediatric investigation plans under assessment at the PDCO.

11.1.2. Neonatology

Summary of committee discussion:

The group discussed paediatric investigation plans under assessment at the PDCO.

11.1.3. Inventory

Summary of committee discussion:

The group convened on the margins of the PDCO plenary meeting to discuss how to best gather input on unmet needs from clinical experts.

11.1.4. Internal PDCO Operations

Summary of committee discussion:

The PDCO discussed feedback received on how to improve the functioning of the PDCO.

11.1.5. External regulatory collaboration

Summary of committee discussion:

The PDCO discussed feedback received on how to improve the interaction of the PDCO with other Committees and WPs.

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 25-28 February 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: When not chairing the meeting: No participation in final deliberations and voting on:	- 3.1.15. -Autologous CD4 and CD8 T-cells that have been transduced with a self-inactivating lentiviral vector expressing an affinity enhanced NY-ESO-1 specific T-Cell Receptor - Orphan - EMEA-002476-PIP02 -19 -3.2.1. Ambrisentan - EMEA-C2-000434-PIP01-08-M06 - 3.2.5. Mepolizumab - EMEA-C-000069-PIP04-13-M02 - 3.3.18. ROLAPITANT - EMEA-001768-PIP02-15-M03
Karl-Heinz Huemer	Member	Austria	No interests declared	
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	
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	
Pia Annunen	Alternate	Finland	No participation in discussions, final deliberations and voting on:	-3.1.17. Relatlimab / nivolumab - EMEA-002727-PIP01-19;
Sylvie Benchetrit	Member	France	No interests declared	
Dominique Ploin	Alternate	France	No interests declared	
Sabine Scherer	Member	Germany	No interests declared	
Yuansheng	Alternate	Germany	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Sun				
Eleni Katsomiti	Member	Greece	No interests declared	
Ágnes Gyurasics	Member (CHMP member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	
Sara Galluzzo	Member	Italy	No interests declared	
Dina Apele-Freimane	Member	Latvia	No 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	
Dana Gabriela Marin	Member (CHMP alternate)	Romania	No interests declared	
Peter Sisovsky	Member	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 restrictions applicable to this meeting	N/A
Jorrit Gerritsen	Alternate	Healthcare Professionals' Representative	No interests declared	
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	N/A

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Catherine Cornu	Alternate	Healthcare Professionals' Representative	No participation in final deliberations and voting on:	- 3.3.12. Pitolisant - Orphan - EMEA-001176-PIP01-11-M04;
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Doina Plesca	Alternate	Healthcare Professionals' Representative	No interests declared	
Günter Karl-Heinz Auerswald	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	N/A
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:	
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Maria Estela Moreno Martin	Expert - in person*	Spain	No interests declared	
Meeting run with support from relevant EMA staff				

* Experts were only 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/