29 March 2019
EMA/PDCO/149030/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes of the meeting on 26 February-01 March 2019

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

26 February 2019, 14:00- 19:00, room 3A

27 February 2019, 08:30- 19:00, room 3A

28 February 2019, 08:30- 19:00, room 3A

01 March 2019, 08:30- 13:00, room 3A

Disclaimers

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

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

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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Table of contents

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. 23 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. Adoption of agenda

The agenda was adopted and published on the EMA website.

1.3. Adoption of the minutes

The minutes of the January 2019 PDCO meeting were adopted and published on the EMA website.

2. Opinions

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. N-hydroxy-5-methylfuran-2-sulfonamide - EMEA-002378-PIP01-18

Bristol-Myers Squibb International Corporation; Treatment of acute heart failure

Day 120 opinion

Cardiovascular Diseases

Summary of committee discussion:

The PDCO adopted a positive opinion, including a deferral.

2.1.2. Ozanimod - EMEA-001710-PIP03-17

Celgene Europe Limited; Treatment of ulcerative colitis

Day 120 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The Applicant's response to the Day 90 issues was acknowledged. A positive opinion was adopted.

2.1.3. Anti-IL-21 humanized immunoglobulin G1-kappa monoclonal antibody - EMEA-002374-PIP01-18

Boston Pharmaceuticals, Inc.; Treatment of systemic lupus erythematosus (SLE)

Day 120 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

At its February 2019 meeting, the PDCO noted that all remaining points raised at Day 90 had been addressed and agreed a PIP with a deferral for anti-IL-21 humanized immunoglobulin G1-kappa monoclonal antibody in the condition of 'Treatment of systemic lupus erythematosus (SLE)'.

2.1.4. Voclosporin - EMEA-002264-PIP01-17

Aurinia Pharmaceuticals Ltd.; Treatment of systemic lupus erythematosus / Treatment of active lupus nephritis

Day 120 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO noted that the remaining issues raised at Day 90 were resolve. Therefore the PDCO agreed at its February 2019 meeting on a PIP for voclosporin for 'Treatment of systemic lupus erythematosus (SLE)' (indication limited to treatment of lupus nephritis in paediatric patients with systemic lupus erythematosus) with a deferral.

2.1.5. Oteseconazole - EMEA-002392-PIP01-18

Mycovia Pharmaceuticals Inc; Treatment of vulvovaginal candidiasis

Day 120 opinion

Infectious Diseases

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed on a positive opinion for oteseconazole in the condition of 'Treatment of vulvovaginal candidiasis'.

2.1.6. Ofatumumab - EMEA-002397-PIP01-18

Novartis Europharm Limited; Treatment of multiple sclerosis / Treatment of relapsing remitting multiple sclerosis

Day 120 opinion

Neurology

Summary of committee discussion:

The PDCO re-discussed the application taking into consideration the additional information received on the issues previously identified. A positive opinion was adopted.

2.1.7. Abemaciclib - EMEA-002342-PIP01-18

Eli Lilly and Company Limited; Ewing's Sarcoma (ES) / Treatment of relapsed/refractory Ewing sarcoma (ES) in children and young adults, in combination with irinotecan and temozolomide

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this procedure at Day 120 during the February 2019 plenary. The PDCO agreed with all the conclusions reached at Day 90. In conclusion, the PDCO adopted a positive opinion at Day 120.

2.1.8. Autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains - Orphan - EMEA-002369-PIP01-18

Celgene Europe B.V.; Treatment of mature B-cell neoplasms / Treatment of paediatric B cell maturation antigen (BCMA)+ relapsed or refractory B non-Hodgkin lymphoma

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this procedure at Day 120 during the February 2019 plenary. The PDCO adopted a positive opinion at Day 120.

2.1.9. Vinorelbine tartrate (liposomal) - EMEA-002365-PIP01-18

TLC Biopharmaceuticals B.V.; treatment of rhabdomyosarcoma / Maintenance therapy after 1st relapse treatment, Treatment of relapsed or refractory rhabdomyosarcoma, Maintenance therapy for high-risk rhabdomyosarcoma patients achieving complete remission after frontline treatment

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this PIP in line with the outcome of the Day 90 discussion. A positive opinion was adopted.

2.1.10. Aflibercept - EMEA-000236-PIP05-18

Bayer AG; Retinopathy of prematurity (ROP) / Aflibercept is indicated for the treatment of retinopathy of prematurity (ROP)

Day 120 opinion

Ophthalmology

Summary of committee discussion:

The Committee adopted a positive opinion of a paediatric development of aflibercept in the condition of "treatment of retinopathy of prematurity".

2.1.11. Nintedanib - Orphan - EMEA-001006-PIP05-18

Boehringer Ingelheim International GmbH; Treatment of fibrosing interstitial lung diseases (ILD) / Treatment of fibrosing interstitial lung diseases (ILD) in paediatric patients

Day 120 opinion

Pneumology - Allergology / Oncology

Summary of committee discussion:

Based on the assessment of this application and the discussion at Day 90, the Committee adopted a positive opinion on the agreement of a Paediatric Investigation Plan and a deferral for nintedanib in the condition 'Treatment of fibrosing interstitial lung diseases'.

2.1.12. Ad26.ZEBOV - EMEA-002307-PIP01-17

Janssen Cilag International N.V.; Prevention of Ebola virus disease / Prevention of EVD in children aged ≥1 year

Day 120 opinion

Vaccines / Infectious Diseases

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, a PIP was agreed.

2.1.13. MVA-BN-Filo - EMEA-002308-PIP01-17

Janssen Cilag International N.V.; Prevention of Ebola virus disease / Prevention of EVD in children aged ≥1 year

Day 120 opinion

Vaccines / Infectious Diseases

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, a PIP was agreed.

2.1.14. Rosuvastatin calcium / fenofibrate - EMEA-002509-PIP01-18

Mylan Healthcare GmbH; Mixed dislipidemia, i.e. hypertriglyceridemia combined with hypercholesterolemia

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The PDCO re-discussed at Day 60 the product specific waiver request for this fixed dose combination for the condition of 'Treatment of elevated cholesterol with elevated triglycerides'. The PDCO considered the waiver based on the ground that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments acceptable. A positive opinion was adopted.

