29 June 2018
EMA/PDCO/437683/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes of the meeting on 26-29 June 2018

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

26 June 2018, 14:00- 19:00, room 3A

27 June 2018, 08:30- 19:00, room 3A

28 June 2018, 08:30- 19:00, room 3A

29 June 2018, 08:30- 13:00, room 3A

Disclaimers

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

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

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

Note on access to documents

Some documents mentioned in the minutes cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

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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 and will be published on the EMA website.

1.3. Adoption of the minutes

The minutes of the May 2018 PDCO were adopted and will be published on the EMA website.

2. Opinions

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

2.1. Opinions on Products

2.1.1. Octenidine dihydrochloride - EMEA-001384-PIP02-17

Schülke & Mayr GmbH; Maintenance of oral hygiene / For temporary reduction of bacterial count in the oral cavity, for inhibition of plaque formation, in cases of

insufficient oral hygiene capacity

Day 30 opinion

Other / Infectious Diseases

Summary of committee discussion:

The PDCO agreed to grant a product-specific waiver on its own motion for all subsets of the paediatric population in the specified condition on the ground of lack of significant therapeutic benefit over existing treatments.

2.1.2. His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Lys(γ-Glu-palmitoyl)-Ser-Glu-Tyr-Leu-Asp-Ser- Glu-Arg-Ala-Arg-Asp-Phe-Val-Ala-Trp-Leu-Glu-Ala-Gly-Gly-OH - EMEA-002287-PIP01-17

MedImmune Limited; Treatment of Type 2 Diabetes Mellitus

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

During its plenary on 29 June 2018, the PDCO discussed the applicant's responses to the outstanding issues from the day 90 discussion in May 2018 for this dual glucagon-like peptide-1 (GLP-1) / glucagon (GCG) receptor agonist for the treatment of type 2 diabetes.
In summary, the applicant's responses and clarifications were deemed acceptable by the PDCO and a positive opinion was adopted by the Committee.

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

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

Day 120 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The committee confirmed the outcome of the Day 90 discussion. As all remaining issues had been clarified a positive opinion was adopted.

2.1.4. Risankizumab - EMEA-001776-PIP03-17

AbbVie Ltd; Crohn's Disease

Day 120 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

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

2.1.5. Risankizumab - EMEA-001776-PIP04-17

AbbVie Ltd; Ulcerative Colitis

Day 120 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

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

2.1.6. Cefiderocol - EMEA-002133-PIP01-17

Shionogi Limited; Treatment of Gram-negative bacterial infections

Day 120 opinion

Infectious Diseases

Summary of committee discussion:

The applicant provided acceptable justification/clarification on the issues which were outstanding at Day 90.
In conclusion, based on the assessment of this application, the PDCO adopted a positive opinion on the paediatric plan proposed by the applicant.

2.1.7. Glasdegib - Orphan - EMEA-002199-PIP01-17

Pfizer Limited; Treatment of acute myeloid leukaemia (AML)

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO's view expressed at Day 90 was endorsed.
The PDCO recommends granting a waiver for glasdegib (maleate) for all subsets of the paediatric population from birth to less than 18 years of age in the condition of treatment of acute myeloid leukaemia, specifically on the ground that the product is likely to be unsafe in younger children (from birth to closure of the epiphyses) and on the grounds that the product does not represent a significant therapeutic benefit for children with closed epiphyses because clinical studies are not feasible because of the relative rarity of AML in this subgroup.

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.

2.1.8. Olaparib - Orphan - EMEA-002269-PIP01-17

AstraZeneca AB; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system [CNS], haematopoietic, and lymphoid tissue). / Treatment of paediatric patients from 6 months to ≤18 years old with homologous recombination repair (HRR) mutated solid tumours

Day 120 opinion

Oncology

Summary of committee discussion:

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

2.1.9. Setrusumab - Orphan - EMEA-002169-PIP01-17

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

Day 120 opinion

Other

Summary of committee discussion:

PDCO agreed at their June 2018 meeting a positive opinion on the PIP for setrusumab in the treatment of Osteogenesis Imperfecta.

2.1.10. Ferric Pyrophosphate Citrate - EMEA-002261-PIP01-17

Rockwell Medical, Inc.; Treatment of iron deficient anaemia in haemodialysis patients

Day 120 opinion

Uro-nephrology / Haematology-Hemostaseology

Summary of committee discussion:

The remaining issues were solved and the PDCO adopted a positive opinion for this PIP for treatment of anaemia of chronic kidney disease.

2.1.11. Ad26.Mos4.HIV - EMEA-002160-PIP01-17

Janssen-Cilag International NV; Prevention of HIV-1 infection in children from 9 to less than 18 years of age

Day 120 opinion

Vaccines / Infectious Diseases

Summary of committee discussion:

The applicant provided acceptable justification/clarification on the remaining minor, issues which were outstanding at Day 90.

As all the issues were resolved, based on the assessment of this application, the PDCO adopted a positive opinion on the paediatric plan proposed by the applicant. Completion of the paediatric study is deferred.

2.1.12. Clade C gp140, co-formulated with aluminum phosphate adjuvant - EMEA-002221-PIP01-17

Janssen-Cilag International NV; Prevention of HIV-1 infection in children from 9 to less than 18 years of age

Day 120 opinion

Vaccines / Infectious Diseases

Summary of committee discussion:

The applicant provided acceptable justification/clarification on the remaining, minor, issues which were outstanding at Day 90.

As all the issues were resolved, based on the assessment of this application, the PDCO adopted a positive opinion on the paediatric plan proposed by the applicant. Completion of the paediatric study is deferred.

2.1.13. Mosaic gp140, co-formulated with aluminum phosphate adjuvant / Clade C gp140, co-formulated with aluminum phosphate adjuvant - EMEA-002161-PIP01-17

Janssen-Cilag International NV; Prevention of HIV-1 infection in children from 9 to less than 18 years of age

Day 120 opinion

Vaccines / Infectious Diseases

Summary of committee discussion:

The applicant provided acceptable justification/clarification on the remaining, minor, issues which were outstanding at Day 90.

