1 June 2018
EMA/PDCO/372867/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes of the meeting on 29 May-01 June 2018

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

29 May 2018, 14:00- 19:00, room 03-A

30 May 2018, 08:30- 19:00, room 03-A

31 May 2018, 08:30- 19:00, room 03-A

01 June 2018, 08:30 - 13:00, room 03-A

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 and will be published on the EMA website.

1.3. Adoption of the minutes

The minutes of the April 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. Bimekizumab - EMEA-002189-PIP01-17

UCB Biopharma SPRL; Treatment of moderate to severe chronic plaque psoriasis in children from the age of 6 years and older

Day 120 opinion

Dermatology

Summary of committee discussion:

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

2.1.2. Dasiglucagon - Orphan - EMEA-002233-PIP01-17

Zealand Pharma A/S; Treatment of hypoglycaemia

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

During its plenary on 01 June 2018, the PDCO discussed the applicant's responses to the outstanding issues from the day 90 PDCO discussion, in April 2018, for dasiglucagon for the acute treatment of severe hypoglycaemia.
The PDCO deemed the applicant's responses acceptable and therefore adopted a positive Opinion for PIP 2233.

2.1.3. Ustekinumab - EMEA-000311-PIP05-17

Janssen-Cilag International NV; Treatment of Ulcerative Colitis

Day 120 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The applicant's responses to the D90 issues were considered acceptable. A positive opinion was adopted.

2.1.4. Itacitinib - Orphan - EMEA-002178-PIP01-17

Incyte Biosciences UK Ltd.; Treatment of steroid naïve paediatric population with acute graft versus host disease after allogeneic hematopoietic stem cell transplantation

Day 120 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

Based on the assessment of this application, the PDCO agreed at their May 2018 meeting a PIP for itacitinib in treatment of acute graft versus host disease with a waiver and a deferral.

2.1.5. Recombinant IgG degrading enzyme of Streptococcus pyogenes (IdeS) - Orphan - EMEA-002183-PIP01-17

Hansa Medical AB; Patients with chronic kidney disease in need of kidney transplantation / Prevention of graft rejection following solid organ transplantation

Day 120 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The applicant had provided the requested clarifications and satisfactorily addressed the PDCO's concerns. A PIP was agreed for IdeS (a recombinant IgG degrading enzyme of Streptococcus pyogenes) for the "prevention of graft rejection following solid organ transplantation".

2.1.6. solriamfetol - EMEA-002184-PIP01-17

Jazz Pharmaceuticals UK Ltd; Treatment of obstructive sleep apnoea, Treatment of narcolepsy, Treatment of excessive daytime sleepiness in narcolepsy patients

Day 120 opinion

Neurology

Summary of committee discussion:

The PDCO re-discussed the application including the latest information received since Day 90.
The waiver request for OSA was found adequately justified and approvable. Taking the above points into account the PDCO adopted a positive opinion endorsing this PIP.

2.1.7. Palbociclib - EMEA-002146-PIP01-17

Pfizer Limited; treatment of refractory or recurrent Ewing sarcoma

Day 120 opinion

Oncology

Summary of committee discussion:

An Oral Explanation Meeting (OEM) was held with the applicant on Thursday 31 May 2018.
In conclusion, the PDCO recommended granting a paediatric investigation plan in the condition treatment of Ewing sarcoma.

2.1.8. Purified inactivated rabies virus - EMEA-002234-PIP01-17

Sanofi Pasteur S.A.; Prevention of rabies disease, treatment of exposure to rabies virus

Day 120 opinion

Vaccines

Summary of committee discussion:

Based on the assessment of this application, the PDCO adopted a positive opinion on the paediatric plan proposed by the applicant. The paediatric development is entirely non-deferred, includes all age groups from birth to less than 18 years of age.

2.1.9. Dapagliflozin - EMEA-000694-PIP03-17

AstraZeneca AB; I50 Heart Failure

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for dapagliflozin for all subsets of the paediatric population (0 to 18 years of age) in the condition of Prevention of cardiovascular events in patients with chronic heart failure.
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.