2.1.15. Serlopitant - EMEA-002496-PIP01-18

Menlo Therapeutics Inc.; Treatment of prurigo nodularis

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 serlopitant for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'treatment of prurigo nodularis'. 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. The PDCO identified treatment of pruritus as an unmet need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.16. Delafloxacin - EMEA-001080-PIP03-18

A. Menarini - Industrie Farmaceutiche Riunite - s.r.l.; Treatment of community acquired pneumonia (CAP)

Day 60 opinion

Infectious 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 delafloxacin for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'Treatment of community

acquired pneumonia (CAP)' 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.

2.1.17. ^{177}Lu-PSMA-617 - EMEA-002419-PIP02-18

Succurro Clinical Research Limited; Prostate-specific membrane antigen (PSMA)-expressing metastatic, castration-resistant, prostate cancer

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this full product specific waiver request for the radioactive therapeutic agent ^{177}Lu-PSMA-617, developed in adults for the condition of 'treatment of prostate-specific membrane antigen (PSMA)-expressing prostate cancer'. Overall, the PDCO considered the request on the ground that the disease does not occur in children acceptable. A positive opinion was adopted.

2.1.18. L-asparaginase - Orphan - EMEA-000341-PIP03-18

ERYTECH Pharma S.A.; Treatment of pancreatic cancer

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO's views expressed at Day 30 were endorsed. Based on the assessment of this application and the discussions at the Paediatric Committee, the PDCO agrees with the Applicant's request for a waiver. The PDCO recommends granting a waiver for L-asparaginase for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of 'treatment of pancreatic 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.

2.1.19. Rivoceranib (mesylate) - Orphan - EMEA-002489-PIP01-18

LSK BioPharma Limited; Treatment of gastric cancer / Treatment of adult patients with advanced or metastatic gastric cancer

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO confirmed the conclusions reached at Day 30 and adopted a positive opinion. 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 rivoceranib (mesylate) for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'treatment of gastric cancer and gastroesophageal junction adenocarcinoma'.
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. Rogaratinib - EMEA-002439-PIP01-18

Bayer AG; Treatment of urothelial 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 rogaratinib for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of urothelial carcinoma.
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. N2'-Deacetyl-N2'-[4-methyl-4-(oxobutyldithio)-1-oxopentyl]-maytansine-hu769_4D4 Antibody - EMEA-002504-PIP01-18

Sanofi-Aventis Recherche & Développement; Treatment of all conditions included in the category of malignant neoplasms expressing CEACAM5 protein

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO's views expressed at Day 30 were endorsed. Based on the assessment of this application and the discussions at the Paediatric Committee, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for N2'-Deacetyl-N2'-[4-methyl-4-(oxobutyldithio)-1-oxopentyl]-maytansine-hu769_4D4 Antibody for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of 'Treatment of all conditions included in the category of malignant neoplasms (excluding central nervous system, haematopoietic and lymphoid tissue 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. Tislelizumab - EMEA-002480-PIP01-18

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

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO's view expressed at Day 30 was endorsed. Therefore, based on the assessment of this application and the discussions at the Paediatric Committee, the PDCO agrees with the Applicant's request for a waiver. The PDCO recommends granting a waiver for tislelizumab for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition 'treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue)' on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to 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.

2.1.23. Cenegermin - Orphan - EMEA-001729-PIP02-18

Dompé farmaceutici S.p.A.; Treatment of dry eye disease

Day 60 opinion

Ophthalmology

Summary of committee discussion:

The PDCO's view expressed at Day 30 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 cenegermin for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of dry eye disease.

2.1.24. Orvepitant - EMEA-002510-PIP01-18

NeRRe Therapeutics Ltd; Treatment of refractory chronic cough

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

Based on the assessment of this application and the discussions at the Paediatric Committee , the PDCO agrees with the Applicant's request for a waiver. The PDCO recommends granting a waiver for orvepitant for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of refractory chronic cough on the grounds that this condition does not occur 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 might be 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.

2.1.25. Secukinumab - EMEA-000380-PIP05-18

Novartis Europharm Limited; Hidradenitis Suppurativa

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The Committee decided to grant a full waiver on its own motion for all subsets of the paediatric population (0 to 18 years of age) for the treatment of Hidradenitis Suppurativa on the grounds that clinical studies with secukinumab cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2.1.26. Gadopiclenol - EMEA-001949-PIP02-18

GUERBET; Diagnostic / Detection and visualization of disorders or lesions with suspected abnormal vascularity in various body regions

Day 60 opinion

Diagnostic

Summary of committee discussion:

During its February 2019 plenary meeting, the PDCO adopted a positive opinion at Day 60 for this diagnostic agent gadopiclenol for the detection and visualisation of lesions within the head and neck, thorax, abdomen, pelvis, and musculoskeletal system.

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. Sebelipase alfa - EMEA-C-001331-PIP01-12-M02

Alexion Europe SAS; Treatment of Lysosomal acid lipase deficiency

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism / Gastroenterology-Hepatology

Summary of committee discussion:

The PDCO took note of outcomes of preceding partial compliance check procedures:
• EMEA-C1-001331-PIP01-12-M01
The PDCO adopted on 01 March 2019 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0173/2015) of 07 August 2015.

2.2.2. Denosumab - EMEA-C-000145-PIP01-07-M09

Amgen Europe B.V.; Treatment of giant cell tumour of bone

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO took note of outcomes of preceding partial compliance check procedures:
• EMEA-C1-000145-PIP01-07-M02
The PDCO adopted on 1 March 2019 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0098/2018) of 16/3/2018.

2.2.3. Conestat alfa - EMEA-C-000367-PIP01-08-M08

Pharming Group N.V.; Treatment of hereditary angioedema (HAE)

Day 60 opinion

Other

Summary of committee discussion:

The PDCO took note of outcomes of preceding partial compliance check procedures:
• EMEA-C1-000367-PIP01-08-M01
• EMEA-C-000367-PIP01-08-M07
The PDCO adopted on 1 March 2019 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision P/0343/2018 of 8 November 2018.