As all the issues were resolved, based on the assessment of this application, the PDCO adopted a positive opinion on the paediatric plan proposed by the applicant. Completion of the paediatric study is deferred.

2.1.14. Amlodipine / irbesartan - EMEA-002352-PIP01-18

Sanofi- Aventis Research & Development; Treatment of essential hypertension

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

Based on the assessment of this application the PDCO agrees with the applicant's request

for a waiver. The PDCO recommends granting a waiver for irbesartan / amlodipine for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of hypertension.

2.1.15. Venglustat - Orphan - EMEA-001716-PIP03-18

Genzyme Europe B.V.; ICD-10: Q61.2; Polycystic kidney, autosomal dominant; Congenital malformations of the urinary system (Q60-Q64)

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism / Uro-nephrology

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO does not agree with the applicant's request for a waiver for the reasons detailed in the Day 30 summary.
The PDCO emphasises that there is an unmet paediatric need for the treatment of PKD. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available.
A negative opinion was adopted.

2.1.16. Luspatercept - EMEA-001521-PIP02-18

Celgene Europe Ltd; Treatment of Myelofibrosis

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The Paediatric Committee agrees with the applicant's request for a waiver.
The PDCO recommends granting a waiver for luspatercept for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of myelofibrosis on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible.

2.1.17. Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3- zeta chimeric antigen receptor - Orphan - EMEA-002335-PIP01-18

Kite Pharma EU B.V.; Treatment of Mantle Cell Lymphoma

Day 60 opinion

Oncology

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, it is appropriate for PDCO to grant a full waiver for Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3- zeta chimeric

antigen receptor for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of Mantle Cell Lymphoma.

2.1.18. Navitoclax - EMEA-000478-PIP02-18

AbbVie Ltd; Treatment of myelofibrosis

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO confirmed the outcome of the Day 30 discussion and granted a full waiver for navitoclax for the treatment of myelofibrosis for all paediatric age groups on the ground that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

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 navitoclax for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of myelofibrosis.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need.

2.1.19. Veliparib - Orphan - EMEA-000499-PIP05-18

AbbVie Ltd; Treatment of ovarian carcinoma, Treatment of fallopian tube carcinoma, Treatment of peritoneal carcinoma

Day 60 opinion

Oncology

Summary of committee discussion:

The applicant’s responses to the D30 issues were considered acceptable and 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 ovarian cancer, treatment of fallopian tube cancer, treatment of peritoneal 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.

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. Sunitinib malate - EMEA-C-000342-PIP01-08-M07

Pfizer Limited; Treatment of gastro-intestinal stromal tumours

Day 30 letter

Oncology

Summary of committee discussion:

The PDCO discussed this procedure at Day 60 during the June 2018 plenary meeting. The completed studies were checked for compliance.
The PDCO adopted on 29 June 2018 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0147/2018) of 7 May 2018.

2.2.2. Siponimod fumaric acid co-crystal - EMEA-C1-000716-PIP01-09-M02

Novartis Europharm Limited; Treatment of Multiple Sclerosis

Day 30 letter

Neurology

Summary of committee discussion:

The submitted data are in compliance with the measures and timelines of the paediatric investigation plan as set in the latest EMEA Decision P/0098/2017 of 11 April 2017.

2.2.3. Nusinersen - EMEA-C-001448-PIP01-13-M03

Biogen Idec Ltd; Treatment of spinal muscular atrophy

Day 30 opinion

Neurology

Summary of committee discussion:

The PDCO adopted on 29 June 2018 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision P/0123/2018.

2.2.4. Nonacog gamma - EMEA-C-001139-PIP01-11-M02

Baxalta Innovations GmbH; Treatment of haemophilia B (congenital factor IX deficiency)

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO took note of preceding procedures and reports on partially completed compliance EMEA-C1-001139-PIP01-11-M01.

The PDCO adopted on 29 June 2018 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0021/2016) of 29 January 2016.

2.2.5. Macitentan - EMEA-C2-001032-PIP01-10-M02

Actelion Registration Ltd; Treatment of pulmonary arterial hypertension

Day 30 letter

Cardiovascular Diseases

Summary of committee discussion:

The PDCO discussed the completed study and considered that it is compliant with the latest Agency's Decision (P/0049/2016) of 18 March 2016.
The PDCO finalised on 29/06/2018 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. Cilastatin sodium / relebactam / imipenem monohydrate - EMEA-C1-001809-PIP01-15

Merck Sharp & Dohme (Europe), Inc.; Treatment of Gram-negative bacterial infections

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/0163/2016) of 15 June 2016.
The PDCO finalised on 29 June 2018 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.

2.2.7. Trifarotene - EMEA-C-001492-PIP01-13-M01

GALDERMA R&D; Treatment of acne

Day 30 opinion

Dermatology

Summary of committee discussion:

The PDCO adopted on 29 June 2018 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0099/2017) of 11 April 2017.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Landiolol hydrochloride - EMEA-001150-PIP02-13-M02

AOP Orphan Pharmaceuticals AG; Treatment of supraventricular arrythmias

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The PDCO adopted a negative opinion on the modification of the agreed PIP; the requirements agreed in the previous modification remain unchanged and binding.

2.3.2. Tralokinumab - EMEA-001900-PIP02-17-M01

LEO Pharma A/S; Treatment of Atopic Dermatitis

Day 60 opinion

Dermatology

Summary of committee discussion:

The applicant response was considered acceptable by the PDCO.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0083/2018 of 16 March 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.3. Olipudase alfa - Orphan - EMEA-001600-PIP01-13-M01

Genzyme Europe B.V.; ICD-10: E75.2; Endocrine, nutritional and metabolic diseases, Metabolic disorders, Disorders of sphingolipid metabolism and other lipid storage disorders, Other sphingolipidosis, Niemann-Pick Disease.

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, 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/0053/2015 of 6 March 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.4. Osilodrostat - Orphan - EMEA-000315-PIP02-15-M02

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

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The Committee discussed the clarification provided by the applicant after D30. PDCO agreed with the modification.

