15 September 2017
EMA/PDCO/612728/2017 Rev. 1
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes of the meeting on 12-15 September 2017

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

12 September 2017, 13:00 - 19:00, room 3A

13 September 2017, 08:30 - 19:00, room 3A

14 September 2017, 08:30 - 19:00, room 3A

15 September 2017, 08:30 - 13:00, room 2A

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 with amendments.

1.3. Adoption of the minutes

The minutes of the August 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. Ibrutinib - Orphan - EMEA-001397-PIP05-17

Janssen-Cilag International N.V.; Mantle cell lymphoma

Day 30 opinion

Oncology

Summary of committee discussion:

The PDCO discussed the application for a waiver for all subsets of the paediatric population for ibrutinib, an inhibitor of Bruton's tyrosine kinase, for the condition 'treatment of mantle cell lymphoma'.
A product-specific waiver for the same condition 'treatment of mantle cell lymphoma' and the hard capsules, the only pharmaceutical form available at that time, was granted by the PDCO in 2013 (Decision P/0149/2013).
A PIP for the condition 'treatment of mature B-cell neoplasms' that includes patients from 1 to less than 18 years of age was also granted in 2015.
Subsequently, film tablets were developed, and this product-specific waiver is being, therefore, requested to cover this new pharmaceutical form.
The PDCO therefore agreed with the applicant's request for a waiver and recommended granting a waiver for ibrutinib, film-coated tablets, for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of mantle cell lymphoma based on the grounds that the disease does occur only in the adult population.

2.1.2. Ibrutinib - Orphan - EMEA-001397-PIP06-17

Janssen-Cilag International N.V.; lymphoplasmacytic lymphoma / Waldenström's macroglobulinaemia

Day 30 opinion

Oncology

Summary of committee discussion:

The PDCO discussed the application for a waiver for all subsets of the paediatric population for ibrutinib, an inhibitor of Bruton's tyrosine kinase, for the condition 'treatment of lymphoplasmacytic lymphoma'.
A product-specific waiver for the same condition 'treatment of lymphoplasmacytic lymphoma' and the hard capsules, the only pharmaceutical form available at that time, was granted by the PDCO in 2014 (Decision P/0271/2014).
A PIP for the condition 'treatment of mature B-cell neoplasms' that includes patients from 1 to less than 18 years of age was also granted in 2015.
Subsequently, film tablets were developed, and this product-specific waiver is being, therefore, requested to cover this new pharmaceutical form.
The PDCO therefore agreed with the applicant's request for a waiver and recommended granting a waiver for ibrutinib, film-coated tablets, for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of lymphoplasmacytic lymphoma'based on the grounds that the disease does occur only in the adult population.

2.1.3. Crisaborole - EMEA-002065-PIP01-16

Pfizer Ltd; Mild to moderate atopic dermatitis

Day 120 opinion

Dermatology

Summary of committee discussion:

The Committee adopted a positive opinion, including deferral.

2.1.4. Ligelizumab - EMEA-001811-PIP02-15

Novartis Europharm Ltd.; Treatment of chronic spontaneous urticaria

Day 120 opinion

Dermatology

Summary of committee discussion:

The majority of issues identified at Day 90 are now resolved satisfactorily.
The Committee adopted a positive opinion, including deferral.

2.1.5. (2S)-2-{[(2R)-2-[({[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-l]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino}butanoic acid - Orphan - EMEA-002054-PIP01-16

Albireo AB; 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 acknowledged.
A positive opinion was adopted.

2.1.6. maribavir - Orphan - EMEA-000353-PIP02-16

Shire Pharmaceuticals Ireland Limited; Treatment of CMV infection / Treatment of CMV infection in transplant patients from birth to <18 years of age

Day 120 opinion

Infectious Diseases

Summary of committee discussion:

The applicant provided on 28 August 2017 a response to the draft opinion, which clarified the issues raised at Day 90. The applicant also agreed with most of the PDCO's outstanding requests.
In conclusion, the PDCO adopted a positive opinion on the paediatric plan proposed by the applicant.

2.1.7. acalabrutinib - Orphan - EMEA-001796-PIP03-16

ACERTA PHARMA, BV; Treatment of mature B cell neoplasms / Treatment of children from 1 to <18 years of age with previously untreated mature B-cell neoplasms (eg, diffuse large B-cell lymphoma [DLBCL], Burkitt lymphoma [BL] and primary mediastinal B-cell lymphoma

[PMBCL])., Treatment of children from 1 to <18 years of age with relapsed/refractory mature B-cell neoplasms (eg, diffuse large B-cell lymphoma [DLBCL], Burkitt lymphoma [BL] and primary mediastinal B-cell lymphoma [PMBCL]).

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed on 14 September 2017 the application for agreement of a PIP for acalabrutinib, based on the modified application submitted on 26 June 2017 and taking into account the outstanding issues communicated after the day 90-discussion, the applicant's written responses to the outstanding issues. The comments from the applicant on the draft opinion were also taken into account.
All outstanding issues were considered solved.
Finally, regarding the condition and scope the Committee noted that the scope of the application represents a group of diseases, summarised as mature B-cell neoplasms in the WHO classification. At this time, acalabrutinib holds several orphan designations. Orphan designation for one or more of the specific diseases included in the scope of this PIP can likely be obtained.
In conclusion, the PDCO recommends granting a paediatric investigation plan for acalabrutinib for children from 1 to less than 18 years of age, a deferral for the treatment of mature B-cell neoplasms.