2.2.4. Peanut allergen extract - EMEA-C1-001481-PIP01-13-M03

DBV Technologies S.A.; Treatment of peanut allergy

Day 60 letter

Pneumology - Allergology

Summary of committee discussion:

The PDCO finalised this partially completed compliance procedure on 1 March 2019.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Corifollitropin alfa - EMEA-000306-PIP01-08-M04

Merck Sharp & Dohme B.V.; Inability to achieve pregnancy, Treatment of hypogonadotrophic hypogonadism / female adults, boys

Day 60 opinion

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0197/2016 of 18/07/2016).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.2. Rivaroxaban - EMEA-000430-PIP01-08-M11

Bayer AG; Treatment of thromboembolic events, Prevention of thromboembolic events / Treatment (secondary prevention) of venous thromboembolism

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0194/2017 of 03/07/2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.3. Ertugliflozin L-PGA - EMEA-001533-PIP01-13-M02

Merck Sharp & Dohme (Europe), Inc.; 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 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/0324/2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.4. Migalstat hydrochloride - Orphan - EMEA-001194-PIP01-11-M04

Amicus Therapeutics UK Limited; Treatment of Fabry disease

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, and the clarifications provided by the Applicant, the PDCO considered that the proposed changes could be accepted, with some additional requirements. The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0328/2016 of 02/12/2016).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.5. Recombinant parathyroid hormone: rhPTH (1-84) - Orphan - EMEA-001526-PIP01-13-M03

Shire Pharmaceuticals Ireland Limited; Hypoparathyroidism / Treatment of hypoparathyroidism

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Overall, the PDCO considered that the proposed changes could be accepted, provided additional requirements are included in the PIP Opinion.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0325/2017 of 31/10/2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.6. Luspatercept - Orphan - EMEA-001521-PIP01-13-M03

Celgene Europe B.V.; Anaemias due to chronic disorders / Treatment of anaemia in patients with beta-thalassemia intermedia and major

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO re-discussed the procedure at Day 60 during the February 2019 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/0122/2018 of 11 April 2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.7. Nonacog beta pegol (glycopegylated recombinant coagulation factor IX) - Orphan - EMEA-000731-PIP01-09-M03

Novo Nordisk A/S; ICD10-D67-Hereditary factor IX deficiency / Treatment and prophylaxis of bleeding in patient with Haemophilia B (congenital factor IX deficiency)

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0329/2014).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.8. Roxadustat - EMEA-001557-PIP01-13-M03

Astellas Pharma Europe B.V.; treatment of anaemia due to chronic disorders

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0233/2018 of 15 August 2018).

2.3.9. Tofacitinib citrate - EMEA-000576-PIP01-09-M10

Pfizer Limited; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis) / Juvenile idiopathic arthritis

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0203/2018 of 17/07/2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.10. Ceftolozane / tazobactam - EMEA-001142-PIP01-11-M03

Merck Sharp & Dohme (Europe), Inc.; Treatment of abdominal and gastrointestinal infections, Treatment of urinary tract infections / Treatment of complicated urinary tract infections (cUTI), Treatment of complicated intra-abdominal infections (cIAI)

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0088/2017 of 29/03/2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.11. Etravirine - EMEA-000222-PIP01-08-M09

Janssen-Cilag International NV; Treatment of human immunodeficiency virus type-a (HIV)-1 infection / indicated in combination with boosted protease inhibitor and other antiretroviral medicinal products for the treatment of HIV-1 infection in antiretroviral treatment-experienced adolescents and children from 2 months of age and older

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0163/2015 of 7 August 2015).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.12. Oritavancin diphosphate - EMEA-001270-PIP01-12-M02

Menarini International Operations Luxembourg S.A.; Treatment of skin and subcutaneous tissue bacterial infections

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The Applicant's response is considered acceptable; the opinion was amended accordingly. Furthermore, the PDCO updated the condition / indication name in line with the current terminology, i.e. 'Treatment of acute bacterial skin and skin structure infections'.
The PDCO adopted a positive opinion.

2.3.13. Inebilizumab - Orphan - EMEA-001911-PIP01-15-M02

Viela Bio; Neuromyelitis optica spectrum disorder (NMOSD)

Day 60 opinion

Neurology

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed change could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0136/2018 of 7 May 2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.14. Regorafenib - EMEA-001178-PIP01-11-M04

Bayer AG; Treatment of all conditions contained in the category of malignant neoplasms (except haematopoietic and lymphoid tissue) / Treatment of paediatric patients with a solid malignant tumour(s) integrated with anti-cancer therapy

Day 60 opinion

Oncology

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0091/2017 of 11/4/2017).

2.3.15. Idarucizumab - EMEA-001438-PIP01-13-M01

Boehringer Ingelheim international GmbH; Prevention of dabigatran associated haemorrhage Treatment of dabigatran associated haemorrhage

Day 60 opinion

Other

Summary of committee discussion:

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

2.3.16. Selexipag - EMEA-000997-PIP01-10-M02

Janssen Cilag International NV; pulmonary arterial hypertension / Treatment of pulmonary arterial hypertension

Day 60 opinion

Other

Summary of committee discussion:

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

The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0154/2013 of 05/07/2013).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.17. Fevipiprant - EMEA-001315-PIP02-16-M01

Novartis EuroPharm Limited; Asthma / Treatment of uncontrolled persistent asthma

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan and on the discussion on Day 30, the PDCO considered that the proposed changes cannot be supported. The PDCO adopted a negative opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0124/2018 of 11 April 2018). Consequently, the measures and timelines of the agreed paediatric investigation plan remain unchanged.