2.3.5. Romosozumab - EMEA-001075-PIP04-15-M01

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

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/0066/2016 of 29/1/2016).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.6. Roxadustat - EMEA-001557-PIP01-13-M02

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

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO adopted a negative opinion.

2.3.7. Ciprofloxacin Hydrochloride - EMEA-001563-PIP02-15-M01

Aradigm Limited; Treatment of chronic pulmonary infections caused by Pseudomonas aeruginosa

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO re-discussed its views expressed on day 30 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/0023/2017 of 13 February 2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.8. Oseltamivir phosphate - EMEA-000365-PIP01-08-M10

Roche Registration Limited; Treatment and prevention of influenza in healthy and immunocompromised patients from 0 to less than 18 years of age

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The responses submitted by the applicant after D30 discussions were reviewed by the PDCO.
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/01080/2017 of 11/4/2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.9. Balovaptan - EMEA-001918-PIP01-15-M01

Roche Registration Ltd; ICD1O F84: Treatment of autism spectrum disorder / Treatment of core social and communication deficits in people with autism spectrum disorder aged 2 years or older

Day 60 opinion

Neurology

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed 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/0073/2017 of 27/1/2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.10. (Z)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-4-(2-(sulfamoylamino)ethylamino)-1,2,5-oxadiazole-3-carboximidamide - EMEA-002072-PIP01-16-M01

Incyte Corporation; Treatment of select unresectable or metastatic solid tumours with epacadostat in combination with pembrolizumab in paediatric patients between the ages of 6 months and 18 years of age / Select unresectable or metastatic solid tumours in paediatric patients >6 months and < 18 years

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO's views expressed on day 30 were re-discussed, taking into account the applicant's clarifications.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0283/2017 of 04/10/2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.11. Avelumab - Orphan - EMEA-001849-PIP02-15-M02

Merck KGaA; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoetic and lymphoid tissue neoplams), Treatment of malignant neoplasms of lymphoid tissue, Treatment of malignant neoplasms of the central nervous system / Treatment of paediatric patients from birth to less than 18 years old with a refractory or relapsed tumour of the central nervous system or with a tumour of the central nervous system as part of first line treatment, Treatment of paediatric patients from birth to less than 18 years old with a relapsed or refractory solid tumour or with a solid tumour as part of the first line treatment, Treatment of paediatric patients from birth to less than 18 years old with a refractory or relaphsed Hodgkin or non-Hodgkin lymphoma, or with Hodgkin or non-Hodgkin lymphoma as part of first line treatment

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO's view expressed at Day 30 was 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/0361/2017 of 01/12/2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.12. Eribulin - EMEA-001261-PIP01-11-M05

Eisai Europe Ltd; Soft Tissue Sarcoma

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this procedure at Day 60 during the June 2018 plenary meeting. The Committee noted that the applicant addressed most of the points raised during the Day 30 discussion.

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan and the information provided after the 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/0330/2016 of 2 December 2016).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.13. Paclitaxel - EMEA-001308-PIP01-12-M02

Celgene Europe Limited; Treatment of Solid malignant tumours / Treatment of a paediatric solid malignant tumour

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO's view expressed on 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/0017/2017 of 31/01/2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.14. Pixantrone (as dimaleate) - EMEA-000713-PIP02-10-M05

CTI Life Sciences Limited; ICD-09 C83 Diffuse non-Hodgkin's Lymphoma (including C83.7 Burkitt Lymphoma, C83.5 Lymphoblastic Lymphoma, C83.3 Large-cell Lymphoma) / Treatment of Non-Hodgkin's Lymphoma

Day 60 opinion

Oncology

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed

paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.

The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0310/2016 of 4 November 2016) and on the granting of a product-specific waiver.
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.15. Andexanet alfa - EMEA-001902-PIP01-15-M03

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

Day 60 opinion

Other

Summary of committee discussion:

The applicant's responses to the Day 30 issues were 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/0120/2018 of 11 April 2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.16. Febuxostat - EMEA-001417-PIP01-12-M04

Menarini International Operations Luxembourg S.A.; 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:

The PDCO confirmed the outcome of the Day 30 discussion and agreed to grant a full waiver for febuxostat for the treatment and prevention of hyperuricaemia for all paediatric age groups on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2.3.17. Benralizumab - EMEA-001214-PIP01-11-M08

AstraZeneca AB; Treatment of asthma

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

The committee's views expressed on day 30 were endorsed.
The PDCO therefore adopted a favourable opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0107/2018 of 11 April 2018).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.18. Vortioxetine - EMEA-000455-PIP02-10-M04

H. Lundbeck A/S; Major Depressive Disorder

Day 60 opinion

Psychiatry

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 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. Fc- and CDR-modified humanized monoclonal antibody against C5 - Orphan - EMEA-001943-PIP01-16-M01

Alexion Europe SAS; Treatment of atypical Haemolytic Uremic Syndrome

Day 60 opinion

Uro-nephrology / Haematology-Hemostaseology

Summary of committee discussion:

Between Day 30 and Day 60 the applicant provided further details.
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/0034/2017 of 30/01/2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.20. Influenza virus surface antigens - A/turkey/Turkey/1/05 (H5N1) - EMEA-000599-PIP01-09-M06

Seqirus S.r.l.; Prevention of Influenza / Active immunisation against H5N1 subtype of

Influenza A virus

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 thus 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/0057/2017 of 17 March 2017).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.21. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - EMEA-001830-PIP01-15-M01

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

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 thus 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/0085/2016 of 18 March 2016).
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.4. Opinions on Re-examinations

No items

2.5. Opinions on Review of Granted Waivers

No items

2.6. Finalisation and adoption of opinions

No items

2.7. Partial Compliance Checks completed by EMA

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

has been informed in writing.

2.7.1. Tocilizumab - EMEA-C1-000309-PIP04-17-M01

Roche Registration Limited; Treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) in adults and paediatric patients 2 years of age and older

Day 30 letter

Immunology-Rheumatology-Transplantation

The PDCO noted a completion of this partial compliance check.