2.1.8. Lactobacillus reuteri - Orphan - EMEA-001895-PIP01-15

Infant Bacterial Therapeutics AB; Prevention of necrotising enterocolitis

Day 120 opinion

Other / Neonatology - Paediatric Intensive Care / Gastroenterology-Hepatology

Summary of committee discussion:

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

2.1.9. Hydrochlorothiazide / Irbesartan / Amlodipine - EMEA-002167-PIP01-17

WIN MEDICA S.A.; Essential hypertension / Treatment of essential hypertension as substitution therapy in adult patients whose blood pressure is adequately controlled on the combination of amlodipine, irbesartan and hydrochlorothiazide, taken either as three single -component formulations or as a dual-component and a single component formulation

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

At their September 2017 meeting the PDCO confirmed the conclusions reached at D30 and agreed a waiver for amlodipine / irbesartan / hydrochlorothiazide for all subsets of the

paediatric population (0 to 18 years of age) in the condition 'Treatment of hypertension' based on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2.1.10. Meldonium dihydrate - EMEA-002212-PIP01-17

ELC GROUP s.r.o.; an adjuvant treatment of stable effort angina pectoris for Adults only

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The committee's views expressed on day 30 were re-discussed, including the applicant's clarification, 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 meldonium dihydrate for all subsets of the paediatric population (0 to 18 years of age) in the condition "treatment of angina pectoris" on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adult populations.
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.

2.1.11. Ezetimibe / Rosuvastatin - EMEA-002202-PIP01-17

Krka, d.d., Novo mesto; E78.0 Pure hypercholesterolaemia, I25 Chronic ischaemic heart disease, E78.2 Mixed hyperlipidaemia

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism / Cardiovascular Diseases

Summary of committee discussion:

The committee's views expressed on day 30 were re-discussed and endorsed.
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 Rosuvastatin / Ezetimibe for all subsets of the paediatric population (0 to 18 years of age) in the condition of "Treatment of hypercholesterolaemia" on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

2.1.12. capmatinib - EMEA-002203-PIP01-17

Novartis Europharm Ltd; Treatment of lung malignant neoplasms

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the requested product specific waiver for capmatinib for the 'treatment of lung malignant neoplams' taking into consideration the additional clarifications provided by the applicant after the D30 discussion.
On the basis of this additional information, the members concluded that at this stage it is unclear what could be the possible role of capmatinib in treatment paediatric tumours used in monotherapy or in combination and therefore considered adeguate to limit the scope of this application to 'treatment of lung malignant neoplams'.
In conclusion, 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 capmatinib for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of 'treatment of lung malignant neoplams' on the grounds that the disease occurs only in the adult population.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.13. veliparib - Orphan - EMEA-000499-PIP03-17

AbbVie Ltd; Treatment of breast cancer

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO discussed at Day 60 this request for a waiver on 15 September 2017.
The Committee confirmed all points raised at Day 30.
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 veliparib for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'Treatment of breast cancer'.
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, as an unmet need, paediatric cancers with loss-of-function mutations in BRCA1 or BRCA2 or other mutations impairing DNA repair mechanisms. 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. Oxymetazoline HCL / Pilocarpine HCL - EMEA-002181-PIP01-17

Allergan Pharmaceuticals International Limited; Presbyopia

Day 60 opinion

Ophthalmology

Summary of committee discussion:

A positive opinion was adopted by the PDCO on D60.
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 Oxymetazoline HCL/ Pilocarpine HCL for all subsets of the paediatric population (0 to 18 years of age) in the condition of Presbyopia.

2.1.15. ezetimibe / bempedoic acid - EMEA-002200-PIP01-17

Esperion Therapeutics, Inc.; Treatment of elevated cholesterol

Day 60 opinion

Other / Cardiovascular Diseases

Summary of committee discussion:

The PDCO confirmed the outcome of the Day 30 discussion and adopted a full waiver for all paediatric age groups for the fixed dose combination of bempedoic acid and ezetimibe for the treatment of elevated cholesterol. The PDCO considered that this fixed dose combination would not provide any significant therapeutic benefit to the paediatric population because treatment with the individual components, allowing individual dose titration in every child with regard to their LDL cholesterol levels, is preferable. Moreover, alternative therapies are available.
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 bempedoic acid / ezetimibe for all subsets of the paediatric population (0 to less than 18 years of age) in the condition of treatment of elevated cholesterol.
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.

2.2. 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. fidaxomicin - EMEA-C1-000636-PIP01-09-M05

Astellas Pharma Europe B.V.; Treatment of enterocolitis caused by clostridium difficile

Day 30 letter

Infectious Diseases

Summary of committee discussion:

The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0058/2017) of 17 March 2017.
The PDCO finalised on 15 September 2017 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 (submission date of request for

partial compliance check).