2.3.18. Peanut flour - EMEA-001734-PIP01-14-M04

Aimmune Therapeutics Inc; Peanut Allergy / Peanut oral immunotherapy for the reduction in clinical reactivity to accidental exposure in peanut children and adults

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that all 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/0377/2018 of 7 December 2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.19. Neisseria meningitidis serogroup Y polysaccharide conjugated to tetanus toxoid / Neisseria meningitidis serogroup W-135 polysaccharide conjugated to tetanus toxoid / Neisseria meningitidis serogroup C polysaccharide conjugated to tetanus toxoid / Neisseria meningitidis serogroup A polysaccharide conjugated to tetanus toxoid - EMEA-001930-PIP01-16-M01

Sanofi Pasteur; Prevention of meningococcal disease

Day 60 opinion

Vaccines

Summary of committee discussion:

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, and the clarifications received after Day 30, 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/0359/2017 of 1/12/2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.20. Pibrentasvir / glecaprevir - EMEA-001832-PIP01-15-M02

AbbVie Ltd; Treatment of chronic hepatitis C Day 30 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO concluded that the requested modification was acceptable.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0166/2018 of 15 June 2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.21. Tenofovir alafenamide - EMEA-001584-PIP01-13-M04

Gilead Sciences International Ltd.; Treatment of chronic Hepatitis B / indicated for the treatment of chronic hepatitis B infection in paediatric patients aged 2 years and above

Day 30 opinion

Infectious Diseases

Summary of committee discussion:

The modification was 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/0037/2018 of 30 January 2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.22. 2-[[8-chloro-3-[(4-chlorophenyl)methyl]-4-(difluoromethoxy)-2-ethyl-5-quinolinyl]oxy]acetic acid L-lysine salt - EMEA-002484-PIP01-18

GB001, Inc (A wholly-owned subsidiary of Gossamer Bio, Inc.); Asthma / Use as an add-on controller medication in the treatment of adults, adolescents and children (>5 years of age) with inadequately controlled asthma

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

Based on the discussion on Day 30, the PDCO adopted a request for modification.

2.3.23. Anti-CD7 mAb conjugated to ricin toxin A chain / anti-CD3 mAb conjugated to ricin toxin A chain - Orphan - EMEA-002087-PIP01-16

Xenikos BV; Steroid refractory acute graft versus host disease

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

Based on the Committee discussion on Day 30, the PDCO adopted a request for modification.

2.4. Opinions on Re-examinations

2.4.1. Chemically modified recombinant human sulfamidase - Orphan - EMEA-002380-PIP01-18

Swedish Orphan Biovitrum AB (publ); Mucopolysaccharidosis type IIIA (MPS IIIA)

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The final opinion has been sent to the PDCO for comments in writing. The comments received support the view of Rapporteur, Peer-reviewer and Paediatric-coordinator.
The final opinion has been agreed and adopted via written procedure on 21 March 2019.

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

For the following partial compliance checks, no need to refer them to PDCO Committee for discussion, were identified by the PME coordinator and PDCO Rapporteur. The PDCO has been informed in writing.

2.7.1. Avelumab - EMEA-C2-001849-PIP02-15-M02

Merck KGaA; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumors, haematopoetic and lymphoid tissue neoplasms)

Day 1 letter

Oncology

Summary of committee discussion:

The partial compliance check has been finalised with a confirmation of compliance of all those studies contained in the agreed paediatric investigation plan that were subject of this procedure.

2.7.2. Tisagenlecleucel - EMEA-C2-001654-PIP01-14-M03

Novartis Europharm Limited; Treatment of B cell acute lymphoblastic leukaemia/lymphoblastic lymphoma

Day 30 letter

Oncology

Summary of committee discussion:

The partial compliance check has been finalised with a confirmation of compliance of all those studies contained in the agreed paediatric investigation plan that were subject of this procedure.

2.7.3. Vericiguat - EMEA-C1-001636-PIP01-14-M01

Bayer AG; Treatment of left ventricular failure

Day 30 letter

Cardiovascular Diseases

Summary of committee discussion:

The partial compliance check has been finalised with a confirmation of compliance of all those studies contained in the agreed paediatric investigation plan that were subject of this procedure.

2.7.4. Osilodrostat - EMEA-C2-000315-PIP02-15-M02

Novartis Europharm Limited; Treatment of adrenal cortical hyperfunctions

Day 30 letter

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The partial compliance check has been finalised with a confirmation of compliance of all those studies contained in the agreed paediatric investigation plan that were subject of this procedure.

2.7.5. Fc- and CDR-modified humanised monoclonal antibody against C5 - EMEA-C1-001943-PIP01-16-M01

Alexion Europe SAS; Treatment of atypical haemolytic uremic syndrome

Day 30 letter

Uro-nephrology / Haematology-Hemostaseology

Summary of committee discussion:

The partial compliance check has been finalised with a confirmation of compliance of all those studies contained in the agreed paediatric investigation plan that were subject of this procedure.

3. Discussion of applications

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. Remimazolam - EMEA-001880-PIP01-18

Anaesthetic and allied procedures / Intensive care unit (ICU) sedation, Sedation during medical procedures, general anaesthesia

Day 90 discussion

Anaesthesiology

3.1.2. Efpeglenatide - EMEA-001903-PIP01-15

Type 2 diabetes mellitus

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.3. Dusquetide - EMEA-002306-PIP02-18

Prevention of severe oral mucositis

Day 90 discussion

Gastroenterology-Hepatology

3.1.4. 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

Genzyme Europe B.V.; Treatment of Haemophilia B, Treatment of Heamophilia A / 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, 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 90 discussion

Haematology-Hemostaseology

3.1.5. Ustekinumab - EMEA-000311-PIP06-18

ICD10: M32 Systemic lupus erythematosus (SLE) / Treatment of systemic lupus erythematosus (SLE)

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.6. Tafenoquine - EMEA-002301-PIP01-17

Prevention of malaria

Day 90 discussion

Infectious Diseases

3.1.7. Benzimidazole-containing ENaC inhibitor - EMEA-002394-PIP01-18

Treatment of cystic fibrosis (CF) / indicated to improve lung function and reduce pulmonary exacerbations for patients with CF in conjunction with standard therapies.

