15 December 2017
EMA/PDCO/830920/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes of the meeting on 12-15 December 2017

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

12 December 2017, 14:00- 17:00, room 3E

13 December 2017, 08:30- 19:00, room 3E

14 December 2017, 08:30- 19:00, room 3E

15 December 2017, 08:30- 13:00, room 3E

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).

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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. 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.

1.3. Adoption of the minutes

The minutes of the November 2017 PDCO plenary meeting were adopted with amendments 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. Chloroprocaine Hydrochloride - EMEA-000639-PIP03-16

Sintetica GmbH; Peripheral nerve block (local anesthesia by perineural injection)

Day 120 opinion

Anaesthesiology

Summary of committee discussion:

The PDCO reviewed the application including the new information received since Day 90 and concluded that all issues have now been resolved, the modified PIP is acceptable. A positive opinion has therefore been adopted.

2.1.2. Lucerastat - Orphan - EMEA-002095-PIP01-16

Idorsia Pharmaceuticals Deutschland GmbH; Treatment of Fabry disease

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO endorsed the applicant's clarifications received between D90 and D120. The PDCO recommended granting a positive opinion on a PIP with a deferral for lucerastat in the condition of Treatment of Fabry disease.

2.1.3. 1,4-dihydro-1-[(2R)-2-(2-methoxyphenyl)-2-[(tetrahydro-2H-pyran-4-yl)oxy]ethyl]-α,α,5-trimethyl-6-(2-oxazolyl)-2,4-dioxo-thieno[2,3-d]pyrimidine-3(2H)-acetic acid - EMEA-002109-PIP01-16

Gilead Sciences International Ltd.; K75.8 Other specified inflammatory liver diseases (non-alcoholic steatohepatitis [NASH]) / Treatment of Non-Alcoholic Steatohepatitis (NASH) with mild to severe fibrosis (F1-F4) in paediatric subjects, 8 to < 18 years of age

Day 120 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The PDCO adopted a positive opinion on this PIP on D120.

2.1.4. Maralixibat Chloride - Orphan - EMEA-001475-PIP03-17

Shire Pharmaceuticals Ireland Limited; Treatment of Progressive Familial Intrahepatic Cholestasis

Day 120 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The PDCO discussed this procedure on D120.
The applicant's responses to the D90 issues were considered acceptable.
A positive opinion was adopted.

2.1.5. Glutamine (Levoglutamide) - Orphan - EMEA-001996-PIP02-16

Emmaus Medical Europe Ltd.; Sickle cell disease / Glutamine (Levoglutamide) is indicated for the prevention of sickle cell crises in adults and children older than 5 years suffering from Sickle Cell Disease.

Day 120 opinion

Haematology-Hemostaseology

Summary of committee discussion:

During its plenary on 15 December 2017, the PDCO discussed the applicant's responses to the outstanding issues, as per day 90 discussion in November 2017.
The PDCO considered that sufficient details have now been provided by the applicant in order to favourably agree on the PIP.
The PDCO adopted a positive Opinion for Levoglutamide (L-glutamine oral powder) in the condition of treatment of sickle cell disease (PIP1996-02), during its plenary on 15 December 2017.

2.1.6. Upadacitinib - EMEA-001741-PIP02-16

AbbVie Ltd; Treatment of Ulcerative Colitis

Day 120 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO discussed this procedure on D120. The applicant's responses to the D90 issues were considered acceptable and a positive opinion was adopted.

2.1.7. Obiltoxaximab - EMEA-002144-PIP01-17

SFL Regulatory Affairs Consulting Ltd.; Treatment of bacillary infection, Prevention of bacillary infection / Treatment of inhalation anthrax following exposure to Bacillus anthracis in combination with appropriate antibacterial drugs, Post-exposure prophylaxis of inhalation anthrax when alternative therapies are not available or are not appropriate, N/A

Day 120 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO adopted a positive opinion on the paediatric plan proposed by the applicant.

2.1.8. Gilteritinib (as fumarate) - EMEA-002064-PIP01-16

Astellas Pharma Europe B.V.; Treatment of acute myeloid leukemia / Treatment of FLT3/ITD positive acute myeloid leukemia

Day 120 opinion

Oncology / Haematology-Hemostaseology

Summary of committee discussion:

The PDCO re-discussed the application for gilteritinib for the treatment of acute myeloid leukaemia taking into account the additional clarifications provided by the applicant.

The PDCO therefore recommended granting a paediatric investigation plan for gilteritinib and deferral, for the treatment of acute myeloid leukaemia.

2.1.9. Recombinant Clostridium difficile Toxoid B / Recombinant Clostridium difficile Toxoid A - EMEA-002112-PIP01-16

Pfizer Limited; Prevention of Clostridium difficile infection (CDI) / Active immunization for the prevention of primary Clostridium difficile infection in children and adolescents 2 to 18 years of age

Day 120 opinion

Vaccines

Summary of committee discussion:

Following the Day 90 discussion a draft opinion with remaining issues highlighted was shared with the applicant.
An agreement was thus reached on the last few outstanding issues, the PDCO adopted a positive opinion on the paediatric plan proposed by the applicant.

2.1.10. Rosuvastatin calcium / Acetylsalicylic acid - EMEA-002239-PIP01-17

Adamed Sp. z o.o.; prevention of cardiovascular events

Day 60 opinion

Cardiovascular Diseases

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 Acetylsalicylic acid / Rosuvastatin calcium for all subsets of the paediatric population (0 to 18 years of age) in the condition of prevention of cardiovascular events.
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. Fluorocholine (18F) - EMEA-002129-PIP02-17

UJV Rez, a. s.; Visualisation of choline metabolism in malignant neoplasms

Day 60 opinion

Diagnostic

Summary of committee discussion:

The PDCO's views expressed at D30 were endorsed.
The PDCO considered that (18F) fluorocholine can be a sensitive marker in other cancer types apart from prostatic cancer (targeted for the adult development) and its use is unlikely to remain limited to this type of cancer.
It was also confirmed that this product may have a relevant use in the diagnosis of brain tumours and their differentiation from post radiation necrotic tissue or of their progression. Compared to MRI and FDG PET, for patients with brain tumours, choline PET seems to be most promising for radiotherapy planning. It offers delineation of the biological target volume and the differential diagnosis between radiation necrosis and tumour recurrence.
In conclusion, the PDCO did not agree with the applicant's request for a waiver for (18F) fluorocholine for all subsets of the paediatric population (from to 18 years of age) in the condition 'visualisation of choline metabolism in malignant neoplasms'.