2.2.2. cannabidiol - EMEA-C1-001964-PIP01-16

GW Research Ltd; Treatment of seizures associated with Lennox-Gastaut Syndrome (LGS)

Day 30 letter

Neurology

Summary of committee discussion:

The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0136/2017) of 07 June 2017.
The PDCO finalised on 15 September 2017 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. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with lentiviral vector that encodes for the human ARSA cDNA sequence - EMEA-C1-001765-PIP02-15-M01

Glaxo Smith Kline Trading Services Limited; Treatment of metachromatic leukodystrophy (MLD)

Day 30 letter

Other

Summary of committee discussion:

The PDCO discussed the completed study and considered that it is compliant with the latest Agency's Decision (P/0160/2017) of 30 June 2017.
The PDCO finalised on 15 September 2017 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.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. dabigatran etexilate mesilate - EMEA-000081-PIP01-07-M10

Boehringer Ingelheim International GmbH; Treatment of thromboembolic events, Prevention of thomboembolic events/ Treatment of venous thromboembolic events in paediatric patients (secondary venous thrombotic event prevention)

Day 60 opinion

Cardiovascular Diseases / Haematology-Hemostaseology

Summary of committee discussion:

The PDCO discussed this procedure on D60. The applicant’s responses to the D30 issues were acknowledged and considered 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/0282/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.2. edoxaban (tosylate) - EMEA-000788-PIP02-11-M06

Daiichi Sankyo Europe GmbH; Prevention of arterial thromboembolism, Prevention of venous thromboembolism, Treatment of venous thromboembolism/ Prevention of arterial thromboembolism in paediatric cardiac patients at risk of thrombotic events, Acute treatment & secondary prevention of symptomatic recurrent venous thrombotic events (VTE) in paediatric patients at risk

Day 60 opinion

Cardiovascular Diseases / Haematology-Hemostaseology

Summary of committee discussion:

The PDCO confirmed the outcome of the Day 30 discussion and agreed with the proposed changes.
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/0012/2017 of 31 January 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.3. Dapagliflozin - EMEA-000694-PIP02-14-M02

AstraZeneca AB; Type 1 Diabetes Mellitus / As an adjunct to insulin treatment to improve glycaemic control in adults with type 1 diabetes mellitus when insulin alone does not provide adequate control

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO's views expressed on 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 some 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/0063/2016 of 18 March 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.4. recombinant parathyroid hormone [rhPTH(1-84)] - Orphan - EMEA-001526-PIP01-13-M02

Shire Pharmaceuticals Ireland Limited; ICD10: E 89.2 hypoparathyroidism, post-procedural;E 20.9, unspecified / Treatment of hypoparathyroidism

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/0255/2015 of 30/10/2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.5. Methoxy polyethylene glycol- epoetin beta - EMEA-000172-PIP01-07-M03

Roche Registration Limited; Anaemia associated with chronic kidney disease

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The Committee reviewed the additional information received since Day 30.
In conclusion the PDCO considered that the proposed changes could be accepted and 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.

2.3.6. Recombinant Human A Disintegrin and Metalloprotease with Thrombospondin Type-1 Motifs 13 - Orphan - EMEA-001160-PIP01-11-M01

Baxalta Innovations GmbH; Treatment of thrombotic thrombocytopenic purpura (TTP)

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

Between Day 30 and Day 60 the applicant provided further information. The Committee confirmed the outcome of the discussion at Day 30 and adopted a positive opinion.
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/0048/2012 of 13/01/2012).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.7. Autologous CD34+ haematopoietic stem cells transduced ex vivo with EFS lentiviral vector encoding for the human ADA gene - Orphan - EMEA-001974-PIP01-16-M01

Pr Bobby Gaspar; Treatment of severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID)

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO re-discussed this modification procedure at Day 60 on 15 September 2017.
The Committee took into consideration the answers and further information provided by the applicant.
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 /0077/2017 of 17 March 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.8. Eculizumab - Orphan - EMEA-000876-PIP05-15-M02

Alexion Europe SAS; Myasthenia Gravis / Treatment of Refractory Generalized Myasthenia Gravis

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO re-discussed the requested modification taking into account the responses provided by the applicant after the D30 discussion and the comments received on the draft opinion.
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/0185/2016 of 15/07/2016)
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.9. guselkumab - EMEA-001523-PIP02-14-M01

Janssen Cilag International NV; Treatment of psoriasis / Treatment of severe plaque psoriasis in children ≥6 to <18 years of age who cannot be adequately controlled with topical agents and/or phototherapy

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/x0073/2016 of 18 March 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.10. Tofacitinib - EMEA-000576-PIP01-09-M07

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:

The applicant provided the requested clarifications.
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/0054/2017 of 17 March 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.11. avibactam / ceftazidime - EMEA-001313-PIP01-12-M06

Pfizer Limited; Treatment of bacterial infections / For the treatment of complicated urinary tract infections, For the treatment hospital acquired pneumonia, For the treatment of complicated intra-abdominal infections, For the treatment of Gram-negative bacterial infections

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/0062/2017 of 17 March 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.12. Cabotegravir - EMEA-001418-PIP01-13-M01

ViiV Healthcare UK Limited; Treatment of human immunodeficiency virus (HIV-1) Infection / Treatment of human immunodeficiency virus (HIV-1) Infection, in combination with other antiretroviral agents

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The applicant provided on 25 August 2017 a response to the draft opinion, which satisfactorily clarified all the issues raised at Day 30.
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/0272/2014 of 27 October 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.13. Domagrozumab - Orphan - EMEA-001763-PIP01-15-M01

Pfizer Limited; Duchenne Muscular Dystrophy

Day 60 opinion

Neurology

Summary of committee discussion:

The Paediatric Committee reviewed the additional clarifications provided by the applicant between D30 and D60.
Overall, 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/0108/2016 of 15 April 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.14. Erenumab - EMEA-001664-PIP02-15-M01

Novartis Europharm Limited; Prevention of migraine headaches

Day 60 opinion

Neurology

Summary of committee discussion:

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0370/2016 of 16/12/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.15. Fremanezumab - EMEA-001877-PIP01-15-M01

Teva GmbH; Prevention of migraine headaches

Day 60 opinion

Neurology

Summary of committee discussion:

The PDCO confirmed the position reached 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/0301/2016 of 16/9/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.16. Gemtuzumab Ozogamicin - Orphan - EMEA-001733-PIP02-15-M01

Pfizer Limited; Treatment of Acute Myloid Leukaemia

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed at Day 60 this request for modification on the 15th of September 2017.
The PDCO confirmed all the conclusions reached at the Day 30 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/0078/2016 of 18 March 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.17. andexanet alfa - EMEA-001902-PIP01-15-M01

Portola Pharma UK Limited; prevention of factor Xa inhibitor associated haemorrhage, treatment of factor Xa inhibitor associated haemorrhage / fot the reversal of anticoagulation due to direct and indirect facor Xa inhibitors in patients experiencing an acute major bleeding episode, for the reversal of anticoagulation due to direct and indirect factor Xa inhibitors in patients requiring urgent surgery

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/0199/2016 of 18 July 2016.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.18. Febuxostat - EMEA-001417-PIP01-12-M03

Menarini International Operations Luxembourg S.A.; Prevention/treatment of hyperuricemia / Prevention or treatment of hyperuricemia in patients at intermediate or high risk of Tumor Lysis Sindrome (TLS) affected by hematologic malignancies

Day 60 opinion

Other / 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/0285/2015 of 27/11/2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.19. Tapentadol - EMEA-000325-PIP01-08-M08

Grünenthal GmbH; Treatment of chronic pain

Day 60 opinion

Pain

Summary of committee discussion:

The PDCO's views expressed on day 30 were re-discussed and endorsed taking into account the applicant's clarifications.
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/0148/2017 of 7 June 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.20. Formoterol fumarate dihydrate / Beclometasone dipropionate - EMEA-000548-PIP01-09-M07

Chiesi Farmaceutici S.p.A.; COPD, Asthma / Maintenance therapy of asthma where use of a combination product (inhaled corticosteroid and long-acting beta2-agonist) is appropriate: - patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting beta2-agonist or - patients already adequately controlled on both inhaled corticosteroids and long-acting beta2-agonists.,

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 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/0001/2017 of 5 January 2017).

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

2.3.21. Ivacaftor - Orphan - EMEA-001640-PIP01-14-M03

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

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 which were considered agreeable.
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/0193/2017 of 3 July 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.22. tralokinumab - EMEA-000782-PIP01-09-M04

MedImmune Ltd; Asthma / Reduce exacerbations and to improve asthma control and lung function in patients 12 years and older with severe asthma inadequately controlled with medium or high dose inhaled corticosteroids and another controller

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

The PDCO discussed the applicants responses to the outstanding issues as per day 30 PDCO discussion for the modification procedure for tralokinumab (human monoclonal antibody targeting the cytokine interleukin 13) for the treatment of asthma during its plenary on 15 September 2017.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the changes, as per above PDCO conclusion, 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/0099/2016 of 15/04/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.23. Everolimus - Orphan - EMEA-000019-PIP08-12-M03

Novartis Europharm Limited; Tuberous Sclerosis Complex (TSC) / Treatment of refractory partial-onset seizures associated with tuberous sclerosis complex (TSC)

Day 60 opinion

Uro-nephrology / Neurology

Summary of committee discussion:

The PDCO re-discussed the application.
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.

2.3.24. Influenza virus surface antigens (haemagglutinin and neuraminidase) of the following strains: A/<Official Strain>(H1N1), A/<Official Strain>(H3N2), B/<Official Strain>Yamagata lineage, B/<Official Strain>Victoria lineage based on annual recommendations by WHO, CHMP (EU) and other regional or local authorities - EMEA-001782-PIP01-15-M01

Abbott Biologicals B.V.; Prevention of Influenza infection / Prophylaxis of influenza; especially in those who run an increased risk of associated complications

Day 60 opinion

Vaccines

Summary of committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed.
Based on the review of the rationale submitted by the 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/0182/2015 of 19/06/15).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.25. Liposomal combination of cytarabine and daunorubicin - Orphan - EMEA-001858-PIP02-16-M01

JAZZ PHARMACEUTICALS IRELAND LIMITED; Acute Myeloid Leukemia

Day 30 opinion

Oncology

Summary of committee discussion:

The PDCO discussed the modification request on 14 September 2017.
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, at D30, a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0200/2017 of 21 July 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.26. Entolimod - Orphan - EMEA-002020-PIP01-16-M01

Cleveland Biolabs, Inc; Treatment of acute Radiation Syndrome / Entolimod is indicated for reducing the risk of death following exposure to potentially lethal irradiation.

Day 30 opinion

Other

Summary of committee discussion:

The PDCO discussed this modification on 14 September 2017.
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/0104/2017of 11 April 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.4. Opinions on Re-examinations

2.4.1. Autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 - Orphan - EMEA-001654-PIP01-14-M02

Novartis Europharm Limited; B cell acute lymphoblastic leukaemia (ALL) / Treatment of CD19+ B cell acute lymphoblastic leukaemia (ALL) in paediatric patients whose disease is refractory to a standard chemotherapy regimen, relapsed after stem cell transplantation (SCT) or are ineligible for allogenic SCT.

Day 30 opinion

Oncology

Summary of committee discussion:

The PDCO considered the arguments provided by the applicant The PDCO adopted a favourable Opinion.

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. Omega-3-carboxylic acids - EMEA-001865-PIP02-16

Hypertriglyceridaemia or mixed dyslipidaemia to reduce the risk of atherosclerotic cardiovascular disease (ACVD), Mixed dyslipidaemia with persistent hypertriglyceridaemia.