Day 90 discussion

Pneumology - Allergology

3.1.8. Glycopyrronium bromide / formoterol fumarate dihydrate / beclometasone dipropionate - EMEA-001875-PIP02-18

Treatment of asthma / Regular treatment of asthma in patients not controlled with medium-high doses of inhaled corticosteroids and long-acting beta2-agonists

Day 90 discussion

Pneumology - Allergology

3.1.9. EMEA-002481-PIP01-18

Moderate to severe atopic dermatitis (AD)

Day 60 discussion

Dermatology

3.1.10. Levonorgestrel - EMEA-002474-PIP02-18

Contraception

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.11. Norursodeoxycholic acid - Orphan - EMEA-002485-PIP01-18

Dr. Falk Pharma GmbH; Primary sclerosing cholangitis (PSC)

Day 60 discussion

Gastroenterology-Hepatology

3.1.12. Recombinant human monoclonal antibody against mannan-binding lectin-associated serine protease-2 - Orphan - EMEA-002479-PIP01-18

Omeros London Limited; Treatment in haematopoietic stem cell transplantation / Treatment of haematopoietic stem cell transplant associated thrombotic microangiopathy (HSCT-TMA).

Day 60 discussion

Haematology-Hemostaseology

3.1.13. Artesunate - Orphan - EMEA-002402-PIP02-18

ACE Pharmaceuticals BV; Plasmodia infections / Treatment of severe malaria caused by Plasmodium falciparum in children aged 1 month to 18 years

Day 60 discussion

Infectious Diseases

3.1.14. Equine Immunoglobulin F(ab')2 fragments targeting Shiga toxin - Orphan - EMEA-002444-PIP02-18

Chemo Research, S.L.; Prevention of Shiga-Toxin producing Escherichia Coli haemolytic uremic syndrome

Day 60 discussion

Infectious Diseases

3.1.15. Tazobactam sodium / cefepime hydrochloride - EMEA-002483-PIP01-18

Treatment of complicated Urinary Tract Infections (cUTI)

Day 60 discussion

Neonatology - Paediatric Intensive Care / Infectious Diseases / Uro-nephrology

3.1.16. Crizotinib - EMEA-001493-PIP03-18

ALK-positive inflammatory myofibroblastic tumour (IMT), ALK-positive anaplastic large cell lymphoma (ALCL) / Treatment of paediatric patients with relapsed/refractory systemic ALK-positive ALCL, Treatment of paediatric patients with unresectable or relapsed/refractory ALK-positive IMT

Day 60 discussion

Oncology

3.1.17. Flucytosine - Orphan - EMEA-002437-PIP02-18

Tocagen Inc; Treatment of glioma

Day 60 discussion

Oncology

3.1.18. Vocimagene amiretrorepvec - Orphan - EMEA-002505-PIP02-18

Tocagen Inc.; Treatment of glioma

Day 60 discussion

Oncology

3.1.19. Synthetic double-stranded siRNA oligonucleotide directed against lactate dehydrogenase A mRNA and containing four modified nucleosides which form a ligand cluster of four N-acetylgalactosamine residues - Orphan - EMEA-002493-PIP01-18

Dicerna EU Limited; The treatment primary hyperoxaluria

Day 60 discussion

Uro-nephrology

3.1.20. Atorvastatin / amlodipine / candesartan - EMEA-002520-PIP01-18

Treatment of essential hypertension (ICD9: 401, ICD10: I10), Treatment of Familial hypercholesterolemia (ICD9: 272.0, ICD10: E78.0) / For adults with hypertension and elevated cholesterol already controlled with candesartan, amlodipine and atorvastatin given concurrently at the same dose level as in the fixed dose combination (FDC) (substitution indication).

Day 30 discussion

Cardiovascular Diseases

3.1.21. Recombinant human lecithin cholesterol acyltransferase - Orphan - EMEA-002497-PIP01-18

AstraZeneca AB; Acute STEMI

Day 30 discussion

Cardiovascular Diseases

3.1.22. Glycerol / urea - EMEA-002511-PIP01-18

Treatment of atopic dermatitis / Treatment of dry skin, Prevention of relapse of atopic dermatitis

Day 30 discussion

Dermatology

3.1.23. Inactivated patient's own (autologous) microorganism (e.g. Escherichia coli, Candida spp., Enterococcus spp., Streptococcus spp., Staphylococcus spp., Prevotella intermedia, Fusobacterium nucleatum and others) - EMEA-002442-PIP01-18

Prevention and treatment of chronic or recurrent dermal or mucosal inflammation / Prevention and treatment of chronic or recurrent skin and/or mucosa inflammation in the urogenital, otorhinolaryngeal, bronchial, oral, gingiva or periodontal tract, resistant to treatment or not sufficiently treatable with topical or systemic antibiotics, antivirals, antifungals or anti-inflammatory compounds

Day 30 discussion

Dermatology / Pneumology - Allergology / Oto-rhino-laryngology / Uro-nephrology

3.1.24. Seladelpar - Orphan - EMEA-002527-PIP01-18

CymaBay Ireland Limited; Treatment of primary biliary cholangitis

Day 30 discussion

Gastroenterology-Hepatology

3.1.25. EMEA-002501-PIP01-18

Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital FVIII deficiency)

Day 30 discussion

Haematology-Hemostaseology

3.1.26. EMEA-002529-PIP01-18

Treatment of respiratory syncytial virus infection

Day 30 discussion

Infectious Diseases

3.1.27. Cladribine - EMEA-000383-PIP02-18

Treatment of multiple sclerosis / Adults and Paediatrics

Day 30 discussion

Neurology

3.1.28. Phenobarbital - EMEA-002532-PIP01-18

Epilepsy

Day 30 discussion

Neurology

3.1.29. Abemaciclib - EMEA-002342-PIP02-18

High Grade Glioma (HGG), Neuroblastoma (NBL) / Treatment of relapsed or refractory neuroblastoma in combination with irinotecan and temozolomide in paediatric patients, Treatment of newly diagnosed high grade glioma in combination with temozolomide in paediatric patients

Day 30 discussion

Oncology

3.1.30. Humanized antibody targeting B cell maturation antigen conjugated with maleimidocaproyl monomethyl auristatin F - Orphan - EMEA-002468-PIP02-18