2.1.12. Tucatinib - EMEA-002242-PIP01-17

Cascadian Therapeutics Luxembourg S.A.R.L.; Treatment of breast malignant neoplasms

Day 60 opinion

Oncology

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 tucatinib for all subsets of the paediatric population on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adult populations.

2.1.13. Recombinant human epidermal growth factor - EMEA-002258-PIP01-17

Praxis Pharmaceuticals S.A; Diabetic foot ulcer

Day 60 opinion

Other / Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Based on the assessment of this application, the PDCO agrees with the applicant's request for a waiver.
Furthermore, the PDCO acknowledged the additional justification provided by the applicant. The PDCO recommends granting a waiver for recombinant human epidermal growth factor for all subsets of the paediatric population (0 to 18 years of age) in the

condition of diabetic foot ulcer on the grounds that the complication of diabetic foot ulcer does not (yet) occur in the paediatric population.
A positive opinion has been adopted by the PDCO during their plenary on 15 December 2017.
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.

2.1.14. Ethinyl estradiol / Dienogest - EMEA-002229-PIP01-17

Exeltis France S.A.; Contraception / Oral contraception

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

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 PIP. The PDCO recommends granting a positive PIP opinion for Dienogest / Ethinyl estradiol in the condition of prevention of pregnancy

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. Clostridium Botulinum neurotoxin type A (150 kD), free from complexing proteins - EMEA-C-001039-PIP01-10-M02

Merz Pharmaceuticals GmbH; Treatment of muscle spasticity

Day 60 opinion

Neurology

Summary of committee discussion:

The PDCO re-discussed the request for the compliance check taking into consideration the additional clarifications provided by the applicant after the D30 discussion that allowed to perform the compliance check considered that this is compliant with the latest Agency's Decision (P/0157/2016) of 15 June 2016.
The PDCO adopted on 15/12/2017 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision

2.2.2. Sotagliflozin - EMEA-C1-001517-PIP02-14-M02

Sanofi-aventis R&D; Treatment of type 1 diabetes mellitus

Day 30 letter

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The completed study was checked for compliance and considered compliant with the latest Agency's Decision (P/0337/2017) of 30 October 2017.
The PDCO finalised on 15th December this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be completed until this date.

2.2.3. Clostridium Botulinum neurotoxin type A (150 kD), free of complexing proteins - EMEA-C1-001039-PIP02-12-M02

Merz Pharmaceuticals GmbH; Treatment of sialorrhea

Day 30 letter

Neurology

Summary of committee discussion:

The PDCO discussed the completed study and considered that it is compliant with the latest Agency's Decision (P/0157/2016) of 15 June 2016.
The PDCO finalised this partially completed compliance procedure at Day 30 and confirmed the compliance of the study.

2.2.4. Fenfluramine hydrochloride - EMEA-C1-001990-PIP01-16

Zogenix International Ltd; Treatment of Dravet syndrome

Day 30 letter

Neurology

Summary of committee discussion:

The completed studies were checked for compliance.
The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision.
The PDCO finalised on 15 December 2017 this partially completed compliance procedure.

2.2.5. Avelumab - EMEA-C1-001849-PIP02-15-M01

Merck KGaA; Treatment of malignant neoplasms of lymphoid tissue

Day 30 letter

Oncology

Summary of committee discussion:

The completed studies were checked for compliance.
The PDCO discussed the completed studies and considered that these are compliant with

the latest Agency's Decision (P/0361/2017) of 1 December 2017.
The PDCO finalised on 15 December this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be completed until this date.

2.2.6. Dasatinib (as monohydrate) - EMEA-C-000567-PIP01-09-M04

Bristol-Myers Squibb Pharma EEIG; Treatment of Philadelphia chromosome (BCR-ABL translocation)-positive chronic myeloid leukaemia

Day 30 opinion

Oncology

Summary of committee discussion:

The completed study was checked for compliance.
The PDCO discussed that study was not completed in compliance with the agreed paediatric investigation plan.
The PDCO adopted on 15 December 2017 an opinion refusing the compliance of one or more studies in the agreed paediatric investigation plan as set out in the Agency's Decision (P/0118/2013) of 02 May 2013.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Regadenoson - EMEA-000410-PIP01-08-M02

Rapidscan Pharma Solutions EU Limited; Myocardial perfusion disturbances / Diagnostic evaluation of myocardial perfusion disturbances

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

2.3.2. Gadolinium,[α3,α6,α9-tris[3-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]-3-oxopropyl]-3,6,9,15-tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene-3,6,9-triacetato(3-)-κN3,κN6,κN9,κN15,κO3,κO6,κO9] - EMEA-001949-PIP01-16-M01

GUERBET; Detection and visualization of areas with disruption of the blood brain barrier and/or abnormal vascularity for the central nervous system (CNS), or of any type of diseases from different body regions (soft tissues, bone and internal body

structures/organs) for diagnostic purposes.

Day 60 opinion

Diagnostic

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO concluded that the proposed changes could not be accepted. The PDCO therefore adopted a negative Opinion on the modification of the agreed PIP.
The key elements of the agreed PIP remain unchanged.

2.3.3. Empagliflozin - EMEA-000828-PIP01-09-M06

Boehringer Ingelheim International GmbH; 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/0326/2016 of 02/12/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.4. Linagliptin - EMEA-000498-PIP01-08-M07

Boehringer Ingelheim International GmbH; 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/0324/2016 of 02/12/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.5. Sitagliptin phosphate - EMEA-000470-PIP01-08-M10

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

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

At their December 2017 meeting the PDCO discussed the responses received by the applicant on the PDCO comments raised at D30.