Day 90 discussion

Cardiovascular Diseases

3.1.2. Synthetic double-stranded siRNA oligonucleotide directed against hydroxyacid oxidase 1 mRNA that is covalently linked to a ligand containing three N-acetylgalactosamine residues - Orphan - EMEA-002079-PIP01-16

Alnylam UK Limited; Treatment of Primary Hyperoxaluria Type 1

Day 90 discussion

Gastroenterology-Hepatology

3.1.3. Iron hydroxyethyl amylopectin heptonate - EMEA-002094-PIP01-16

Iron deficiency anemia., Iron deficiency.

Day 90 discussion

Haematology-Hemostaseology

3.1.4. emapalumab - Orphan - EMEA-002031-PIP01-16

Novimmune B.V; Treatment of Haemophagocytic Lymphohistiocytosis

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.5. recombinant humanised IgG4 monoclonal antibody against MSRV-Envelope protein - EMEA-002127-PIP01-17

Treatment of Multiple Sclerosis / Treatment of patients from 10 to less than 18 years old with relapsing-remitting multiple sclerosis

Day 90 discussion

Neurology

3.1.6. ruxolitinib phosphate - EMEA-000901-PIP03-16

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

Day 90 discussion

Oncology

3.1.7. calcifediol - EMEA-002093-PIP01-16

secondary Hyperparathyroidism (SHPT)

Day 90 discussion

Uro-nephrology

3.1.8. N. meningitidis serogroup W polysaccharide conjugated to tetanus toxoid / N. meningitidis serogroup Y polysaccharide conjugated to tetanus toxoid / N. meningitidis serogroup C polysaccharide conjugated to tetanus toxoid / N. meningitidis serogroup A polysaccharide conjugated to tetanus toxoid - EMEA-001930-PIP01-16

Prevention of Meningococcal Disease

Day 90 discussion

Vaccines

3.1.9. Bimekizumab - EMEA-002189-PIP01-17

Treatment of psoriasis / Treatment of moderate to severe chronic plaque psoriasis in children from the age of 6 years and older

Day 60 discussion

Dermatology

3.1.10. Alicaforsen - Orphan - EMEA-002060-PIP02-17

Atlantic Pharmaceuticals (Holdings) Ltd; Treatment of gastrointestinal procedural complications / Treatment of active episodes of antibiotic refractory pouchitis

Day 60 discussion

Gastroenterology-Hepatology

3.1.11. Obeticholic Acid - EMEA-001304-PIP03-17

NASH / NASH with Fibrosis

Day 60 discussion

Gastroenterology-Hepatology

3.1.12. Plazomicin Sulfate - EMEA-001639-PIP02-17

Treatment of infections due to Enterobacteriaceae / Treatment of neonatal sepsis due to

Enterobacteriaceae in patients with limited treatment options, Treatment of complicated urinary tract infections, including acute pyelonephritis, due to Enterobacteriaceae, including cases with concurrent bacteraemia.

Day 60 discussion

Infectious Diseases

3.1.13. Pritelivir - EMEA-002180-PIP01-17

Treatment of recurrent herpes labialis / Topical treatment of recurrent herpes labialis

Day 60 discussion

Infectious Diseases

3.1.14. Mecasermin rinfabate - Orphan - EMEA-000534-PIP03-17

Premacure AB; Chronic lung disease of prematurity

Day 60 discussion

Neonatology - Paediatric Intensive Care

3.1.15. Lasmiditan - EMEA-002166-PIP01-17

Migraine with and without aura

Day 60 discussion

Neurology

3.1.16. taselisib - EMEA-002210-PIP01-17

Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms) / Treatment of children with relapsed or refractory solid tumors with known or anticipated PI3K activation.

Day 60 discussion

Oncology

3.1.17. Tanezumab - EMEA-001635-PIP03-17

Treatment of chronic pain

Day 60 discussion

Pain

3.1.18. Cow's milk protein extract - EMEA-002201-PIP01-17

Treatment of IgE-mediated cow's milk allergy

Day 60 discussion

Pneumology - Allergology

3.1.19. ezetimibe / atorvastatin - EMEA-002207-PIP01-17

treatment of hypercholesterolaemia

Day 30 discussion

Cardiovascular Diseases

3.1.20. vonapanitase - Orphan - EMEA-002195-PIP01-17

Proteon Therapeutics Limited; prevention of arteriovenous fistula failure

Day 30 discussion

Cardiovascular Diseases

3.1.21. EMEA-002216-PIP01-17

Treatment of Atopic Dermatitis

Day 30 discussion

Dermatology

3.1.22. EMEA-002208-PIP01-17

Treatment of psoriasis, Treatment of Crohn's disease, Treatment of ulcerative colitis / Treatment of moderate to severely active Crohn's disease in paediatric patients aged 2 to less than 18 years of age, Treatment of moderate to severely active ulcerative colitis in paediatric patients aged 2 to less than 18 years of age, Treatment of moderate-to-severe plaque psoriasis in paediatric patients aged 6 to less than 18 years of age.

Day 30 discussion

Dermatology / Gastroenterology-Hepatology

3.1.23. inclisiran sodium - EMEA-002214-PIP01-17

Treatment of elevated cholesterol / Inclisiran is indicated to lower LDL-C in adults and children aged 11 years old and older with heterozygous familial hypercholesterolemia in combination with other lipid lowering therapies., Inclisiran is indicated to lower LDL-C in adults and children aged 11 years old and older with homozygous familial hypercholesterolemia in combination with other lipid lowering therapies.