2.1.10. Moxonidine - EMEA-002275-PIP01-17

Abbott Laboratories; Treatment of Hypertension

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The PDCO view expressed at Day 30 was re-discussed and endorsed.
The Committee adopted a negative opinion.

2.1.11. Trandolapril - EMEA-002274-PIP01-17

Abbott Laboratories; Mild or moderate hypertension

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The PDCO view expressed at Day 30 was re-discussed and endorsed.
The Committee adopted a negative opinion.

2.1.12. Patidegib - EMEA-002322-PIP01-17

Blue-Reg Europe on behalf of Pellepharm, Inc; Treatment of basal cell carcinoma (BCC)

Day 60 opinion

Dermatology / Oncology

Summary of committee discussion:

The PDCO discussed this procedure during the May 2018 plenary meeting.
The PDCO confirmed that the appropriate condition for this product is 'treatment of naevoid basal-cell carcinoma syndrome (Gorlin syndrome)'.
The PDCO also considered the clarifications provided by the applicant after the D30 discussion and found them agreeable. The PDCO therefore adopted a favourable Opinion on the request for a product specific waiver for patidegib gel on the grounds that the specific medicinal product is likely to be unsafe in younger children (from birth to closure of the epiphysis) and on the grounds that the specific medicinal product does not represent a significant therapeutic benefit for children with closed epiphysis because clinical studies are not feasible.
The PDCO recommends granting a waiver for patidegib for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of naevoid basal-cell carcinoma syndrome (Gorlin syndrome).
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. Bilastine - EMEA-000347-PIP03-18

FAES FARMA S.A.; Treatment of allergic rhinoconjunctivitis, Treatment of urticaria

Day 60 opinion

Dermatology / Pneumology - Allergology / Oto-rhino-laryngology

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for bilastine for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of allergic rhinoconjunctivitis, Treatment of urticaria.
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.

2.1.14. Abatacept - EMEA-000118-PIP04-17

Bristol-Myers Squibb Pharma EEIG; Treatment of childhood-onset of Sjögren's Syndrome

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed.
Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for abatacept for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of Sjögren's Syndrome.

2.1.15. Liposomal ciclosporin A (L-CsA) - Orphan - EMEA-002344-PIP01-18

Breath Therapeutics GmbH; Treatment of Bronchiolitis obliterans Syndrome (BOS)

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO re-discussed and endorsed its views expressed on day 30. The PDCO has adopted a negative opinion on the proposed full waiver for the treatment of bronchiolitis obliterans syndrome that was claimed by the applicant on the grounds that the disease would not occur in paediatric patients. The PDCO has agreed that the development of the product should be focused on adolescent patients.

2.1.16. Upadacitinib - EMEA-001741-PIP05-17

AbbVie Ltd; Treatment of vasculitides

Day 60 opinion

Immunology-Rheumatology-Transplantation

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 upadacitinib for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of vasculitides.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

2.1.17. Fostamatinib - EMEA-001196-PIP02-17

Rigel Pharmaceuticals Ltd; Treatment of immune thrombocytopenia (idiopathic thrombocytopenic purpura)

Day 60 opinion

Other

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric

Committee the PDCO agreed at their May 2018 meeting with the applicant's request for a waiver. The PDCO recommends granting a waiver for fostamatinib for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of immune thrombocytopenia (idiopathic thrombocytopenic purpura) based on possible lack of safety.

2.1.18. Nitrous oxide - EMEA-002340-PIP01-18

Società Italiana Carburo Ossigeno Spa SICO; In analgesia / sedation in all conditions in which pain relief / sedation with rapid onset and rapid fall in effect is required (short-term surgical interventions, traumatology, burns, dentistry, otorhinolaryngology, childbirth), Under anesthesia, in combination with other anesthetics administered by inhalation or intravenously

Day 60 opinion

Pain / Anaesthesiology

Summary of committee discussion:

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

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. Everolimus - EMEA-C-000019-PIP08-12-M03

Novartis Europharm Limited; Treatment of Tuberous Sclerosis Complex

Day 30 opinion

Neurology

Summary of committee discussion:

The PDCO adopted on 01 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/0316/2017) of 31 October 2017.