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0062/2015 of 13/2/2015).

2.3.6. Baricitinib - EMEA-001220-PIP01-11-M02

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, Treatment of JIA-associated uveitis

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The committee deemed the responses received and the changes implemented in the draft opinion between Day 30 and Day 60 acceptable.
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/0192/2016 of 15/07/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.7. Human normal immunoglobulin - EMEA-001797-PIP01-15-M01

Octapharma Pharmazeutika Produktionsges.m.b.H; Primary Immunodeficiency Diseases

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

Based on the review of the responses, submitted by the applicant after Day 30 discussion, 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/0084/2016 of 18/03/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.8. Ixekizumab - EMEA-001050-PIP01-10-M03

Eli Lilly & Company Limited; Plaque psoriasis, Treatment of chronic idiopathic arthritis

(including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis) / Children with juvenile idiopathic arthritis subtypes of enthesitis-related arthritis (including JoAS) and juvenile psoriatic arthritis., Treatment of severe chronic plaque psoriasis in paediatric patients from the age of 6 years who are not adequately controlled by topical therapies.

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

At their December 2017 meeting the PDCO discussed the responses received from the applicant that addressed the issues raised at D30.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0233/2016 of 22/7/2016).

2.3.9. Tofacitinib - EMEA-000576-PIP01-09-M08

Pfizer Limited; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and 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/0296/2017 of 04/10/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.10. Ceftaroline fosamil - EMEA-000769-PIP01-09-M07

Pfizer Limited; Treatment of cSSTI (complicated skin and soft tissue infections) / Treatment of CAP (community-aquired pneumonia)

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO's views expressed at day 30 were re-discussed and endorsed.
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/0355/2016 of 21 December 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO

Opinion.

2.3.11. Cobicistat / atazanavir sulphate - EMEA-001465-PIP01-13-M02

Bristol-Myers Squibb Pharma EEIG; Treatment of HIV-1 infection / indicated in combination with other ARV medicinal products for the treatment of HIV-1 infected adults and children from 3 years of age without known mutations associated with resistance to atazanavir.

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

After the Day 30 discussion the applicant submitted a more detailed justification
In conclusion, based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that some of the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0181/2017 of 30 June 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.12. Posaconazole - EMEA-000468-PIP02-12-M04

Merck Sharp & Dohme (Europe), Inc.; Prevention of invasive fungal infections / For treatment of invasive fungal infections in the following paediatric patients: -Invasive aspergillosis in patients with disease that is refractroy to amphotericin B or itraconazole or in patients who are intolerant of these medicinal products; Treatment of invasive aspergillosis, -Patients receiving remission-induction chemotherapy for acute myelogenous leukemia (AML) or myelodysplastic syndromes (MDS) expected to result in prolonged neutropenia and who are at high risk of developing invasive fungal infections; - Hematopoietic stem cell transplant (HSCT) recipients who are undergoing high-dose immunosuppressive therapy for graft versus host disease and who are at high risk of developing invasive fungal infections.

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO's views expressed on day 30 were re-discussed, taking into account the applicant's corrected clarifications, and endorsed.
As a consequence, the PDCO considered that the proposed changes could be accepted, based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0092/2017 of 11 April 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.13. Tedizolid phosphate - EMEA-001379-PIP01-12-M03

Merck Sharp & Dohme (Europe) Inc.; Treatment of acute bacterial skin and skin structure infections

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO, taking into account the applicant's clarifications, re-discussed and endorsed its views expressed at day 30.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0264/2016 of 5 October 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.14. Tenofovir alafenamide - EMEA-001584-PIP01-13-M03

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 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO discussed this modification procedure on D60. The applicant's responses to the D30 issues were generally 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/0274/2017 of 4 October 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.15. Lacosamide - EMEA-000402-PIP02-11-M05

UCB Pharma S.A.; Treatment of Epilepsy - Partial-onset seizures [G40.0 - G40.1 - G40.2]

Day 60 opinion

Neurology

Summary of committee discussion:

The PDCO adopted a positive opinion endorsing the requested modifications. The modified PIP opinion supersedes the previous PDCO opinion.

2.3.16. Midostaurin - Orphan - EMEA-000780-PIP01-09-M04

Novartis Europharm Ltd; C92.0 Acute myeloid leukaemia, C94.3 Mast cell leukaemia, C96.2 Malignant mastocytosis / Treatment of paediatric patients with FLT3 mutated AML, newly diagnosed, A waiver is in place for this condition

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the modification request taking into account the applicant's responses provided after D30.

The PDCO therefore adopted a negative Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0011/2017 of 31/01/2017).

2.3.17. Pembrolizumab - EMEA-001474-PIP02-16-M01

Merck Sharp & Dohme (Europe), Inc.; Treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue). Treatment of Hodgkin Lymphoma / Treatment of advanced, untreated or previously treated, malignant melanoma in children from 12 year old to less than 18 years of age. Treatment as monotherapy of a PD-L1 positive paediatric malignant solid tumor in children from 6 months to less than 18 years of age., Treatment of classical Hodgkin lymphoma with incomplete early response to front-linechemotherapy in children from 3 years to less than 18 years of age.Treatment of relapsed or refractory classical Hodgkin lymphoma in children from 5 years to lessthan 18 years of age

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO's views expressed at D30 were confirmed.
The additional information provided by the applicant after D30 were noted.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, as specified at D30, 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/0204/2016 of 01/08/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.18. Burosumab - Orphan - EMEA-001659-PIP01-15-M03

Ultragenyx Pharmaceutical Inc.; X-linked Hypophosphatemia

Day 60 opinion

Other

Summary of committee discussion:

The PDCO has re-discussed the application.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP.
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.19. Conestat alfa - EMEA-000367-PIP01-08-M07

Pharming Group N.V.; D84.1 Defects in the complement system C1 esterase inhibitor (C1-INH) deficiency / Treatment of acute attacks of angioedema associated with hereditary C1 esterase inhibitor deficiency

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 majority of the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0052/2017 of 17/03/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.20. Ivacaftor / lumacaftor - EMEA-001582-PIP01-13-M07

Vertex Pharmaceuticals (Europe) Limited; Treatment of cystic fibrosis

Day 60 opinion

Other

Summary of committee discussion:

The committee re-discussed the request for modification taking into account the applicant's clarifications.
The PDCO therefore adopted a positive opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0198/2017 of 14 July 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.21. Matrix applied characterised autologous cultured chondrocytes - EMEA-000979-PIP01-10-M02

Vericel Denmark ApS; repair of symptomatic, full-thickness cartilage defects of the knee

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

Opinion.