GlaxoSmithKline Trading Services; Treatment of multiple myeloma

Day 30 discussion

Oncology

3.1.31. Mosunetuzumab - EMEA-002524-PIP01-18

Treatment of follicular lymphoma

Day 30 discussion

Oncology

3.1.32. Niraparib - Orphan - EMEA-002268-PIP03-18

Janssen Research & Development; Treatment of prostate malignant neoplasms

Day 30 discussion

Oncology

3.1.33. Carfilzomib - Orphan - EMEA-001806-PIP03-18

Amgen Europe BV; Treatment of multiple myeloma

Day 30 discussion

Oncology / Haematology-Hemostaseology

3.1.34. Amoxicillin - EMEA-002548-PIP01-19

Adults / pantoprazole/clarithromycin/amoxicillin is used for combination therapy for the eradication of Helicobacter pylori in patients with peptic ulceration, with the aim of reducing the frequency of recurrence of duodenal ulcer disease (ulcera duodeni) and gastric ulcer (ulcer ventriculi) caused by this pathogen. The official guidelines for the appropriate use of antibacterial active substances must be taken into account.

Day 30 discussion

Other

3.1.35. Clarithromycin - EMEA-002549-PIP01-19

Adults / pantoprazole/clarithromycin/amoxicillin is used for combination therapy for the eradication of Helicobacter pylori in patients with peptic ulceration, with the aim of reducing the frequency of recurrence of duodenal ulcer disease (ulcera duodeni) and gastric ulcer (ulcer ventriculi) caused by this pathogen. The official guidelines for the appropriate use of antibacterial active substances must be taken into account.

Day 30 discussion

Other

3.1.36. Colecalciferol - EMEA-002553-PIP01-19

Treatment of osteoporosis

Day 30 discussion

Other

3.1.37. Ibandronic acid - EMEA-002331-PIP01-18

Treatment of osteoporosis

Day 30 discussion

Other

3.1.38. Pantoprazole - EMEA-002512-PIP01-18

Adults / pantoprazole/clarithromycin/amoxicillin is used for combination therapy for the eradication of Helicobacter pylori in patients with peptic ulceration, with the aim of reducing the frequency of recurrence of duodenal ulcer disease (ulcera duodeni) and gastric ulcer (ulcer ventriculi) caused by this pathogen. The official guidelines for the appropriate use of antibacterial active substances must be taken into account.

Day 30 discussion

Other

3.1.39. Olopatadine hydrochloride / mometasone furoate - EMEA-002514-PIP01-18

Treatment of allergic rhinitis / rhino-conjunctivitis

Day 30 discussion

Oto-rhino-laryngology

3.1.40. Atogepant - EMEA-002530-PIP01-18

G43 Migraine / Prophylaxis of migraine

Day 30 discussion

Pain

3.1.41. (R)-1-(3-(aminomethyl) phenyl)-N-(5-((3 cyanophenyl)(cyclopropylmethylamino)methyl)-2-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide dihydrochloride - Orphan - EMEA-002449-PIP02-18

BioCryst UK; Treatment of hereditary angioedema (HAE) / Treatment of HAE attacks, Prevention of HAE attacks

Day 30 discussion

Pneumology - Allergology

3.1.42. Budesonide / salbutamol sulfate - EMEA-002533-PIP01-18

Treatment of asthma / the as-needed treatment or prevention of bronchoconstriction in children aged 6 years and older with reversible obstructive airway disease; The reduction of exacerbations in children aged 6 years and older with asthma

Day 30 discussion

Pneumology - Allergology

3.1.43. Tosatoxumab - Orphan - EMEA-002506-PIP01-18

Aridis Pharmaceuticals Inc; Pneumonia caused by Staphylococcus aureus

Day 30 discussion

Pneumology - Allergology

3.1.44. EMEA-002398-PIP01-18

Cystic Fibrosis (CF) / Treatment of cystic fibrosis in individuals with cystic fibrosis who are homozygous for the F508del mutation and are receiving treatment with a CFTR modulator

Day 90 discussion

Pneumology - Allergology

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. Lurasidone hydrochloride - EMEA-C-001230-PIP01-11-M04

Aziende Chimiche Riunite Angelini Francesco - ACRAF S.p.A; Treatment of Schizophrenia

Day 30 discussion

Psychiatry

3.2.2. Potassium hydrogen carbonate / potassium citrate monohydrated - EMEA-C1-001357-PIP01-12-M02

ADVICENNE; Treatment of renal tubular acidosis

Day 30 discussion

Uro-nephrology

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Angiotensin II - EMEA-001912-PIP02-16-M02

La Jolla Pharmaceutical II B.V.; Hypotension associated with distributive or vasodilatory shock

Day 30 discussion

Cardiovascular Diseases

3.3.2. Omecamtiv mecarbil - EMEA-001696-PIP01-14-M01

Amgen Europe B.V.; Treatment of heart failure / Treatment of chronic heart failure New York Association (NYHA) class II-IV with systolic dysfunction, in children and adolescents 6 to <18 years, in combination with standard pharmacological therapy, including angiotensin converting enzyme inhibitors (ACE inhibitors), angiotensin II receptor blockers, and/or beta-blockers

Day 30 discussion

Cardiovascular Diseases

3.3.3. Asfotase alfa - Orphan - EMEA-000987-PIP01-10-M04

Alexion Europe SAS; Hypophosphatasia / Treatment of hypophosphatasia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.4. Deferiprone - Orphan - EMEA-001126-PIP01-10-M03

Consorzio per Valutazioni Biologiche e Farmacologiche (CVBF) - Coordinator for DEEP Project (HEALTH-F4-2010-261483); treatment of chronic iron overload requiring chelation therapy / treatment of iron overload in paediatric patients affected by haemoglobinopathies requiring chronic transfusions and iron chelation

Day 30 discussion

Haematology-Hemostaseology

3.3.5. Ravulizumab - Orphan - EMEA-002077-PIP01-16-M02

Alexion Europe SAS; Paroxysmal nocturnal haemoglobinuria / Treatment of paroxysmal nocturnal haemoglobinuria