2.2.2. Testosterone - EMEA-C2-001529-PIP02-14-M01

Acerus Biopharma Inc.; Treatment of male hypogonadism

Day 30 letter

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO discussed the initiated study and considered that it has been initiated in compliance with the latest Agency's Decision (P/0132/2018) of 16 April 2018.
The PDCO finalised on 1 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 initiated until this date.

2.2.3. Osilodrostat - EMEA-C1-000315-PIP02-15-M01

Novartis Europharm Limited; Treatment of adrenal cortical hyperfunctions

Day 30 letter

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0064/2018) of 17 March 2017.
The PDCO finalised on 1 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.

2.2.4. Autologous CD4+ and CD8+ cells expressing a CD19-specific chimeric antigen receptor - EMEA-C1-001995-PIP01-16-M01

Celgene Europe Limited; Treatment of B-lymphoblastic leukemia/lymphoma

Day 30 letter

Oncology

Summary of committee discussion:

The PDCO discussed the completed clinical study and considered that it is compliant with the latest Agency's Decision (P/0119/2018) of 11 April 2018.
The PDCO finalised on 1 June 2018 this partially completed compliance procedure and confirmed the compliance of the completed clinical study contained in the agreed paediatric investigation plan.

2.2.5. Quizartinib - EMEA-C1-001821-PIP01-15-M01

Daiichi Sankyo Europe GmbH; Treatment of acute myeloid leukaemia

Day 30 letter

Oncology

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/0102/2018.

2.2.6. Birch pollen extract (Betula verrucosa) - EMEA-C1-001879-PIP01-15-M01

ALK Abelló A/S; Treatment of allergic rhinitis / rhino-conjunctivitis

Day 30 letter

Pneumology - Allergology

Summary of committee discussion:

The completed study was checked for compliance. The PDCO discussed the completed study and considered that it is compliant with the latest Agency's Decision P/0030/2018 of 30 January 2018.
The PDCO finalised on 01 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.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Bempedoic acid - EMEA-001872-PIP01-15-M01

Esperion Therapeutics, Inc.; Treatment of elevated cholesterol / Treatment of heterozygous and homozygous familial hypercholesterolemia

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan and in line with the day 30 conclusions, 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/0094/2017) for Bempedoic acid for the treatment of elevated cholesterol during its plenary on 01 June 2018.

2.3.2. Regadenoson - EMEA-000410-PIP01-08-M03

GE Healthcare AS; Diagnostic evaluation of myocardial perfusion disturbances

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The Committee reviewed and re-discussed this modification request including the additional information received since Day 30 and concluded that the proposed changes are not acceptable.

The applicant is encouraged to revise their plans taking these conclusions into account and resubmit a new modification proposal, if necessary, with all proposed changes duly justified in one package.
The PDCO therefore adopted a negative opinion on the modification of the agreed PIP.
The key elements remain unchanged.

2.3.3. Ticagrelor - EMEA-000480-PIP01-08-M11

AstraZeneca AB; thromboembolic events (children), acute coronary syndrome, history of myocardial infarction / reduction in occurrence of vaso-occlusive crises in paediatric patients with sickle cell disease

Day 60 opinion

Cardiovascular Diseases / Haematology-Hemostaseology

Summary of committee discussion:

The PDCO re-discussed this procedure during the May 2018 plenary meeting.
The PDCO considered the clarifications provided by the applicant after the D30 discussion and found them 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/0170/2017 of 3 July 2017.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.4. Brodalumab - EMEA-001089-PIP02-13-M01