2.3.22. Birch pollen extract (Betula verrucosa) - EMEA-001879-PIP01-15-M01

ALK Abelló A/S; J30.1 Allergic rhinitis due to pollen / Treatment of tree pollen allergic rhinitis and/or conjunctivitis

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

The PDCO's views expressed on day 30 were re-discussed, taking into account the applicant's clarifications. The PDCO considered that the proposed changes could be accepted, based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0302/2016 of 4 November 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.23. Reslizumab - EMEA-001202-PIP02-13-M02

Teva Pharmaceuticals Europe; Treatment of asthma / indicated as add- on treatment in adult patients with severe eosinophilic 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, 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/0256/2016 of 5 October 2016.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.24. N-[(1,3-dicyclohexyl-6-hydroxy-2,4-dioxo-1,2,3,4-tetrahydro-5-pyrimidinyl)carbonyl]glycine - EMEA-001452-PIP01-13-M01

GlaxoSmithKline R & D; Treatment of anaemia associated with chronic renal disease

Day 60 opinion

Uro-nephrology / 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/0191/2014 of 06/08/2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.25. Outer Membrane Vescicles (OMV) from Neisseria Meningitidis serogroup B strain NZ98/254 measured as amount of total protein containing the PorA P1.4 / Recombinant Neisseria Meningitidis serogroup B fHbp fusion protein / Recombinant Neisseria Meningitidis serogroup B NadA protein / Recombinant Neisseria Meningitidis serogroup B NHBA fusion protein - EMEA-000139-PIP01-07-M02

GSK Vaccines S.r.l.; Prevention of meningitis

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, 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/38/2011 of 17 January 2011).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.26. Piperaquine tetraphosphate / artenimol - EMEA-000153-PIP01-07-M05

Alfasigma SpA; Treatment of uncomplicated malaria caused by Plasmodium falciparum

Day 30 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.
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.27. L-asparaginase encapsulated in erythrocytes - Orphan - EMEA-000341-PIP02-09-M05

ERYTECH pharma S.A.; Treatment of patients with Acute Lymphoblastic Leukaemia

Day 30 opinion

Oncology

Summary of committee discussion:

The PDCO discussed the modification request on 13 December 2017.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0267/2017 of 04 September 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.4. Opinions on Re-examinations

None

2.5. Finalisation and adoption of opinions

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. Tralokinumab - EMEA-001900-PIP02-17

Treatment of Atopic Dermatitis

Day 90 discussion

Dermatology

3.1.2. Non-Pathogenic Bacterial Lysate of Escherichia coli (DSM 17252) and Enterococcus faecalis (DSM 16440) - EMEA-002155-PIP01-17

Irritable bowel syndrome (IBS)

Day 90 discussion

Gastroenterology-Hepatology

3.1.3. Crizanlizumab - Orphan - EMEA-002141-PIP01-17

Novartis Europharm Limited; Treatment of sickle cell disease / Prevention of vaso-occlusive crises in patients with sickle cell disease

Day 90 discussion

Haematology-Hemostaseology

3.1.4. Plasminogen (human) - Orphan - EMEA-002044-PIP01-16

Prometic BioTherapeutics Ltd; Plasminogen deficiency

Day 90 discussion

Haematology-Hemostaseology

3.1.5. EMEA-001741-PIP03-16

Treatment of Crohn's Disease

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.6. Anifrolumab - EMEA-001435-PIP02-16

Lupus nephritis, Systemic lupus erythematosis

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.7. Insulin human - EMEA-002116-PIP01-17

Intestinal malabsorption in preterm infants / Treatment of intestinal malabsorption in preterm infants

Day 90 discussion

Neonatology - Paediatric Intensive Care / Gastroenterology-Hepatology

3.1.8. Adeno-Associated Viral vector serotype rh.10 carrying the human N-sulfoglucosamine sulfohydrolase cDNA - Orphan - EMEA-002122-PIP02-17

LYSOGENE; Mucopolysaccharidosis type IIIA

Day 90 discussion

Neurology

3.1.9. D-Sorbitol / Naltrexone HCl / (RS)-Bacoflen - Orphan - EMEA-002164-PIP01-17

Pharnext SA; Charcot-Marie-Tooth disease Type 1A / Treatment of Charcot-Marie-Tooth Type 1A in symptomatic paediatric patients

Day 90 discussion

Neurology

3.1.10. Durvalumab - EMEA-002028-PIP01-16

Treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue), Treatment of malignant neoplasms of haematopoietic and lymphoid tissue / Treatment of paediatric patients from birth to less than 18 years old with solid tumours, Treatment of paediatric patients from birth to less than 18 years old with haematological malignancies

Day 90 discussion

Oncology

3.1.11. Pevonedistat - EMEA-002117-PIP01-17

Acute Myeloid Leukemia (AML), Myelodysplastic Syndromes (MDS) / The treatment of paediatric patients with relapsed or refractory (R/R) MDS (including juvenile myelomonocytic leukemia). The treatment of paediatric patients with relapsed or refractory (R/R) AML.