Day 30 discussion

Haematology-Hemostaseology

3.3.6. Baricitinib - EMEA-001220-PIP01-11-M05

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

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.7. Adalimumab - EMEA-000366-PIP02-09-M06

AbbVie Limited; Ulcerative Colitis / Treatment of moderate to severe ulcerative colitis

Day 30 discussion

Immunology-Rheumatology-Transplantation / Ophthalmology / Dermatology / Gastroenterology-Hepatology

3.3.8. Relebactam monohydrate / cilastatin sodium / imipenem monohydrate - EMEA-001809-PIP01-15-M01

Merck Sharp & Dohme (Europe), Inc.; Treatment of bacterial infections caused by gram-negative bacteria

Day 30 discussion

Infectious Diseases

3.3.9. Onasemnogene abeparvovec - Orphan - EMEA-002168-PIP01-17-M01

AveXis Netherlands B.V.; Treatment of spinal muscular atrophy / Treatment of spinal muscular atrophy Type 1

Day 30 discussion

Neurology

3.3.10. Quizartinib - Orphan - EMEA-001821-PIP01-15-M03

Daiichi Sankyo Europe GmbH; Treatment of acute myeloid leukaemia (AML) / For the treatment of paediatric patients aged from 1 month to less than 18 years of age with newly diagnosed AML with FLT3-ITD mutations, For the treatment of paediatric patients aged from 1 month to less than 18 years of age with refractory or relapsed AML with FLT3-ITD mutations after failure of front line intensive chemotherapy regimen, in combination with standard chemotherapy.

Day 30 discussion

Oncology

3.3.11. Ruxolitinib phosphate - EMEA-000901-PIP03-16-M01

Novartis Europharm Limited; Acute graft versus host disease / Treatment of acute graft versus host disease (GvHD) after allogeneic hematopoietic stem cell transplantation (alloSCT) in paediatric patients aged 28 days and above

Day 30 discussion

Oncology

3.3.12. Gilteritinib (as fumarate) - Orphan - EMEA-002064-PIP01-16-M01

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

3.3.13. Clostridium botulinum neurotoxin type A , free from complexing proteins - EMEA-001039-PIP02-12-M03

Merz Pharmaceuticals GmbH; Treatment of sialorrhea / Treatment of chronic troublesome sialorrhea associated with neurological conditions (e.g. cerebral palsy, traumatic brain injury) and/or intellectual disability in children and adolescents aged 2 – 17 years.

Day 30 discussion

Ophthalmology / Neurology

3.3.14. Agomelatine - EMEA-001181-PIP01-11-M04

Les Laboratoires Servier; Major Depressive Episodes

Day 30 discussion

Psychiatry

3.3.15. Finerenone - EMEA-001623-PIP01-14-M02

Bayer AG; Chronic Kidney Disease / Treatment of chronic kidney disease associated with proteinuria in addition to a therapy with angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blockers (ARB)

Day 30 discussion

Uro-nephrology

4. Nominations

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 30 April 2019 for Nomination of Rapporteur and Peer reviewer

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.

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

4.3. Nominations for other activities

No items

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

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

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. Fezolinetant- EMEA-18-2018

Astellas Pharma Europe BV; All classes of medicinal products for treatment of climacteric symptoms associated with decreased oestrogen levels, as occurring at menopause / Treatment of moderate to severe vasomotor symptoms associated with menopause in 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 at this stage.

6.1.2. Estetrol- EMEA-02-2019

Donesta Bioscience B.V.; All classes of medicinal products for treatment of climacteric symptoms associated with decreased oestrogen levels, as occurring at menopause /Treatment of moderate to severe vasomotor symptoms (VMS) in hysterectomized post-menopausal 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: Neonatal encephalopathy.

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

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

7.1.1. Human Papillomavirus type 6 L1 protein / Human Papillomavirus type 11 L1 protein / Human Papillomavirus type 16 L1 protein / Human Papillomavirus type 18 L1 protein – Gardasil - EMEA-000375-PIP01-08-M02

MSD (Europe) Inc; Infection by Human Papillomavirus

Proposed indication: prevention of head & neck cancers (HNC) caused by vaccine HPV types

Summary of committee discussion:

The PDCO was of the view that the proposed indication "prevention of head and neck cancers caused by vaccine HPV types" falls under the scope of the mentioned Decision, as the indication is considered to be covered by the condition "Infection by human papillomavirus" listed in the Agency Decision.

8. Annual reports on deferrals

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

9. Organisational, regulatory and methodological matters

9.1. Mandate and organisation of the PDCO

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

The PDCO Committee noted the nomination of Peter Szitanyi as the new member alternate for Slovakia.

The PDCO Chair thanked the leaving member Janez Jazbec, from Slovenia, for his contribution to the work of the Paediatric Committee.

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 medicinal products with recommended paediatric indications adopted in January 2019. These included Maviret (glecaprevir / pibrentasvir) and Orencia (abatacept). Lower strengths for Orencia (abatacept) solution for injection in pre-filled syringe 50 mg and 87.5 mg were approved for paediatric use from 2 years of age.
The list of procedures with paediatric indications to be evaluated by the CHMP, starting in January 2019, was presented to the PDCO members.

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

9.3.1. Non-clinical Working Group: Comments on ICH S11 – Nonclinical safety testing in support of development paediatric medicines

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 (NCWG) evaluation and discussion.
With regards to ICH S11, the Non-clinical Working Group to the Paediatric Committee (PDCO) had no fundamental disagreements with the overall suggested approach in this ICH S11 guideline. The group welcomes this guideline to improve harmonisation between the different regions and support the proposed weight of evidence approach to determine the potential need for a juvenile study and the considerations around careful selection of relevant endpoints as a function of the concerns driving the study.

9.3.2. Formulation Working Group

PDCO member: Brian Aylward

Summary of committee discussion:

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

9.3.3. Modelling and Simulation Working Party: the outlining of the key element form (KEF) for the modelling & simulation (M&S) study

MSWP Chair: Kirstin Karlsson

Summary of committee discussion:

The PDCO welcomed the presentation by the MSWP Chair, Kirstin Karlsson, on the outlining of the key element form (KEF) for the modelling & simulation study.