LEO Pharma A/S; Treatment of psoriasis

Day 60 opinion

Dermatology

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, and the responses received to the points raised by the PDCO at D30 the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0235/2014 of 8/9/2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.5. Ligelizumab - EMEA-001811-PIP02-15-M02

Novartis Europharm Ltd.; Treatment of chronic spontaneous urticaria

Day 60 opinion

Dermatology

Summary of committee discussion:

The applicant's responses to Day 30 questions were deemed acceptable. The remaining issues between Day 30 and Day 60 were addressed satisfactorily.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0329/2017 of 30 October 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.6. 2-hydroxypropyl-ß-cyclodextrin (HP-ß-CD) - Orphan - EMEA-001866-PIP01-15-M02

Mallinckrodt Pharmaceuticals Ireland Ltd; Treatment of progressive neurological manifestations in children and adolescent patients with Niemann-Pick disease, type C

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan and the additional responses to the day 30 outstanding issues, the PDCO considered that the proposed changes could be accepted.
The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0030/2017 of 31/01/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.7. Empagliflozin - EMEA-000828-PIP01-09-M07

Boehringer Ingelheim International GmbH; Treatment of type 2 diabetes mellitus

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO confirmed the outcome of the Day 30 discussion and agreed with the requested modifications.
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/0028/2018 of 30/01/2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.8. Glycerol phenylbutyrate - Orphan - EMEA-000297-PIP02-12-M02

Horizon Pharma Ireland Limited; E72.2 Indicated for use as adjunctive therapy for chronic management of patients with urea cycle disorders (UCDs) including deficiencies of carbamoyl phosphate-synthase-I (CPS), ornithine carbamoyltransferase (OTC), argininosuccinate synthetase (ASS), argininosuccinate lyase (ASL), arginase I (ARG) and ornithine translocase deficiency hyperornithinaemia-hyperammonaemia homocitrullinuria syndrome (HHH) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan and in line with the day 30 conclusions, 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/0068/2014) for Glycerol phenylbutyrate for the Treatment of urea cycle disorders, during its plenary on 01 June 2018.

2.3.9. Linagliptin - EMEA-000498-PIP01-08-M08

Boehringer Ingelheim International GmbH; Treatment of type 2 diabetes mellitus

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO confirmed the outcome of the Day 30 discussion and agreed with the requested modifications.
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/0032/2018 of 30/01/2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.10. Potassium chloride / Sodium chloride / Citric acid (as citric acid anhydrous) / Sodium citrate / Simeticone / Sodium sulfate (as sodium sulfate / Macrogol 4000) - EMEA-001356-PIP02-12-M02

Alfasigma S.p.A.; any clinical procedures requiring a clean bowel e.g. bowel endoscopy or radiology

Day 60 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

Following the Day 30 discussion the applicant provided the requested information regarding recruitment efforts and progress. The applicant followed the PDCO's opinion expressed 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/0019/2017 of 31/01/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.11. Vonicog alfa - Orphan - EMEA-001164-PIP01-11-M02

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

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The clarification submitted by the applicant was discussed by the PDCO. The applicant proposed completion date was considered agreeable.

2.3.12. Eculizumab - Orphan - EMEA-000876-PIP05-15-M03

Alexion Europe SAS; Treatment of Refractory Generalized Myasthenia Gravis

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO re-discussed the proposed modification taken into account the clarifications provide by the applicant after the D30 discussion.
All the issues were therefore considered solved.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan and the additional clarifications provided after D30, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0323/2017 of 31/10/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.13. Expanded donor-derived allogenic T cells transduced with the retroviral vector expressing the transgenes for inducible caspase9 and the truncated CD19 selectable marker - Orphan - EMEA-001869-PIP01-15-M01

Bellicum Pharma Ltd; Adjunctive treatment in haematopoietic stem cell transplantation