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. Baricitinib - EMEA-001220-PIP03-16

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

Day 90 discussion

Dermatology

3.1.2. 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 90 discussion

Dermatology / Gastroenterology-Hepatology

3.1.3. Inclisiran sodium - EMEA-002214-PIP01-17

Treatment of familial hypercholesterolaemia / Inclisiran is indicated to lower LDL-C in adults and children aged 8 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 8 years old and older with homozygous familial hypercholesterolemia in combination with other lipid lowering

therapies.

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.4. 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 90 discussion

Gastroenterology-Hepatology

3.1.5. Human donor haematopoietic stem and progenitor cells that have been treated ex vivo with the protein transduction domain of the HIV-1 transactivation protein fused to MYC transcription factor - Orphan - EMEA-002185-PIP02-17

Taiga Biotechnologies, Inc; Severe combined immunodeficiency

Day 90 discussion

Immunology-Rheumatology-Transplantation

3.1.6. Ibalizumab - EMEA-002311-PIP01-17

Treatment of human immunodeficiency virus (HIV-1) infection / Ibalizumab, a CD4 domain 2-directed HIV-1 inhibitor, in combination with other antiretroviral(s), is indicated for the treatment of children and adolescents (aged 6 to less than 18 years) infected with HIV-1 resistant to at least 1 agent in 3 different classes.

Day 90 discussion

Infectious Diseases

3.1.7. Sarizotan hydrochloride - Orphan - EMEA-001808-PIP03-17

Newron Pharmaceuticals SpA; Treatment of Rett syndrome

Day 90 discussion

Neurology

3.1.8. Survival Motor Neuron Gene by Self-Complementary Adeno Associated Virus Serotype 9 (AAV9) - Orphan - EMEA-002168-PIP01-17

AveXis EU Ltd; Treatment of spinal muscular atrophy Type 1

Day 90 discussion

Neurology

3.1.9. Afatinib - EMEA-001596-PIP02-17

Treatment of oropharyngeal, laryngeal or nasal epithelial carcinoma, Treatment of paediatric patients with tumours with known ErbB deregulations irrespective of tumour histology, Treatment of lung carcinoma, Treatment of urether and bladder carcinoma / Treatment of paediatric patients aged between ≥ 1 year and ≤ 18 years with recurrent or refractory tumours with known ErbB deregulation and irrespective of tumour histology

Day 90 discussion

Oncology

3.1.10. Entrectinib - EMEA-002096-PIP01-16

Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms) / Treatment of paediatric patients with NTRK fusion-positive solid tumours

Day 90 discussion

Oncology

3.1.11. Ivosidenib - Orphan - EMEA-002247-PIP03-17

Agios Pharmaceuticals, Inc.; Treatment of Acute Myeloid Leukaemia / Treatment of paediatric patients from 2 to less than 18 years of age with newly diagnosed and relapsed or refractory (R/R) AML with an isocitrate dehydrogenase-1 (IDH1) mutation.

Day 90 discussion

Oncology

3.1.12. Sulindac / Eflornithine - Orphan - EMEA-001518-PIP02-16

Cancer Prevention Pharma Ltd.; Treatment of Familial Adenomatous Polyposis

Day 90 discussion

Oncology

3.1.13. Sodium thiosulfate - EMEA-002147-PIP02-17

Prevention of platinum-induced ototoxic hearing loss / Prevention of ototoxicity in patients > 1 month and <18 years of age receiving platinum-based chemotherapy for localised tumours

Day 90 discussion

Oncology / Oto-rhino-laryngology

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

Treatment of cartilage disorders

Day 90 discussion

Other

3.1.15. Palovarotene - EMEA-001662-PIP03-17

Treatment of Multiple Osteochondromas (MO)

Day 90 discussion

Other

3.1.16. Recombinant human acid ceramidase - Orphan - EMEA-002266-PIP01-17

Enzyvant Farber Ireland Ltd; Farber disease

Day 90 discussion

Other

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

Faron Pharmaceuticals Ltd; Treatment of Acute Respiratory Distress Syndrome

Day 90 discussion

Pneumology - Allergology

3.1.18. Ad26.RSV.preF - EMEA-002172-PIP02-17

Prevention of lower respiratory tract disease caused by respiratory syncytial virus (RSV)

Day 90 discussion

Vaccines / Infectious Diseases

3.1.19. EMEA-002329-PIP01-18

Treatment of chronic hand eczema

Day 60 discussion

Dermatology

3.1.20. Givosiran sodium - Orphan - EMEA-002048-PIP02-18

Alnylam UK Limited; Treatment of Acute Hepatic Porphyria (AHP)

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.21. DNA (synthetic adeno-associated virus vector AAV-Spark100-hFIX39-Padua) - EMEA-002362-PIP01-18

Prophylaxis of haemophilia B (hereditary factor IX deficiency)

Day 60 discussion

Haematology-Hemostaseology

3.1.22. Voxelotor - Orphan - EMEA-002356-PIP01-18

SynteractHCR Deutschland GmbH; Treatment of sickle cell disease

Day 60 discussion

Haematology-Hemostaseology

3.1.23. Ustekinumab - EMEA-000311-PIP06-18

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

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.24. Nacubactam - EMEA-002339-PIP01-18

Treatment of Gram-negative bacterial infections / Nacubactam co-administered with meropenem is indicated for the treatment of serious infections including cUTI, HAP, VAP, and BSI caused by Gram-negative bacteria in patients with limited treatment options

Day 60 discussion

Infectious Diseases

3.1.25. Abemaciclib - EMEA-002342-PIP01-18

Ewing's Sarcoma

Day 60 discussion

Oncology

3.1.26. Allogeneic, genetically modified T cells with inactivated T cell alpha beta receptor and CD52 protein, and expressing a CD19-specific chimeric antigen receptor and the synthetic RQR8 protein - EMEA-002348-PIP01-18

B-cell Acute Lymphoblastic Leukemia / Treatment of relapse or refractory B-cell acute

lymphoblastic leukemia

Day 60 discussion

Oncology

3.1.27. Iodine (131-I) murine IgG1 monoclonal antibody against B7-H3 - Orphan - EMEA-002101-PIP02-18

Y-mAbs Therapeutics A/S; Treatment of pediatric neuroblastoma patients with CNS relapse as evidenced by CNS/LM metastases