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.24. Anti-Mucosal Addressin Cell Adhesion Molecule Antibody - EMEA-002218-PIP01-17

Treatment of Ulcerative Colitis, Treatment of Crohn's Disease / Treatment of moderate to severe active Crohn's Disease, Treatment of moderate to severe active Ulcerative Colitis

Day 30 discussion

Gastroenterology-Hepatology

3.1.25. Ibrutinib - Orphan - EMEA-001397-PIP04-17

Janssen-Cilag International N.V.; Treatment of cGVHD / indicated for the treatment of cGVHD in children 1 year of age and older

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.26. Branaplam - EMEA-002204-PIP01-17

Spinal Muscular Atrophy

Day 30 discussion

Neurology

3.1.27. Opicinumab - EMEA-002194-PIP01-17

Treatment of Multiple Sclerosis

Day 30 discussion

Action: For discussion

Neurology

3.1.28. Glasdegib maleate - EMEA-002199-PIP01-17

Treatment of acute myeloid leukaemia (AML) / Glasdegib as monotherapy for prevention of AML relapse in children aged 2 years up to <18 years with high risk for relapse post-alloSCT; Glasdegib in combination with FLAG/DNX as reinduction treatment of R/R AML in children aged 2 years up to <18 years, followed by consolidation therapy with or without SCT, and finally single-agent glasdegib post-consolidation.

Day 30 discussion

Oncology

3.1.29. isatuximab - Orphan - EMEA-002205-PIP01-17

Sanofi-Aventis Recherche & Développement; Treatment of malignant neoplasms of the haematopoietic and lymphoid tissue / Treatment of relapsed, refractory acute lymphoblastic leukemia in combination with standard treatment in paediatric patients with no more than

one prior salvage therapy, Treatment of relapsed, refractory acute myeloblastic leukemia in combination with standard treatment in paediatric patients with no more than one prior salvage therapy

Day 30 discussion

Oncology

3.1.30. resminostat - Orphan - EMEA-002211-PIP01-17

4SC AG; Cutaneous T-Cell Lymphoma

Day 30 discussion

Oncology

3.1.31. Soluble human T cell receptor (TCR) directed against the glycoprotein 100 (gp100) melanoma antigen, linked to the single-chain variable fragment (ScFv) domain of the anti-cluster of differentiation 3 (CD3) antibody - EMEA-002197-PIP01-17

Treatment of ocular melanoma

Day 30 discussion

Oncology

3.1.32. Autologous cartilage derived cultured chondrocytes - EMEA-002217-PIP01-17

Treatment of cartilage disorders

Day 30 discussion

Other

3.1.33. Tolonium chloride - EMEA-002170-PIP01-17

Dental and oral soft tissue infections

Day 30 discussion

Other

3.1.34. EMEA-001976-PIP01-16

Asthma / Once-daily maintenance treatment of asthma as prophylactic therapy in patients aged 12 years and older (and in age 5-11) where use of a maintenance anti-inflammatory medication is appropriate

Day 30 discussion

Pneumology - Allergology

3.1.35. Human Neutrophil Elastase Inhibitor - EMEA-002196-PIP01-17

Treatment of Non-Cystic Fibrosis Bronchiectasis

Day 30 discussion

Pneumology - Allergology

3.1.36. ivacaftor / tezacaftor - EMEA-002191-PIP01-17

Treatment of Cystic Fibrosis

Day 30 discussion

Pneumology - Allergology

3.1.37. EMEA-002222-PIP01-17

Treatment of schizophrenia

Day 30 discussion

Psychiatry

3.1.38. Plant-derived Quadrivalent VLP Influenza vaccine - EMEA-002220-PIP01-17

prophylaxis of seasonal influenza / For active immunization of persons six months of age and older for the prevention of disease caused by influenza A subtype viruses and type B viruses covered by the vaccine.

Day 30 discussion

Vaccines

3.1.39. EMEA-002215-PIP01-17

Disease caused by Streptococcus pneumoniae

Day 30 discussion

Vaccines

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. rivaroxaban - EMEA-C4-000430-PIP01-08-M10

Bayer AG; Treatment of thromboembolic events

Day 30 discussion

Cardiovascular Diseases

3.2.2. rabeprazole (sodium) - EMEA-C-000055-PIP01-07-M05

Eisai Ltd.; Treatment of gastro-oesophageal reflux disease

Day 30 discussion

Gastroenterology-Hepatology

3.2.3. turoctocog alfa pegol - EMEA-C1-001174-PIP02-12-M02

Novo Nordisk A/S; Treatment of hereditary Factor VIII deficiency

Day 30 discussion

Haematology-Hemostaseology

3.2.4. Treosulfan - EMEA-C1-000883-PIP01-10-M04

medac Gesellschaft für klinische Spezialpräparate mbH; Conditioning treatment prior to haematopoietic progenitor cell
transplantation

Day 30 discussion

Immunology-Rheumatology-Transplantation / Oncology

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Azilsartan medoxomil - EMEA-000237-PIP01-08-M07

Takeda Development Centre (Europe) Ltd.; Treatment of hypertension / Essential (primary) hypertension, Secondary hypertension