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO discussed this procedure during the May 2018 plenary meeting.
The PDCO considered the clarifications provided by the applicant after the D30 discussion and found them agreeable.
PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision P/0138/2017 of 7 June 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.14. Rimiducid - Orphan - EMEA-001870-PIP01-15-M01

Bellicum Pharma Ltd.; Treatment of graft versus host disease

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO discussed this procedure during the May 2018 plenary meeting.
The PDCO considered the clarifications provided by the applicant after the D30 discussion and found them agreeable.
Taking the above into account, the PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision P/0137/2017 of 7 June 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.15. Tofacitinib - EMEA-000576-PIP01-09-M09

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

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

Between Day 30 and Day 60 the applicant provided further information. At the Day 60 discussion the PDCO confirmed the outcome of 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/0035/2018 of 30/01/2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.16. Arimoclomol citrate - Orphan - EMEA-001748-PIP01-15-M01

Orphazyme A/S; Treatment of Niemann-Pick Disease, Type C

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 and the responses provided by the applicant to the points raised by the PCO at D30, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0079/2016 of 18/3/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.17. Pitolisant - Orphan - EMEA-001176-PIP01-11-M03

BIOPROJET PHARMA; Narcolepsy with or without cataplexy

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

2.3.18. Tasimelteon - Orphan - EMEA-001531-PIP01-13-M04

Vanda Pharmaceuticals; ICD-10 G47.24 Circadian rhythm sleep disorder, free-running type (Non-24) / Non24-Hour Sleep-Wake Disorder (Non-24) in the totally blind

Day 60 opinion

Neurology

Summary of committee discussion:

The PDCO discussed at their May 2018 meeting the responses received by the applicant and despite some changes can be accepted the PDCO had still a number of comments to make.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0053/2016 of 18/3/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.19. Cobimetinib - EMEA-001425-PIP01-13-M03

Roche Registration Limited; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue) with Ras, Raf or MEK pathway activation / Treatment of children with a paediatric solid malignant tumour with known or expected Ras, Raf or MEK pathway activation, at first relapse or refractory to initial treatment

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the proposed modification taking into consideration the clarifications provided by the applicant after D30.
In conclusion, 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/0065/2017 of 17/03/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.20. Larotrectinib - Orphan - EMEA-001971-PIP02-16-M01

Bayer AG; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haemtopoietic and lymphoid tissue neoplasms). / Treatment of paediatric patients from birth to less than 18 years of age with advanced solid tumours harbouring an NTRK fusion.

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the proposed modification taking into account the additional justification provided by the applicant, after the D30 discussion. The PDCO's view expressed at D30 on the other proposed changes 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/0179/2017 of 03/07/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.21. Sirolimus - Orphan - EMEA-001416-PIP01-12-M02

Santen Incorporated; Treatment of non-infectious uveitis affecting the posterior segment of the eye

Day 60 opinion

Ophthalmology

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/0064/2017 of 17 March 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.22. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with lentiviral vector that encodes for the human ARSA cDNA sequence - Orphan - EMEA-001765-PIP02-15-M02

GlaxoSMithKline Trading Services Limited; Treatment of Metachromatic leukodystrophy (MLD)

Day 60 opinion

Other

Summary of committee discussion:

The PDCO discussed this procedure during the May 2018 plenary meeting.
The PDCO considered the clarifications provided by the applicant after the D30 discussion and found them agreeable.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision P/0160/2017 of 30 June 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.23. Calcium chloride / Aprotinin / Fibrinogen / Thrombin - EMEA-001079-PIP01-10-M04

Kedrion S.p.A.; Treatment and prevention of haemorrhage resulting from a surgical procedure

Day 60 opinion

Other

Summary of committee discussion:

The PDCO considered that the applicant's responses to the D30 issues were 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/0280/2014 of 30 October 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.24. Mexiletine hydrochloride - Orphan - EMEA-002012-PIP01-16-M01

Lupin (Europe) Ltd.; Symptomatic treatment of myotonic disorders

Day 60 opinion

Other

Summary of committee discussion:

The applicant submitted clarifications and withdrew many of the initially proposed changes.
The committee discussed and endorsed the applicant's revised changes which take into consideration PDCO's comments expressed on 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/0155/2017 of 2 June 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.25. Gabapentin - EMEA-001310-PIP01-12-M03

PHARM Srl; Treatment of chronic pain in paediatric patients aged from 3 months to less than 18 years

Day 60 opinion

Pain

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.26. Potassium hydrogen carbonate / Potassium citrate monohydrate - EMEA-001535-PIP01-13-M01

Advicenne; Cystinuria (ICD 10: E72.0)

Day 60 opinion

Uro-nephrology

Summary of committee discussion:

The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision but some parts of the opinion were left unchanged.
The new PDCO opinion on the modified agreed PIP supersedes the previous PDCO opinion.

2.3.27. Sucroferric oxyhydroxide - EMEA-001061-PIP01-10-M03

Vifor Fresenius Medical Care Renal Pharma France; Hyperphosphataemia / Control of serum phosphorus levels in paediatric and adolescent subjects with chronic kidney disease (CKD)

Day 60 opinion

Uro-nephrology

Summary of committee discussion:

The PDCO confirmed the outcome of the discussion 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/0205/2015 of 04/09/2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.28. 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-M03

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

Day 60 opinion

Vaccines

Summary of committee discussion:

The PDCO discussed the clarification 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/0044/2018 of 16/02/2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.29. Recombinant Varicella Zoster Virus (VZV) glycoprotein E antigen - EMEA-001426-PIP01-13-M02

GlaxoSmithKline Biologicals SA; Prevention of VZV reactivation / Prevention of herpes zoster in immunocompromised subjects aged 1 to 17 years

Day 60 opinion

Vaccines

Summary of committee discussion:

Additional justifications were received from the applicant on 11 May 2015. Altogether the applicant's proposal was considered acceptable.
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/0228/2017 of 9 August 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.30. Tocilizumab - EMEA-000309-PIP04-17-M01

Roche Registration Ltd.; Treatment of SSc (ICD 10-M34)/scleroderma and associated disorders (MedDRA)., Cytokine release syndrome / Treatment of juvenile Systemic Sclerosis (jSSc) in children 5 years of age and older, 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 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

Based on the review of the evidence provided by the applicant and the background information related to the procedure the PDCO at their May 2018 meeting supported the current modification of the agreed paediatric investigation plan.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0217/2017 of 9 August 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.
The applicant should continue monitoring in post-marketing the safety of multiple administration and effect of response to CAR T cell therapy.

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. Crisaborole- EMEA-C3-002065-PIP01-16-M01

Pfizer Ltd.; Treatment of atopic dermatitis

Day 1 letter

Dermatology

Summary of committee discussion:

The Coordinator and rapporteur confirm that the initiation of Study is considered compliant with the terms of the latest Decision (P/0101/2018) of 15 March 2018. The PDCO was informed about the outcome of this procedure.

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

Wilson Therapeutics AB; Treatment of Wilson disease

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.2. EMEA-002287-PIP01-17

Treatment of Type 2 Diabetes Mellitus

Day 90 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

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

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

Day 90 discussion

Gastroenterology-Hepatology

3.1.4. Risankizumab - EMEA-001776-PIP03-17

Crohn's Disease

Day 90 discussion

Gastroenterology-Hepatology

3.1.5. Risankizumab - EMEA-001776-PIP04-17

Ulcerative Colitis

Day 90 discussion

Gastroenterology-Hepatology

3.1.6. Cefiderocol - EMEA-002133-PIP01-17

Treatment of Gram-negative bacterial infections

Day 90 discussion

Infectious Diseases

3.1.7. Glasdegib maleate - Orphan - EMEA-002199-PIP01-17

Pfizer Limited; Treatment of acute myeloid leukaemia (AML)