Day 60 discussion

Oncology

3.1.28. Pegvorhyaluronidase alfa - Orphan - EMEA-001883-PIP03-17

Halozyme Inc; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms) / Pegvorhyaluronidase alfa is indicated in combination with cytotoxic cancer therapies for the treatment of paediatric patients aged 6 months to less than 18 years with relapsed or refractory solid tumours that accumulate high levels of hyaluronan

Day 60 discussion

Oncology

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

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

Day 60 discussion

Pneumology - Allergology

3.1.30. Rapastinel - EMEA-002357-PIP01-18

Major depressive disorder

Day 60 discussion

Psychiatry

3.1.31. Split influenza virus, inactivated containing antigens equivalent to the B-like strain (Yamagata lineage) / Split influenza virus, inactivated containing antigens equivalent to the B-like strain (Victoria lineage) / Split influenza virus, inactivated containing antigens equivalent to the A/H3N2-like strain / Split influenza virus, inactivated containing antigens equivalent to the A/H1N1-like strain - EMEA-002359-PIP01-18

Prevention of influenza infection

Day 60 discussion

Vaccines

3.1.32. Indapamide hemihydrate / perindopril tert-butylamine / rosuvastatin calcium / acetylsalicylic acid - EMEA-002366-PIP01-18

Treatment of cardiovascular disease / For the secondary prevention of cardiovascular accidents as substitution therapy in patients adequately controlled with the mono-components given concomitantly at equivalent therapeutic doses.

Day 30 discussion

Cardiovascular Diseases

3.1.33. Rosuvastatin Calcium / Omega-3-acid ethyl esters 90 - EMEA-002384-PIP01-18

ICD10:E78.2

Day 30 discussion

Cardiovascular Diseases

3.1.34. EMEA-002350-PIP01-18

Treatment of psoriasis / Treatment of moderate to severe plaque psoriasis in paediatric patients 6 years of age and older

Day 30 discussion

Dermatology

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

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

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.36. Asciminib - EMEA-002347-PIP01-18

Treatment of Philadelphia positive Chronic Myelogenous Leukemia in chronic phase

Day 30 discussion

Haematology-Hemostaseology

3.1.37. Concizumab - Orphan - EMEA-002326-PIP03-18

Novo Nordisk A/S; Treatment of congenital haemophilia B, Treatment of congenital haemophilia A

Day 30 discussion

Haematology-Hemostaseology

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

Treatment of Systemic Lupus Erythematosus (SLE)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.39. Fenebrutinib - EMEA-002349-PIP01-18

Chronic idiopathic arthritis (including RA, axial spondyloarthritis, PsA, and JIA) / Treatment of active JIA (i.e., seropositive [RF positive] polyarthritis, seronegative [RF negative] polyarthritis, enthesitis related arthritis, psoriatic arthritis, persistent sJIA without systemic features, oligoarthritis [persistent and extended], and undifferentiated arthritis) in patients 2 years of age to less than 18 years of age

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.40. Guselkumab - EMEA-001523-PIP03-18

Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, spondyloarthritis, PsA and juvenile idiopathic arthritis [JIA])

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.41. Rilpivirine (as free base) - EMEA-000317-PIP02-18

Treatment of human immunodeficiency virus (HIV-1) infection / In combination with cabotegravir long acting, treatment of HIV-1 infection in pediatric patients from 6 to less than 18 years of age who are virologically suppressed (HIV-1 RNA <50 copies/mL) and

no known or suspected resistance to either rilpivirine or cabotegravir

Day 30 discussion

Infectious Diseases

3.1.42. Suvratoxumab (anti-Staphylococcus aureus alpha toxin monoclonal antibody) - EMEA-002337-PIP01-18

Prevention of nosocomial pneumonia caused by Staphylococcus aureus

Day 30 discussion

Infectious Diseases

3.1.43. Arimoclomol citrate - Orphan - EMEA-001748-PIP02-18

Orphazyme A/S; Treatment of amyotrohic lateral sclerosis, Treatment of sporadic inclusion body myositis

Day 30 discussion

Neurology

3.1.44. Avapritinib - Orphan - EMEA-002358-PIP02-18

Blueprint Medicines Corporation; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms) / Treatment of paediatric patients with advanced solid tumors harboring mutations in either KIT or PDGFRα

Day 30 discussion

Oncology

3.1.45. Elotuzumab - EMEA-002377-PIP01-18

Treatment of multiple myeloma

Day 30 discussion

Oncology

3.1.46. Nadofaragene firadenovec - EMEA-002376-PIP01-18

Mesothelioma

Day 30 discussion

Oncology

3.1.47. Spartalizumab - EMEA-002351-PIP01-18

Treatment of melanoma / Treatment of adolescent patients with melanoma containing BRAF V600 activating mutations

Day 30 discussion

Oncology

3.1.48. Tepotinib - EMEA-002345-PIP01-18

Treatment of lung malignant neoplasms / Adults

Day 30 discussion

Oncology

3.1.49. Dexamethasone / Levofloxacin - EMEA-002375-PIP01-18

Prevention and treatment of inflammation and prevention of infection associated with cataract surgery

Day 30 discussion

Ophthalmology

3.1.50. Odiparcil - Orphan - EMEA-002256-PIP01-17

Inventiva SA; Treatment of mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome)

Day 30 discussion

Other

3.1.51. (R)-azasetron (as besylate) - Orphan - EMEA-002165-PIP02-18

Sensorion SA; Ototoxicity, poisoning due to cisplatin, Sudden Sensorineural Hearing Loss / Treatment of Sudden Sensorineural Hearing Loss, Prevention of cisplatin-induced ototoxicity