Day 90 discussion

Oncology

3.1.12. Tremelimumab - EMEA-002029-PIP01-16

Treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue), Treatment of malignant neoplasms of haematopoietic and lymphoid tissue / Treatment of paediatric patients from birth to less than 18 years old with solid tumours, Treatment of paediatric patients from birth to less than 18 years old with haematological malignancies

Day 90 discussion

Oncology

3.1.13. 17α,21-dihydroxy-16α-methyl-pregna-1,4,9(11)-triene-3,20-dione - Orphan - EMEA-001794-PIP02-16

ReveraGen BioPharma Ltd; Treatment of duchenne muscular dystrophy

Day 90 discussion

Other

3.1.14. Tanezumab - EMEA-001635-PIP03-17

Treatment of chronic pain

Day 90 discussion

Pain

3.1.15. Vilanterol trifenatate / Umeclidinium bromide / Fluticasone furoate - EMEA-002153-PIP01-17

ICD-10 J45.5x severe persistent asthma

Day 90 discussion

Pneumology - Allergology

3.1.16. Baricitinib - EMEA-001220-PIP03-16

Treatment of atopic dermatitis / Treatment of patients with moderate to severe atopic dermatitis

Day 60 discussion

Dermatology

3.1.17. Bis-choline tetrathiomolybdate - Orphan - EMEA-002232-PIP01-17

Wilson Therapeutics AB; Treatment of Wilson disease

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.18. Semaglutide - EMEA-001441-PIP03-17

Treatment of obesity

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.19. Orphan - EMEA-002233-PIP01-17

Zealand Pharma A/S; Treatment of hypoglycaemia

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.20. Ustekinumab - EMEA-000311-PIP05-17

Treatment of Ulcerative Colitis

Day 60 discussion

Gastroenterology-Hepatology

3.1.21. (6aR,10aR)-1-Hydroxy-6,6-dimethyl-3-(2-methyl-2-octanyl)-6a,7,10,10a-tetrahydro-6H-benzo[c]chromene-9-carboxylic acid. - Orphan - EMEA-002069-PIP02-17

Corbus Pharmaceuticals Holdings Inc; Treatment of systemic sclerosis

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.22. Riociguat - Orphan - EMEA-000718-PIP03-17

Bayer AG; Treatment of Systemic Sclerosis / Treatment of Diffuse Cutaneous Systemic Sclerosis (dcSSc)

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.23. The whole range of unmanipulated autologous mononuclear cells derived from human umbilical cord blood (Hau-UCB-mnc) - Orphan - EMEA-001799-PIP02-17

BrainRepair UG (haftungsbeschränkt); Periventriculaleukomalacia (PVL) ICD-10-CM P91.2

Day 60 discussion

Neonatology - Paediatric Intensive Care

3.1.24. Human donor hematopoietic stem and progenitor cells (HSPC) that have been treated ex vivo with Tat-MYC fusion protein - Orphan - EMEA-002185-PIP02-17

Taiga Biotechnologies, Inc.; Severe Combined Immunodeficiency

Day 60 discussion

Other / Immunology-Rheumatology-Transplantation

3.1.25. Purified Rabies virus, - EMEA-002234-PIP01-17

Prevention of rabies disease, treatment of exposure to rabies virus

Day 60 discussion

Vaccines

3.1.26. Candesartan cilexetil / Amlodipine besylate - EMEA-002248-PIP01-17

Treatment of essential hypertension (ICD9: 401, ICD10: I10)

Day 30 discussion

Cardiovascular Diseases

3.1.27. Ezetimibe / Rosuvastatin - EMEA-002257-PIP01-17

Treatment of hypercholesterolemia / The combination of Rosuvastatin and Ezetimibe is indicated for the treatment of hypercholesterolemia as substitution therapy in adult patients adequately controlled with the individual substances given concurrently at the same dose level as in the fixed dose combination, but as separate products.

Day 30 discussion

Cardiovascular Diseases

3.1.28. Treprostinil sodium - Orphan - EMEA-002254-PIP01-17

SciPharm Sàrl; Treatment of (inoperable) chronic thromboembolic pulmonary hypertension (CTEPH)

Day 30 discussion

Cardiovascular Diseases

3.1.29. Birch bark extract - Orphan - EMEA-001299-PIP03-17

Amryt Research Limited; Treatment of epidermolysis bullosa

Day 30 discussion

Dermatology

3.1.30. A genetically modified Lactococcus lactis - EMEA-002237-PIP01-17

Treatment of Type 1 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.31. Levothyroxine sodium - EMEA-002259-PIP01-17

Benign thyroid nodules, Goitre, Hypothyroidism

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.32. Metformin hydrochloride / dapagliflozin - EMEA-001151-PIP02-17

Type 2 diabetes (E11)

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.33. Metformin hydrochloride / saxagliptin / dapagliflozin - EMEA-002249-PIP01-17

Type 2 diabetes (E11) Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.34. Pemafibrate - EMEA-001573-PIP02-17

Treatment of hypertriglyceridaemia, Prevention of cardiovascular events in patients with elevated triglycerides levels

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Cardiovascular Diseases

3.1.35. Venglustat - EMEA-002260-PIP01-17

ICD-10: G20; Disease of the nervous system; Extrapyramidal and movement disorders (G20-G26); Parkinson disease.

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Neurology

3.1.36. EMEA-001710-PIP03-17

Treatment of ulcerative colitis

Day 30 discussion

Gastroenterology-Hepatology

3.1.37. Risankizumab - EMEA-001776-PIP03-17

Crohn's Disease

Day 30 discussion

Gastroenterology-Hepatology

3.1.38. Risankizumab - EMEA-001776-PIP04-17

Ulcerative Colitis

Day 30 discussion

Gastroenterology-Hepatology

3.1.39. Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human βA-T87Q-globin gene - Orphan - EMEA-001665-PIP02-17

Bluebird bio France; Sickle Cell Disease

Day 30 discussion

Haematology-Hemostaseology

3.1.40. Eptinezumab - EMEA-002243-PIP01-17

Prevention of migraine headaches

Day 30 discussion

Neurology

3.1.41. Entinostat Polymorph B - EMEA-002272-PIP01-17

Treatment of breast cancer

Day 30 discussion

Oncology

3.1.42. Niraparib - Orphan - EMEA-002268-PIP01-17

Janssen Research & Development; Treatment of prostate malignant neoplasms

Day 30 discussion

Oncology

3.1.43. Ruxolitinib phosphate - EMEA-000901-PIP04-17

Chronic graft versus host disease / Treatment of chronic Graft vs Host Disease (GvHD) after allogeneic hematopoietic stem cell transplantation (alloSCT) in paediatric patients aged 28 days and above.