9.4. Cooperation within the EU regulatory network

9.4.1. European Network of Paediatric Research (Enpr) - European Medicines Agency (EMA): Outcome of Working Group on Trial Preparedness

PDCO member: Angeliki Siapkara

Summary of committee discussion:

The draft outcome document of the Enpr-EMA Working Group on trial preparedness was presented. PDCO members were encouraged to review the document and to provide feedback.

9.5. Cooperation with International Regulators

9.5.1. Report from the Paediatric Cluster Teleconference

Summary of committee discussion:

The Committee was informed about the discussions at the Paediatric Cluster teleconference on 21 February and the ad-hoc additional T-conference on 26 February 2019.

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

9.6.1. Outcome of the WHO/Paediatric HIV Vatican Meeting

Summary of committee discussion:

The PDCO was informed about the outcome of two meetings held in December 2018:

- The High-Level Dialogue to Assess Progress on and Intensify Commitment to Scaling Up Diagnosis and Treatment of Paediatric HIV that took place in the Vatican City.
- The 4th Paediatric ARV Drug Optimization (PADO) Meeting that was held in Geneva.

9.7. PDCO work plan

No items

9.8. Planning and reporting

9.8.1. Strategic Review and Learning Meeting (SRLM) under the Romanian Presidency to be held in Malta on 13-14 June 2019

PDCO members: Dana Gabriela Marin, John Joseph Borg

Summary of committee discussion:

The PDCO welcomed the information that the Strategic Review and Learning Meeting (SRLM) under the Romanian Presidency will be hosted by Malta on 13-14 June 2019.

10. Any other business

10.1.1. Survey on additional information requested during PIP procedures

Summary of committee discussion:

The PDCO was informed about results of a survey showing how often additional information are requested during a PIP procedure.

10.1.2. EMA relocation to Amsterdam, the Netherlands – Questions & Answers (Q&As)

Summary of committee discussion:

As a follow-up to previous discussions on the EMA relocation in 2019 to Amsterdam, the Netherlands, the EMA Secretariat further updated the PDCO on the new meeting premises in the interim building in Amsterdam to use as of March 2019. The EMA Secretariat shared with PDCO the orientation guide for delegates.

10.1.3. Workshop on Allergen Immunotherapy (AIT) for Children, 16 January 2019

Scope: Adoption of the minutes

Summary of committee discussion:

The PDCO discussed and agreed on the summary of Multi-stakeholder Meeting on Allergen Immuno-therapy (AIT) for Children in January 2019 and added the Committee's conclusions with regard to the standard PIP for allergen products for specific immunotherapy.
The summary will now be circulated to all participants of the multi-stakeholder meeting.

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

The group was informed about the main topics that were discussed at the 7th ACCELERATE Paediatric Oncology Conference. Additionally, the group discussed topics related to currently ongoing paediatric oncology procedures.

11.1.2. Neonatology

Summary of committee discussion:

The break-out session discussed comments received during the public consultation of the "Concept paper on the need for revision of the guideline on the investigation of medicinal products in the term and preterm neonate".

11.1.3. Inventory

Summary of committee discussion:

The group continues the discussion on the assessment of unmet needs.

11.1.4. Juvenile Idiopathic Arthritis

Summary of committee discussion:

PDCO members discussed challenges and possible ways forward regarding PIPs in the therapeutic area of juvenile idiopathic arthritis.

The Chair thanked all participants and closed the meeting.

12. List of participants

List of participants including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 26 February-01 March 2019 meeting

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Dirk Mentzer	Chair	Germany	No interests declared	
Karl-Heinz Huemer	Member	Austria	No interests declared	
Koenraad Norga	Member (Vice-Chair)	Belgium	When chairing the meeting: To be replaced for discussions, final deliberations and voting When not chairing the meeting: No participation in final deliberations and voting	Humanized antibody targeting B cell maturation antigen conjugated with maleimidocaproyl monomethyl auristatin F - Orphan - EMEA-002468-PIP02-18
Karen Van Malderen	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Georgios Savva	Member	Cyprus	No interests declared	
Tereza Bazantova	Member	Czech Republic	No interests declared	
Kirstine Moll Harboe	Member	Denmark	No interests declared	
Irja Lutsar	Member	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	
Anastasia 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	
Alessandro Jenkner	Alternate	Italy	No interests declared	
Dina Apele-Freimane	Member	Latvia	No restrictions applicable to this meeting	
Sigita Burokiene	Member	Lithuania	No interests declared	
Goda Vaitkeviciene	Alternate	Lithuania	No interests declared	
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No interests declared	
Herbert Lenicker	Alternate	Malta	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Maaike van Dartel	Member	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	
Angeliki Siapkara	Member	United Kingdom	No interests declared	
Martina Riegl	Alternate	United Kingdom	No interests declared	
Fernando Cabanas	Member	Healthcare Professionals' Representative	No interests declared	
Jorrit Gerritsen	Alternate	Healthcare Professionals' Representative	No interests declared	
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Catherine Cornu	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Doina Plesca	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Günter Karl-Heinz Auerswald	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Michal Odermarsky	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Viviana Giannuzzi	Alternate	Patients' Organisation Representative	No restrictions applicable to this meeting	
Eleni Ghaki Gaki	Expert - in person*	United Kingdom	No interests declared	
Homera	Expert - in	United	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Fahimeda Binte Ali	person*	Kingdom		
Kirstin Karlsson	Expert - in person*	Sweden	No restrictions applicable to this meeting	
María Estela Moreno Martín	Expert - in person*	Spain	No interests declared	
Rune Kjeken	Expert - via telephone*	Norway	No restrictions applicable to this meeting	
Johanna Lähteenvuo	Expert - via telephone*	Finland	No interests declared	
Pauliina Lehtolainen-Dalkilic	Expert - via telephone*	Finland	No interests declared	
Ollie Tenhunen	Expert - via telephone*	Finland	No interests declared	
Anja Schiel	Expert - via telephone*	Norway	No interests declared	
Helga Haugom Olsen	Expert - via telephone*	Norway	No interests declared	
A representative from the European Commission attended the meeting				
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/