Day 30 discussion

Oto-rhino-laryngology

3.1.52. Fasinumab - EMEA-002059-PIP01-16

Chronic pain

Day 30 discussion

Pain

3.1.53. EMEA-002324-PIP01-17

Treatment of Cystic Fibrosis

Day 30 discussion

Pneumology - Allergology

3.1.54. EMEA-002191-PIP02-17

Treatment of Cystic Fibrosis

Day 30 discussion

Pneumology - Allergology

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

Prevention of Ebola Virus Disease / Prevention of EVD in children aged ≥1 year

Day 30 discussion

Vaccines / Infectious Diseases

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

Prevention of Ebola Virus Disease / Prevention of EVD in children aged ≥1 year

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. Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human betaA-T87Q-globin gene - EMEA-C1-001665-PIP01-14-M02

bluebird bio (Germany) GmbH; Treatment of β-thalassaemia

Day 30 discussion

Haematology-Hemostaseology

3.2.2. Upadacitinib - EMEA-C1-001741-PIP01-14-M01

AbbVie Ltd; Treatment of Chronic Idiopathic Arthritis (including rheumathoid arthritis, psoriatic arthritis, spondyloarthritis and juvenile idiopathic arthritis)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.2.3. Fenfluramine hydrochloride - EMEA-C2-001990-PIP01-16

Zogenix International Ltd; Treatment of Dravet syndrome

Day 30 discussion

Neurology

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. 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-M02

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 30 discussion

Diagnostic

3.3.2. Dapagliflozin - EMEA-000694-PIP01-09-M07

AstraZeneca AB; Treatment of Type 2 Diabetes

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.3. Ertugliflozin L-PGA - EMEA-001533-PIP01-13-M01

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

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.4. Exenatide - EMEA-000689-PIP01-09-M08

AstraZeneca AB; Non-insulin dependent diabetes mellitus (treatment including thiazolidinediones), Non-insulin dependent diabetes mellitus (excluding treatment with thiazolidinediones), Non-insulin dependent diabetes mellitus - in combination with insulin (with or without oral antidiabetics) / Treatment of type 2 Diabetes Mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.5. Recombinant Human alpha-galactosidase A - Orphan - EMEA-001828-PIP01-15-M01

Protalix Ltd; Treatment of Fabry disease

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.6. Polyethylene Glycol 3350 / Potassium Chloride / Sodium Chloride / Ascorbic Acid / Sodium Ascorbate / Sodium Sulfate - EMEA-001705-PIP02-15-M01

Norgine Limited; Bowel cleansing prior to clinical procedures

Day 30 discussion

Gastroenterology-Hepatology

3.3.7. Tofacitinib - EMEA-000576-PIP03-12-M01

Pfizer Limited; Ulcerative colitis / Treatment of children and adolescents aged 2 to <18 years of age with moderate to severe ulcerative colitis, who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent.

Day 30 discussion

Gastroenterology-Hepatology

3.3.8. Caplacizumab (anti-von Willebrand Factor Nanobody) - Orphan - EMEA-001157-PIP01-11-M02

Ablynx NV; Treatment of acquired thrombotic thrombocytopenic purpura

Day 30 discussion

Haematology-Hemostaseology

3.3.9. Eftrenonacog alfa - Orphan - EMEA-000914-PIP01-10-M04

Swedish Orphan Biovitrum AB (publ); Hereditary Factor IX Deficiency - D67

Day 30 discussion

Haematology-Hemostaseology

3.3.10. Human fibrinogen concentrate - EMEA-001931-PIP01-16-M01

Biotest AG; Treatment of congenital fibrinogen deficiency

Day 30 discussion

Haematology-Hemostaseology

3.3.11. Belimumab - EMEA-000520-PIP02-13-M02

Glaxo Group Limited; Treatment of systemic lupus erythematosus

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.12. Emapalumab - Orphan - EMEA-002031-PIP01-16-M02

Novimmune B.V; Treatment of Haemophagocytic Lymphohistiocytosis

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.13. Ustekinumab - EMEA-000311-PIP03-11-M04

Janssen-Cilag International NV; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, spondyloarthritis, PsA and juvenile idiopathic arthritis [JIA]) / Treatment of juvenile idiopathic arthritis (juvenile psoriatic arthritis [jPsA]

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.14. Isavuconazonium (sulfate) - Orphan - EMEA-001301-PIP02-12-M02

Basilea Pharmaceutica International Ltd.; Treatment of mucormycosis, Treatment of invasive aspergillosis

Day 30 discussion

Infectious Diseases

3.3.15. Rilpivirine (as hydrochloride) - EMEA-000317-PIP01-08-M10

Janssen-Cilag International NV; Treatment of human immunodeficiency virus (HIV-1) infection / Rilpivirine is indicated in combination with other antiretroviral (ARV) medicinal products, for the treatment of human immunodeficiency virus (HIV-1) infection in ARV-naïve paediatric patients from 2 to less than 18 years with a baseline viral load below 100,000 HIV-1 RNA copies/mL

Day 30 discussion

Infectious Diseases

3.3.16. Simeprevir - EMEA-000625-PIP01-09-M03

Janssen-Cilag International NV; Treatment of Chronic Viral Hepatitis C (HCV) / Treatment of chronic hepatitis C genotype 1 and genotype 4 infection in paediatric patients aged 3 to less than 18 years

Day 30 discussion

Infectious Diseases

3.3.17. Tenofovir alafenamide / emtricitabine / cobicistat / darunavir - EMEA-001825-PIP01-15-M02

Janssen-Cilag International NV; Treatment of human immunodeficiency virus type-1 (HIV-1) infection / Treatment of HIV-1 infection in paediatric subjects weighing 25 kg or more above 6 years of age

Day 30 discussion

Infectious Diseases

3.3.18. Tenofovir Alafenamide / Emtricitabine / Cobicistat / Elvitegravir - EMEA-001460-PIP01-13-M03

Gilead Sciences International Ltd.; Treatment of human immunodeficiency virus (HIV-1) infection / Genvoya is indicated for the treatment of HIV-1 infection in paediatric patients from 6 years to less than 18 years.