Day 30 discussion

Oncology

3.1.44. T-cell bispecific antibody targeting carcinoembryonic antigen expressed on tumor cells and CD3 epsilon chain present on T-cells - EMEA-002252-PIP01-17

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

Day 30 discussion

Oncology

3.1.45. Veliparib - Orphan - EMEA-000499-PIP04-17

AbbVie Ltd; Treatment of lung carcinoma (SCLC and NSCLC)

Day 30 discussion

Oncology

3.1.46. Bilastine - EMEA-000347-PIP02-16

Treatment of allergic conjunctivitis

Day 30 discussion

Ophthalmology

3.1.47. Human Plasminogen - Orphan - EMEA-002253-PIP01-17

Kedrion S.p.A.; Treatment of Ligneous Conjunctivitis and prevention of pseudomembranes recurrence in patients affected by Ligneous Conjunctivitis

Day 30 discussion

Ophthalmology

3.1.48. Recombinant humanised monoclonal IgG2 lambda antibody against human sclerostin - Orphan - EMEA-002169-PIP01-17

Mereo Biopharma 3 Ltd; Treatment of osteogenesis imperfecta / Treatment of osteogenesis imperfecta, types 1, 3 and 4

Day 30 discussion

Other

3.1.49. Gabapentin / Trazodone hydrochloride - EMEA-002263-PIP01-17

Painful diabetic neuropathy

Day 30 discussion

Pain

3.1.50. Gefapixant citrate salt - EMEA-002267-PIP01-17

R05 - Symptoms and signs involving the circulatory and respiratory systems › Cough

Day 30 discussion

Pneumology - Allergology

3.1.51. Interferon beta-1a - Orphan - EMEA-002238-PIP01-17

Faron Pharmaceuticals Ltd; Treatment of Acute Respiratory Distress Syndrome

Day 30 discussion

Pneumology - Allergology

3.1.52. EMEA-002172-PIP02-17

Prevention of lower respiratory tract disease caused by respiratory syncytial virus

Day 30 discussion

Vaccines / Infectious Diseases

3.2. Discussions on Compliance Check

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

3.2.1. Tolvaptan - EMEA-C1-001231-PIP02-13-M05

Otsuka Pharmaceutical Europe Ltd.; Treatment of polycystic kidney disease

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.2.2. Avacopan - EMEA-C2-002023-PIP01-16-M02

ChemoCentryx, Ltd.; Treatment of ANCA-associated vasculitis

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.2.3. Fremanezumab - EMEA-C1-001877-PIP01-15-M01

Teva GmbH;

Day 30 discussion

Neurology

3.2.4. Galcanezumab - EMEA-C3-001860-PIP03-16

Eli Lilly Nederland B.V.; Prevention of migraine headaches

Day 30 discussion

Neurology

3.2.5. Ozanimod - EMEA-C2-001710-PIP02-14-M02

Celgene Europe Limited; Treatment of Multiple Sclerosis

Day 30 discussion

Neurology

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Alirocumab - EMEA-001169-PIP01-11-M04

Sanofi-aventis Recherche & Developpement; Treatment of elevated cholesterol / Treatment of heterozygous and homozygous familial hypercholesterolemia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.2. Osilodrostat - Orphan - EMEA-000315-PIP02-15-M01

Novartis Europharm Limited; Treatment of adrenal cortical hyperfunctions / Treatment of Cushing's disease in adolescents and children aged 6 years and older

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.3. Sodium zirconium cyclosilicate - EMEA-001539-PIP01-13-M03

AstraZeneca AB; Treatment of hyperkalemia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.4. Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human betaA-T87Q-globin gene - Orphan - EMEA-001665-PIP01-14-M02

bluebird bio France; β-thalassaemia

Day 30 discussion

Haematology-Hemostaseology

3.3.5. Lonoctocog alfa - EMEA-001215-PIP01-11-M06

CSL Behring GmbH; Haemophilia A

Day 30 discussion

Haematology-Hemostaseology

3.3.6. Octocog alfa - EMEA-001064-PIP01-10-M03

Bayer AG; Treatment of hereditary factor VIII deficiency / Treatment and prophylaxis of bleeding in patients with haemophilia A

Day 30 discussion

Haematology-Hemostaseology

3.3.7. Rolapitant - EMEA-001768-PIP02-15-M01

Tesaro UK Ltd; Chemotherapy-Induced Nausea and Vomiting (CINV) in Subjects Receiving Highly Emetogenic Chemotherapy (HEC) / Prevention of delayed nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy in adults given as part of combination therapy

Day 30 discussion

Haematology-Hemostaseology

3.3.8. Golimumab - EMEA-000265-PIP02-11-M02

Janssen Biologics B.V.; Treatment of ulcerative colitis

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.9. Denosumab - EMEA-000145-PIP01-07-M09

Amgen Europe B.V.; Prevention of skeletal related events in patients with bone metastases, Treatment of hypercalcemia of malignancy, Treatment of chronic idiopathic artritis, Treatment of bone loss associated with sex hormone ablative therapy, Treatment of giant cell tumour of bone / Treatment of giant cell tumour of bone in children (12-17 years old)

Day 30 discussion

Immunology-Rheumatology-Transplantation / Endocrinology-Gynaecology-Fertility-Metabolism / Oncology

3.3.10. Fidaxomicin - EMEA-000636-PIP01-09-M07

Astellas Pharma Europe B.V.; Treatment of enterocolitis caused by clostridium difficile / Treatment of Clostridium difficile infections (CDI) also known as C. difficile-associated diarrhoea (CDAD)