Day 30 discussion

Cardiovascular Diseases

3.3.2. Tolvaptan - EMEA-001231-PIP02-13-M05

Otsuka Pharmaceutical Europe Ltd.; Polycystic Kidney Disease (PKD), Dilutional hyponatraemia / Treatment of chronic (>48 hours) dilutional hyponatraemia resistant to fluid restriction (i.e., euvolemic and hypervolemic hyponatremia) associated with heart failure, cirrhosis or SIADH., Treatment of progression of ADPKD, Treatment of progression of ARPKD

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.3. Teduglutide ([gly2] recombinant human glucagon-like peptide) - Orphan - EMEA-000482-PIP01-08-M04

Shire Pharmaceuticals Ireland Limited; ICD-9-CM Diagnosis 579.3 - Other and unspecified post-surgical non-absorption - Syndrome Short Bowel / Treatment of Short Bowel Syndrome

Day 30 discussion

Gastroenterology-Hepatology

3.3.4. Fc- and CDR-modified humanised monoclonal antibody against C5 - Orphan - EMEA-002077-PIP01-16-M01

Alexion Europe SAS; Treatment of Paroxysmal Nocturnal Haemoglobinuria

Day 30 discussion

Haematology-Hemostaseology

3.3.5. sarilumab - EMEA-001045-PIP01-10-M01

sanofi-aventis recherche et développement; Treatment of chronic idiopathic arthritis (including rheumatoid arthrtis, spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.6. Secukinumab - EMEA-000380-PIP01-08-M04

Novartis Europharm Ltd; Psoriasis / Moderate to severe plaque psoriasis in adults who are candidates for systemic therapy

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.7. Upadacitinib - EMEA-001741-PIP01-14-M01

AbbVie Ltd; Treatment of Chronic Idiopathic Arthritis / Treatment of Juvenile Idiopathic Arthritis

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.8. Adalimumab - EMEA-000366-PIP02-09-M05

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

Day 30 discussion

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

3.3.9. lumicitabine - EMEA-001758-PIP01-15-M02

Janssen-Cilag International NV; Treatment of lower respiratory tract disease caused by human respiratory syncytial virus

Day 30 discussion

Infectious Diseases

3.3.10. Telavancin hydrochloride - EMEA-000239-PIP01-08-M03

Theravance Biopharma Ireland Ltd.; Nosocomial Pneumonia (NP)

Day 30 discussion

Infectious Diseases

3.3.11. Thrombomodulin alfa - EMEA-001363-PIP01-12-M01

Asahi Kasei Pharma America Corporation; Treatment of sepsis / Treatment of patients with severe sepsis (respiratory failure and/or septic shock) with coagulopathy

Day 30 discussion

Infectious Diseases

3.3.12. Bumetanide - EMEA-001303-PIP01-12-M02

Les Laboratoires Servier; Treatment of Autism Spectrum Disorder

Day 30 discussion

Neurology

3.3.13. eculizumab - Orphan - EMEA-000876-PIP03-14-M01

Alexion Europe SAS; Neuromyelitis optica spectrum disorders / Treatment of Relapsing Neuromyelitis Optica Spectrum Disorders in the paediatric population

Day 30 discussion

Neurology

3.3.14. lacosamide - EMEA-000402-PIP03-17-M01

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

3.3.15. ozanimod - EMEA-001710-PIP02-14-M02

Celgene Europe Limited; Treatment of multiple sclerosis / Treatment of relapsing remitting forms of multiple sclerosis

Day 30 discussion

Neurology

3.3.16. avelumab (recombinant human monoclonal IgG1 antibody directed against Programmed Death Ligand-1 (anti-PD-L1)) - Orphan - EMEA-001849-PIP02-15-M01

Merck KGaA; Treatment of all conditions included in the category of solid malignant neoplasms (including central nervous system tumours and lymphoma)

Day 30 discussion

Oncology

3.3.17. Naltrexone HCl / Bupropion HCl - EMEA-001373-PIP01-12-M03

Orexigen Therapeutics Ireland Limited; Treatment of obesity

Day 30 discussion

Other

3.3.18. Palovarotene - Orphan - EMEA-001662-PIP01-14-M01

Clementia Pharmaceuticals Inc.; Treatment of Fibrodysplasia Ossificans Progressiva (FOP)

Day 30 discussion

Other

3.3.19. Tapentadol - EMEA-000018-PIP01-07-M14

Grünenthal GmbH; Treatment of acute pain

Day 30 discussion

Pain

3.3.20. mirabegron - EMEA-000597-PIP02-10-M06

Astellas Pharma Europe B.V.; Treatment of idiopathic overactive bladder / Symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in patients with overactive bladder syndrome

Day 30 discussion

Uro-nephrology

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 28 November 2017 for Nomination of Rapporteur and Peer reviewer

Summary of committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

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

Summary of committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

4.3. Nominations for other activities

Summary of committee discussion:

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

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

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

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

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. Fully human anti-human PCSK9 monoclonal antibody - EMEA-001169-PIP01-11

sanofi-aventis R&D; Treatment of elevated cholesterol/Reduction in the frequency of apheresis in HeFH patients

Summary of committee discussion:

The planned extension of indication as proposed by the applicant was not understood by the Paediatric Committee as it was rather seen as an outcome measure. Nevertheless, this assessment is within the remit of the CHMP. The PDCO confirmed that “Reduction in the frequency of apheresis in HeFH patients”, if confirmed as an indication, would be considered included within the condition “Treatment of elevated cholesterol” of the already agreed PIP.

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

None

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 presented the list of procedures with paediatric indications to be evaluated by the CHMP, starting in August 2017.