Day 30 discussion

Infectious Diseases

3.3.19. Tenofovir disoproxil / rilpivirine / emtricitabine - EMEA-000774-PIP01-09-M03

Gilead Sciences International Ltd.; Treatment of human immunodeficiency virus (HIV-1) infection

Day 30 discussion

Infectious Diseases

3.3.20. Autologous haematopoeitic stem cells transduced with lentiviral vector Lenti-D encoding the human ATP-binding cassette, sub-family D (ALD), member 1 (ABCD1) from cDNA - Orphan - EMEA-001244-PIP01-11-M02

bluebird bio France; Adrenoleukodystrophy

Day 30 discussion

Neurology

3.3.21. Perampanel - EMEA-000467-PIP01-08-M10

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

Day 30 discussion

Neurology

3.3.22. Retigabine - EMEA-000116-PIP01-07-M09

Glaxo Group Limited; Treatment of Lennox-Gastaut Syndrome, Treatment of epilepsy with partial onset seizures

Day 30 discussion

Neurology

3.3.23. Ponatinib (as hydrochloride) - Orphan - EMEA-001186-PIP01-11-M02

Incyte Biosciences UK Ltd.; Chronic myeloid leukaemia, Philadelphia chromosome positive acute lymphoblastic leukaemia / Treatment of the paediatric population with Ph+ ALL who are resistant or intolerant to prior TKI therapy, or who have the T315I mutation., Treatment of the paediatric population with chronic (CP), accelerated (AP), or blast phase (BP) CML who are resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy, or who have the T315I mutation

Day 30 discussion

Oncology

3.3.24. Quizartinib - Orphan - EMEA-001821-PIP01-15-M02

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

Day 30 discussion

Oncology

3.3.25. Eliglustat - Orphan - EMEA-000461-PIP02-11-M03

Genzyme Europe B.V.; Treatment of Gaucher Disease Type 1, Treatment of Gaucher Disease Type 3

Day 30 discussion

Other

3.3.26. Vamorolone - Orphan - EMEA-001794-PIP02-16-M01

ReveraGen BioPharma Ltd; Treatment of Duchenne muscular dystrophy

Day 30 discussion

Other

3.3.27. Dupilumab - EMEA-001501-PIP02-13-M03

sanofi-aventis recherche & développement; Asthma

Day 30 discussion

Pneumology - Allergology

3.3.28. Mepolizumab - Orphan - EMEA-000069-PIP04-13-M02

GSK Trading Services Limited; Vasculitides / Treatment of paediatric patients aged 6 to 17 years with eosinophilic granulomatosis with polyangiitis (EGPA) using corticosteroid therapy with or without concomitant immunosuppressant therapy.

Day 30 discussion

Pneumology - Allergology

3.3.29. Mometasone (furoate) / Indacaterol (acetate) - EMEA-001217-PIP01-11-M05

Novartis Europharm Limited; Treatment of asthma

Day 30 discussion

Pneumology - Allergology

3.3.30. Brexpiprazole - EMEA-001185-PIP01-11-M05

Otsuka Europe Development and Commercialisation Limited, Zweigniederlassung, Frankfurt am Main; Treatment of schizophrenia in adolescents 13 to 17 years of age

Day 30 discussion

Psychiatry

3.3.31. Cariprazine hydrochloride - EMEA-001652-PIP01-14-M02

Gedeon Richter Plc.; F20 Schizophrenia

Day 30 discussion

Psychiatry

3.3.32. Loxapine - EMEA-001115-PIP01-10-M06

Ferrer Internacional, S.A.; For rapid control of agitation in patients with schizophrenia, For rapid control of agitation in patients with bipolar disorder

Day 30 discussion

Psychiatry

3.3.33. Lanthanum carbonate hydrate - EMEA-000637-PIP02-10-M06

Shire Pharmaceutical Contracts Ltd; Hyperphosphataemia

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 21 August 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

No items

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. Dupilumab – EMEA-06-2018

Sanofi-aventis Recherche & Développement; All classes of medicinal products for treatment of chronic obstructive pulmonary disease (COPD) (excluding chronic lung diseases associated with long-term airflow limitation, such as asthma, bronchopulmonary dysplasia, primary cilia dyskinesia, obstructive lung disease related to graft-versus-host disease after [bone-marrow] transplantation)/Add-on maintenance treatment to reduce the risk of COPD exacerbations and improve lung function in patients with moderate-to-very severe COPD

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. Vonicog alfa - Orphan - EMEA-001164-PIP01-11-M01

Baxalta Innovations GmbH; Von Willebrand Disease / Treatment and control of haemorrhage (spontaneous and surgical) and prevention of bleeding in surgery in paediatric patients (age of < 18 years) diagnosed with VWD when desmopressin (DDAVP) treatment alone is ineffective or not indicated

Proposed indication: Prophylaxis and treatment of bleeding in paediatric patients diagnosed with von Willebrand disease when desmopressin (DDAVP) treatment alone is ineffective or contraindicated

Day 30 letter

Haematology-Hemostaseology

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 May 2018 was presented to the PDCO members.

The members were also informed about 2 medicinal products, Myalepta and Briviact for which the CHMP adopted a positive opinion recommending a paediatric indication during their meeting in May 2018.

9.2.2. Guideline on the development of new medicinal products for the treatment of Ulcerative Colitis

PDCO member: Peter Szitanyi

Summary of committee discussion:

The guideline was presented and adopted by the PDCO.

9.2.3. Guideline on the development of new medicinal products for the treatment of Crohn's Disease

PDCO member: Peter Szitanyi

Summary of committee discussion:

The guideline was presented and adopted by the PDCO.

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. Extrapolation Reflection Paper – status update

PDCO member: Dirk Mentzer

Summary of committee discussion:

PDCO endorsed the final version of the extrapolation reflection paper.

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:

The PDCO was informed about the discussions and agreed action points of this year's Enpr-EMA meeting with all stakeholders.

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

None

10. Any other business

10.1.1. Training on paediatric requirements/legislations/initiatives in other regions – US and Japan

Summary of committee discussion:

The PDCO was informed about paediatric research initiatives in Japan.

10.1.2. PDCO with Rome Foundation - Irritable Bowel Syndrome and Functional Constipation in children - collaborative papers

PDCO member: Johannes Taminiau

Summary of committee discussion:

The different criteria proposed by the Rome Foundation to conduct clinical trials in juvenile IBS C and D were presented (including inclusion criteria, clinical endpoints, trial design) [Saps M, Tilburg M, Lavigne J, Miranda A, Benninga M, Taminiau J, et al. Recommendations for pharmacological clinical trials in children with irritable bowel syndrome: the Rome foundation pediatric subcommittee on clinical trials. Neurogastroenterol Motil.2016; 28:1619 - 1631].