Day 30 discussion

Infectious Diseases

3.3.11. Erenumab - EMEA-001664-PIP02-15-M02

Novartis Europharm Limited; Prevention of migraine headaches

Day 30 discussion

Neurology

3.3.12. Lacosamide - EMEA-000402-PIP03-17-M02

UCB Pharma S.A.; Treatment of Generalized Epilepsy and Epilepsy Syndromes: Epilepsy - generalized idiopathic epilepsy and epilepsy syndromes [G40.3] Epilepsy - Other generalized epilepsy and epileptic syndromes [G40.4] / Adjunctive therapy in the treatment of primary generalized tonic-clonic seizures (PGTCS) in pediatric patients with idiopathic generalized epilepsy (IGE)(4 years to <18 years), Adjunctive therapy in the treatment of epileptic syndromes associated with generalized seizures in pediatric patients with epilepsy birth to <18 years (specific epileptic syndrome(s) to be based on future clinical development further to exploratory study results)

Day 30 discussion

Neurology

3.3.13. Pyridopyrimidione SMN2 Splicing Modifier - EMEA-002070-PIP01-16-M01

Roche Registration Limited; Treatment of spinal muscular atrophy

Day 30 discussion

Neurology

3.3.14. Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated low affinity nerve growth factor receptor (ΔLNGFR) and herpes simplex I virus thymidine kinase (HSV-Tk Mut2) - Orphan - EMEA-001370-PIP02-13-M01

MolMed S.p.A; Adjunctive treatment in haematopoietic cell transplantation

Day 30 discussion

Oncology

3.3.15. Binimetinib - EMEA-001454-PIP03-15-M01

PIERRE FABRE MEDICAMENT; Treatment of melanoma / Binimetinib in combination with encorafenib is indicated for the treatment of patients aged 12 years and older with unresectable or metastatic melanoma harbouring BRAF V600 mutations.

Day 30 discussion

Oncology

3.3.16. Encorafenib - EMEA-001588-PIP01-13-M01

PIERRE FABRE MEDICAMENT; Treatment of melanoma / Encorafenib in combination with binimetinib is indicated for the treatment of patients aged 12 years and older with unresectable or metastatic melanoma harbouring BRAF V600 mutations.

Day 30 discussion

Oncology

3.3.17. Nivolumab - EMEA-001407-PIP01-12-M01

Bristol-Myers Squibb Pharma EEIG; Treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue) / Treatment of patients with unresectable or metastatic melanoma in the age group from 12 to less than 18 years old. Treatment of a paediatric malignant solid tumour in paediatric patients from 6 months to less than 18 years old

Day 30 discussion

Oncology

3.3.18. Nivolumab - EMEA-001407-PIP02-15-M02

Bristol-Myers Squibb Pharma EEIG; Treatment of malignant neoplasms of lymphoid tissue, Treatment of malignant neoplasms of the central nervous system / Treatment of paediatric patients with relapsed or refractory Hodgkin lymphoma in the age group from 5 years to < 18 years., Treatment of paediatric patients with a relapsed or refractory non-Hodgkin lymphoma in the age group from 6 months to less than 18 years old., Treatment of paediatric patients from 6 months to less than 18 years of age with a recurrent or progressive high-grade glioma.

Day 30 discussion

Oncology

3.3.19. Pembrolizumab - EMEA-001474-PIP01-13-M01

Merck Sharp & Dohme (Europe), Inc.; Treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue). / Treatment of advanced, untreated or previously treated, malignant melanoma in children from 12 year old to less than 18 years of age. Treatment as monotherapy of a PD-L1 positive paediatric malignant solid tumor in children from 6 months to less than 18 years of age

Day 30 discussion

Oncology

3.3.20. Selumetinib - EMEA-001585-PIP01-13-M02

AstraZeneca AB; Treatment of Thyroid Cancer, Treatment of Neurofibromatosis-Type 1 / Selumetinib in combination with adjuvant radioactive iodine therapy is medicated for the treatment of adolescents newly diagnosed with differentiated thyroid cancer who are at h1gh risk of primary treatment failure. Selumetinib is indicated for the treatment of inoperable NFl related plexiform neurofibroma in children and adolescents

Day 30 discussion

Oncology

3.3.21. Ivacaftor - Orphan - EMEA-000335-PIP01-08-M12

Vertex Pharmaceuticals (Europe) Limited; Treatment of Cystic Fibrosis

Day 30 discussion

Other

3.3.22. Dermatophagoides farinae / Dermatophagoides pteronyssinus - EMEA-001258-PIP01-11-M03

ALK-Abelló A/S; Treatment of allergic rhinitis, Treatment of asthma / indicated in house dust mite allergic asthma

Day 30 discussion

Pneumology - Allergology

3.3.23. Ivacaftor - Orphan - EMEA-001640-PIP01-14-M04

Vertex Pharmaceuticals (Europe) Ltd.; Treatment of Cystic Fibrosis

Day 30 discussion

Pneumology - Allergology

3.3.24. Mometasone furoate / Indacaterol acetate (dose expressed as free base) - EMEA-001217-PIP01-11-M04

NOVARTIS EUROPHARM LTD.; Treatment of asthma

Day 30 discussion

Pneumology - Allergology

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 27 February 2018 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:

None

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.

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. Trans-Capsaicin - EMEA-17-2017

Centrexion Therapeutics Corp; All classes of medicinal products for treatment of primary and secondary osteoarthrosis/Reduction in pain due to osteoarthritis

Summary of committee discussion:

The applicability of the class waiver as referred to in the Agency's Decision

CW/0001/2015 to the planned therapeutic indication was not confirmed since the mechanism of action of the medicinal product is not directly targeting osteoarthrosis, but the pain associated with osteoarthrosis.

Other potential paediatric interests of this medicine suggested by PDCO: painful joint conditions such as post-traumatic or osteochondritis dissecans lesions, oligoarthritis in juvenile idiopathic arthritis, post-operative pain.

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. Tafamidis meglumine - EMEA-000884-PIP01-10

Pfizer Limited; neuropathic heredofamilial amyloidosis

Proposed indication: cardiomyopathy (due to wild-type or variant transthyretin)

Summary of committee discussion:

Rapporteur was nominated. The procedure will be discussed in January 2018.

8. Annual reports on deferrals

Note: The annual reports on deferrals to be noted by the members of the PDCO are flagged in the Annex B.