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. CMDh letter to PDCO after Art. 29 referral – Ozanex (ozenoxacin)

PDCO member: Marianne Orholm, Maria Fernandez Cortizo

Summary of committee discussion:

A response letter to CMD(h) after Art. 29 referral – Ozanex (ozenoxacin) was presented to, discussed and adopted by the PDCO.

9.3.4. Guideline on clinical investigation of medicinal products in the treatment of epileptic disorders

PDCO member: Sylvie Benchetrit;

Summary of committee discussion:

The outline of the draft guideline was presented to the Committee, members' comments are invited.

9.3.5. Draft agenda PCWP/HCPWP joint meeting to be held at EMA on 20 September 2017

Summary of committee discussion:

Draft agenda was tabled for information.

9.3.6. Draft Agenda - Session on antimicrobial resistance EMA Working Parties with Patients' and PCWP and HCPWP joint meeting to be held at EMA on 19 September 2017

Summary of committee discussion:

Draft agenda was tabled for information.

9.3.7. Guideline on the development of new medicinal products for the treatment of Crohn's Disease – postponed to the PDCO October 2017 meeting

PDCO members: Peter Szitanyi and Johannes Taminiau

Summary of committee discussion:

Postponed

9.3.8. Reflection paper on the use of extrapolation in paediatric medicines development - postponed

PDCO member: Dirk Mentzer

Summary of committee discussion:

Postponed to October PDCO plenary

9.3.9. Call for membership of the Patients and Consumers Working Party and Healthcare Professional's Working Party

PDCO member: Dirk Mentzer

Summary of committee discussion:

Call for membership of the Patients and Consumers Working Party and Healthcare Professional's Working Party was launched.

Nominations received: Francesca Rocchi (Healthcare Professional's Working Party); Paola Baiardi and Dimitrios Athanasiou (Patients and Consumers Working Party).

9.3.10. Paediatric Addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections

PDCO members: Maria Fernandez Cortizo, Irja Lutsar, Marianne Orholm

Summary of committee discussion:

The version of the addendum including comments received by some PDCO members was presented to the committee. PDCO members will shortly receive another revised version and are kindly requested to submit their final comments latest by 28th September to the PDCO rapporteur.

9.4. Cooperation within the EU regulatory network

None

9.5. Cooperation with International Regulators

None

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

None

9.7. PDCO work plan

None

9.8. Planning and reporting

9.8.1. Presentation regarding T cells expressing Chimeric Antigen Receptors (CAR-Ts)

Summary of committee discussion:

The Committee was updated on general issues relating to CAR-T cells and on the current situation with the CAR-T PIPs.

9.8.2. Business Pipeline Report - Forecast for 2017 - Update Q3/2017

Summary of committee discussion:

Tabled for information

10. Any other business

10.1. Training for PDCO members and alternates

Training for the PDCO members and alternates was held on the 1st day of the plenary meeting.

11. Breakout sessions

11.1. Paediatric oncology

Summary of committee discussion:

The working group discussed the upcoming paediatric strategy forum on medicine development for mature B cell malignancies in children to be held at the EMA on 14-15 November and ICH S9 Q&A.

11.2. Neonatology

Summary of committee discussion:

The working group discussed the neonatal topics planned for the upcoming Strategic Review and Learning Meeting (SRLM) to be held in Tallinn on 4-6 October.

11.3. Inventory

Summary of committee discussion:

The paediatric inventory group convened on the margins of the PDCO plenary to prepare the topics for discussion on the inventory of paediatric needs for the upcoming Strategic Review and Learning Meeting (SRLM) to be held in Tallinn on 4-6 October.

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 12 – 15 September 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-C1-001765-PIP02-15-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	
Marianne Orholm	Member	Denmark	No interests declared	
Kirstine Moll Harboe	Alternate	Denmark	No interests declared	
Irja Lutsar	Member	Estonia	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
Anastasia Mountaki	Alternate	Greece	No interests declared	
Ágnes Gyurasics	Member (CHMP member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	
Alessandro Jenkner	Alternate	Italy	No interests declared	
Dina Apele-Freimane	Member	Latvia	No interests declared	
Sigita Burokiene	Member	Lithuania	No interests declared	
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No interests declared	
Herbert Lenicker	Alternate	Malta	No interests declared	
Maaike van Dartel	Member	Netherlands	No interests declared	
Siri Wang	Member	Norway	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ine Skottheim Rusten	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	
Stefan Grosek	Member	Slovenia	No interests declared	
Fernando de Andrés Trelles	Member	Spain	No interests declared	
Maria Jesús Fernández Cortizo	Alternate	Spain	No interests declared	
Ninna Gullberg	Member	Sweden	No interests declared	
Eva Agurell	Alternate	Sweden	No restrictions applicable to this meeting	
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 restrictions applicable to this meeting	
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Catherine Cornu	Alternate	Healthcare Professionals' Representative	No participation in final deliberations and voting on:	EMEA-002079-PIP01-16 EMEA-000019-PIP08-12-M03
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	
Paola Baiardi	Alternate	Patients' Organisation Representative	No participation in final deliberations and voting on:	EMEA-C1-001765-PIP02-15-M01
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Viviana Giannuzzi	Alternate	Patients' Organisation Representative	No interests declared	
Uwe Müller	Expert - in person*	Germany - PEI	No interests declared	
Charlotta Bergquist	Expert - via telephone*	Sweden	No restrictions applicable to this meeting	
Shiva Ramroop	Expert - in person*	United Kidgdom	No restrictions applicable to this meeting	
Eleni Gaki	Expert - in person*	United Kidgdom	No interests declared	

* 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/