Day 90 discussion

Oncology

3.1.8. 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 90 discussion

Oncology

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

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

Day 90 discussion

Other

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

Treatment of iron deficient anaemia in haemodialysis patients

Day 90 discussion

Uro-nephrology / Haematology-Hemostaseology

3.1.11. EMEA-002160-PIP01-17

Prevention of HIV-1 infection in children from 9 to less than 18 years of age

Day 90 discussion

Vaccines / Infectious Diseases

3.1.12. Clade C gp140 - EMEA-002221-PIP01-17

Prevention of HIV-1 infection in children from 9 to less than 18 years of age

Day 90 discussion

Vaccines / Infectious Diseases

3.1.13. Mosaic gp140 / Clade C gp140 - EMEA-002161-PIP01-17

Prevention of HIV-1 infection in children from 9 to less than 18 years of age

Day 90 discussion

Vaccines / Infectious Diseases

3.1.14. Evinacumab - EMEA-002298-PIP01-17

Treatment of elevated cholesterol / Treatment of homozygous familial hypercholesterolemia (HoFH)

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.15. Ianalumab - EMEA-002338-PIP01-18

Treatment of autoimmune hepatitis in patients aged 12 years to <18 years in whom steroids and/or azathioprine are contraindicated, are not tolerated, or do not provide an adequate response

Day 60 discussion

Gastroenterology-Hepatology

3.1.16. EMEA-002240-PIP02-17

Treatment of Urinary Tract Infections

Day 60 discussion

Infectious Diseases

3.1.17. EMEA-001970-PIP02-17

Treatment of Clostridium difficile infection / indicated to reduce recurrence of Clostridium difficile infection (CDI) in paediatric patients who have received antibacterial drug treatment for recurrent CDI

Day 60 discussion

Infectious Diseases

3.1.18. Isoflurane - EMEA-002320-PIP01-17

Sedation

Day 60 discussion

Neonatology - Paediatric Intensive Care

3.1.19. Bupivacaine - EMEA-000877-PIP03-17

Postsurgical analgesia

Day 60 discussion

Pain

3.1.20. Calcifediol - EMEA-002093-PIP02-17

Treatment of secondary hyperparathyroidism (SHPT) in non-dialysis chronic kidney disease (ND-CKD) patients with low serum 25-hydroxyvitamin D levels

Day 60 discussion

Uro-nephrology

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

Treatment of essential hypertension

Day 30 discussion

Cardiovascular Diseases

3.1.22. EMEA-002329-PIP01-18

Treatment of chronic hand eczema

Day 30 discussion

Dermatology

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

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

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.24. 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); Polycystic kidney, adult type.

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Uro-nephrology

3.1.25. EMEA-002362-PIP01-18

Prophylaxis of haemophilia B (hereditary factor IX deficiency)

Day 30 discussion

Haematology-Hemostaseology

3.1.26. Luspatercept - EMEA-001521-PIP02-18

Treatment of Myelofibrosis

Day 30 discussion

Haematology-Hemostaseology

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

SynteractHCR Deutschland GmbH; Treatment of sickle cell disease

Day 30 discussion

Haematology-Hemostaseology

3.1.28. Ustekinumab - EMEA-000311-PIP06-18

Treatment of systemic lupus erythematosus (SLE)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.29. 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 30 discussion