The main statistical arguments published in a letter written in response to this article were presented [Collignon, O., and F. Pétavy. "Statistical considerations about the design and endpoints of randomized clinical trials for children with irritable bowel syndrome." Neurogastroenterology & Motility 30.5 (2018): e13266].

10.1.3. EC/EMA action plan to further improve the implementation of the Paediatric Regulation

Scope: Outcomes and action plan

Summary of committee discussion:

The Committee discussed initiatives and actions to be included in the draft action plan.

10.1.4. Joint CHMP & PDCO Strategic Review & Learning Meeting Vienna 26-28 September 2018

PDCO member: Karl-Heinz Huemer

Summary of committee discussion:

The PDCO Committee was updated on the preliminary program and PDCO topics.

10.1.5. EMA Workshop on development of antibacterial medicinal products for paediatric patients 20-21 June 2018

PDCO member: Irja Lutsar

Summary of committee discussion:

The Paediatric Committee was updated on the preliminary program and PDCO topics.

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

The group discussed the approach to the relapsed/refractory and first-line setting for novel products in oncology PIPs.

11.1.2. Neonatology

Summary of committee discussion:

The neonatology group discussed an ongoing PIP application with relevance to the

neonatal population.

11.1.3. Inventory

Summary of committee discussion:

The inventory group was convened in the margins of the plenary meeting to continue discussion on the methodology for the assessment of unmet needs.

The Chair thanked all participants and closed the meeting.

12. List of participants

List of participants including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 26-29 June 2018 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-001426-PIP01-13-M02 EMEA-001765-PIP02-15-M02
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	
Jaroslav Sterba	Member	Czech Republic	No interests declared	
Peter Szitanyi	Alternate	Czech Republic	No interests declared	
Kirstine Moll Harboe	Member	Denmark	No interests declared	
Mona Ring Gatke	Alternate	Denmark	No interests declared	
Ann Marie Kaukonen	Member	Finland	No interests declared	
Sylvie Benchetrit	Member	France	No interests declared	
Dominique Ploin	Alternate	France	No interests declared	
Sabine Scherer	Member	Germany	No interests declared	
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	
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	
Goda Vaitkeviciene	Alternate	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	
Anette Solli Karlsen	Alternate	Norway	No interests declared	
Marek Migdal	Member	Poland	No interests declared	
Helena Fonseca	Member	Portugal	No interests declared	
Hugo Tavares	Alternate	Portugal	No interests declared	
Dana Gabriela Marin	Member (CHMP alternate)	Romania	No interests declared	
Peter Sisovsky	Member	Slovakia	No interests declared	
Stefan Grosek	Member	Slovenia	No interests declared	
Fernando de Andrés Trelles	Member	Spain	No interests declared	
Maria Jesús Fernández Cortizo	Alternate	Spain	No interests declared	
Ninna Gullberg	Member	Sweden	No interests declared	
Eva Agurell	Alternate	Sweden	No interests declared	
Angeliki Siapkara	Member	United Kingdom	No interests declared	
Martina Riegl	Alternate	United Kingdom	No interests declared	
Fernando Cabanas	Member	Healthcare Professionals' Representative	No interests declared	
Riccardo Riccardi	Alternate	Healthcare Professionals' Representative	No participation in final deliberations and voting on:	EMEA-001308-PIP01-12-M02 EMEA-001425-PIP01-13-M03
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Michal Odermarsky	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Viviana Giannuzzi	Alternate	Patients' Organisation Representative	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jan Mueller-Berghaus	Expert - in person*	Germany	No interests declared	
Hans Lodewijk Hillege	Expert - in person*	Netherlands	No interests declared	
Fahimeda Ali	Expert - in person*	United Kindgom	No interests declared	
Johannes Hendrikus Ovelgonne	Expert - via TC	Netherlands	No interests declared	
Juliana Min	Expert - in person*	United Kingdom	No interests declared	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

* Experts were only evaluated against the agenda topics or activities they participated in

13. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

Paediatric investigation plan (PIP) (section 2.1 Opinion on PIPs and section 3.1 Discussions on PIPs)
A paediatric investigation plan (PIP) is a development plan aimed at ensuring that the necessary data are obtained through studies in children, when it is safe to do so, to support the authorisation of a medicine for children. Pharmaceutical companies submit proposals for PIPs to the European Medicines Agency's Paediatric Committee (PDCO). This Committee is responsible for agreeing or refusing the plan.

Compliance checks (section 2.2 Opinions on Compliance check, section 3.2 Discussions on Compliance check)
A compliance check may be necessary before any application for marketing authorisation (even for an adult indication) can be considered valid, if there was no deferral for at least one of the studies agreed in the PIP, or after the due date of initiation or completion of a study/measure. The same applies to some regulatory applications for authorised products, as described above.

Modification of an Agreed Paediatric Investigation Plan (section 2.3 Opinions on Modification of an agreed PIP, section 3.3 Discussions on Modification of an agreed PIP)
The development plan for a medicine can be modified at a later stage as knowledge increases. Modifications can also be made if the applicant encounters such difficulties with the implementation of a PIP, which render it unworkable or no longer appropriate.
In some cases, studies can be deferred until after the studies in adults have been conducted. This ensures that research in children is done only when it is safe and ethical to do so. Even when studies are deferred, the PIP will include details of the paediatric studies and their timelines.

Class waiver (section 6 Discussion on the applicability of class waiver)
As some diseases do not affect children (for example Parkinson's disease), the development of medicines for these diseases should not be performed in children. In these cases, a PIP is not required and it will be waived**.** For more information on the classes of diseases subject to waivers, see class waivers.

Annual reports on deferrals (section 8)
If the medicinal product is approved in the EU, annual reports on the deferred measures in the PIP must be submitted to the Agency.

More detailed information on the above terms can be found on the EMA website:
www.ema.europa.eu/