9. Organisational, regulatory and methodological matters

9.1. Mandate and organisation of the PDCO

9.2. Coordination with EMA Scientific Committees or CMDh-v

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

Summary of committee discussion:

The list of procedures with paediatric indications to be evaluated by the CHMP, starting in November 2017 was presented to the PDCO members.

The members were also informed about 2 medicinal products, Adynovi and Genvoya for which the CHMP adopted a positive opinion recommending a paediatric indication during their meeting in November 2017.

9.2.1.1. Joint CHMP/PDCO session

Summary of committee discussion:

During the session the committees discussed a procedure related to paediatric oncology.

9.2.2. Pharmacovigilance Risk Assessment Committee (PRAC)

Questions from PRAC to PDCO following a MS request for PRAC Advice: Ethylmorphine and Tramadol

Summary of committee discussion:

The PDCO discussed and adopted a response to the PRAC's questions.

9.2.3. Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh)

CMDh Question to PDCO

PDCO member: Hugo Tavares

Summary of committee discussion:

The background to the request was presented to the PDCO and the Committee discussed the proposed wording and level of detail.

A formal written response to CMDh will be prepared for adoption at the next meeting.

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:

The chair of the Formulation Working Group identified the products which will require Formulation Working Group evaluation and discussion.

9.3.3. Guideline on the development of new medicinal products for the treatment of Crohn's Disease and ulcerative colitis – POSTPONED

9.3.4. Guideline on the clinical evaluation of vaccines

Summary of committee discussion:

The PDCO was updated on the progress of the revision of the guideline.

9.3.5. Guideline on the clinical investigation of recombinant and human plasma-derived factor VIII products - POSTPONED

9.3.6. Pilot phase on the Inventory of unmet needs - POSTPONED

PDCO member: Karl-Heinz Huemer

9.3.7. Draft 2017 revision FAQs on paediatric information in the SmPC

Summary of committee discussion:

EMA presented the proposed changes to the SmPC Advisory Group's FAQs on paediatric information in the SmPC. The proposal was welcomed by the PDCO.

9.4. Cooperation within the EU regulatory network

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

Summary of committee discussion:

No update

9.4.2. Allergen products

Summary of committee discussion:

It was agreed to establish communication and collaboration with the established task force on clinical trials in children of the European Academy of Allergy and Clinical Immunology through active participation of PDCO members at its meetings.

9.5. Cooperation with International Regulators

9.5.1. Food and Drug Administration (FDA)

Dates for 2018 FDA Pediatric Cluster Teleconference

Summary of committee discussion:

The committee was informed about the dates of the paediatric cluster t-conferences with FDA for the first 6 months in 2018.

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

None

9.7. PDCO work plan

9.7.1. Draft PDCO Work plan 2018

Summary of committee discussion:

The Committee adopted the PDCO Work plan for 2018.

9.8. Planning and reporting

9.8.1. Business Pipeline Report - Forecast for 2017 - Update Q4/2017

Summary of committee discussion:

Tabled for information

10. Any other business

10.1. AOB topic

10.1.1. Preparedness of the system and capacity increase

Summary of committee discussion:

The PDCO noted the update and next steps.

10.1.2. Involvement of young people at PDCO – POSTPONED

Summary of committee discussion:

Postponed to January PDCO meeting.

11. Breakout sessions

Cancelled

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 12 – 15 December 2017 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	EMEA-002153-PIP01-17 EMEA-000139-PIP01-07-M02 EMEA-001452-PIP01-13-M01
Karen Van Malderen	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Adriana Andrić	Member	Croatia	No interests declared	
Suzana Mimica Matanovic	Alternate	Croatia	No interests declared	
Georgios Savva	Member	Cyprus	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jaroslav Sterba	Member	Czech Republic	No interests declared	
Peter Szitanyi	Alternate	Czech Republic	No interests declared	
Marianne Orholm	Member	Denmark	No interests declared	
Kirstine Moll Harboe	Alternate	Denmark	No interests declared	
Irja Lutsar	Member	Estonia	No interests declared	
Ann Marie Kaukonen	Member	Finland	No interests declared	
Maija Pihlajamaki	Alternate	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	
Immanuel Barth	Alternate	Germany	No interests declared	
Eleni Katsomiti	Member	Greece	No interests declared	
Ágnes Gyurasics	Member (CHMP member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	
Sara Galluzzo	Member	Italy	No interests declared	
Alessandro Jenkner	Alternate	Italy	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Dina Apele-Freimane	Member	Latvia	No restrictions applicable to this meeting	
Sigita Burokiene	Member	Lithuania	No interests declared	
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No interests declared	
Maaike van Dartel	Member	Netherlands	No interests declared	
Siri Wang	Member	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	
Janez Jazbec	Alternate	Slovenia	No participation in discussion, final deliberations and voting on:	EMEA-000341-PIP02-09-M05
Maria Jesús Fernández Cortizo	Alternate	Spain	No interests declared	
Ninna Gullberg	Member	Sweden	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
Riccardo Riccardi	Alternate	Healthcare Professionals' Representative	No participation in discussion, final deliberations and voting on:	EMEA-002260-PIP01-17
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	
Günter Karl-Heinz Auerswald	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Paola Baiardi	Alternate	Patients' Organisation Representative	No participation in final deliberations and voting on:	EMEA-002153-PIP01-17 EMEA-000139-PIP01-07-M02 EMEA-001452-PIP01-13-M01
Michal Odermarsky	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Viviana Giannuzzi	Alternate	Patients' Organisation Representative	No restrictions applicable to this meeting	
Stefan Vieths	Expert - in person*	Germany	No interests declared	
Andreas Bonertz	Expert - in person*	Germany	No interests declared	
Susanne Kaul	Expert - via telephone*	Germany	No interests declared	
Juliana Min	Expert - in person*	United Kingdom	No interests declared	
Catriona Baker	Expert - in person*	United Kingdom	No interests declared	
Nicola Parkinson	Expert - in person*	United Kingdom	No interests declared	
Sara Homer	Expert - in person*	United Kingdom	No interests declared	
Adrien Inoubli	Expert - in person*	France	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/