Infectious Diseases

3.1.30. Abemaciclib - EMEA-002342-PIP01-18

Ewing's Sarcoma

Day 30 discussion

Oncology

3.1.31. EMEA-002348-PIP01-18

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

Day 30 discussion

Oncology

3.1.32. 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 30 discussion

Oncology

3.1.33. 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 30 discussion

Oncology

3.1.34. Navitoclax - EMEA-000478-PIP02-18

Treatment of myelofibrosis

Day 30 discussion

Oncology

3.1.35. 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 30 discussion

Oncology

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

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

Day 30 discussion

Oncology

3.1.37. Anti-alpha v beta 6 monoclonal antibody - Orphan - EMEA-002332-PIP01-18

Biogen Idec Ltd; Idiopathic Pulmonary Fibrosis

Day 30 discussion

Pneumology - Allergology

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

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

Day 30 discussion

Pneumology - Allergology

3.1.39. EMEA-002121-PIP02-18

Treatment of insomnia

Day 30 discussion

Psychiatry

3.1.40. Rapastinel - EMEA-002357-PIP01-18

Major depressive disorder

Day 30 discussion

Psychiatry

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

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

Day 30 discussion

Haematology-Hemostaseology

3.2.2. Cilastatin sodium / relebactam / imipenem monohydrate - EMEA-C1-001809-PIP01-15

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

Day 30 discussion

Infectious Diseases

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

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

AOP Orphan Pharmaceuticals AG; Treatment of supraventricular arrythmias

Day 30 discussion

Cardiovascular Diseases

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

LEO Pharma A/S; Treatment of Atopic Dermatitis

Day 30 discussion

Dermatology

3.3.3. Exenatide - EMEA-001755-PIP01-15-M01

LES LABORATOIRES SERVIER; Treatment of type 2 diabetes mellitus in patients from 10 to less than 18 years old

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.4. 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 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.5. 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 yers and older

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

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

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

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

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

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

Day 30 discussion

Haematology-Hemostaseology

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

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

Day 30 discussion

Infectious Diseases

3.3.9. 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 30 discussion

Infectious Diseases

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

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

Day 30 discussion

Neurology

3.3.11. (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 30 discussion

Oncology

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

Merck KGaA; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumors, haematopoetic and lymphoid tissue 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 relapsed Hodgkin or non-Hodgkin lymphoma, or with Hodgkin or non-Hodgkin lymphoma as part of first line treatment

Day 30 discussion

Oncology

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

Eisai Europe Ltd; Soft Tissue Sarcoma

Day 30 discussion

Oncology

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

Celgene Europe Limited; Treatment of a paediatric solid malignant tumour

Day 30 discussion

Oncology

3.3.15. 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

Day 30 discussion

Oncology

3.3.16. 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 30 discussion

Other

3.3.17. 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 30 discussion

Other / Oncology

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

AstraZeneca AB; Treatment of asthma

Day 30 discussion

Pneumology - Allergology

3.3.19. Peanut Allergen Extract - EMEA-001481-PIP01-13-M02

DBV Technologies S.A; Peanut allergy

Day 30 discussion

Pneumology - Allergology

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

H. Lundbeck A/S; Major Depressive Disorder

Day 30 discussion

Psychiatry

3.3.21. 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 30 discussion

Uro-nephrology / Haematology-Hemostaseology

3.3.22. 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 30 discussion

Vaccines

3.3.23. Pandemic influenza vaccine (H5N1) - EMEA-001830-PIP01-15-M01

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

Day 30 discussion

Vaccines

4. Nominations

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

4.1. List of letters of intent received for submission of applications with start of procedure 24 July 2018 for Nomination of Rapporteur and Peer reviewer

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

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

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

4.3. Nominations for other activities

None

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

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

6. Discussion on the applicability of class waivers

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

6.1. Discussions on the applicability of class waiver for products

None

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

None

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 list of procedures with paediatric indications to be evaluated by the CHMP, starting in April 2018 was presented to the PDCO members.

The members were also informed about 1 medicinal product, Sprycel for which the CHMP adopted a positive opinion recommending a paediatric indication during their meeting in April 2018, including a new pharmaceutical form (powder for oral suspension) associated with a new strength (10 mg/ml) for treatment of paediatric patients.

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

9.2.2.1. Joint CHMP/PDCO session

Summary of committee discussion:

Discussion at the joint session was cancelled since the concerned CHMP Rapporteurs were invited to participate to the related PDCO discussion.

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.

9.4. Cooperation within the EU regulatory network

None

9.5. Cooperation with International Regulators

9.5.1. WHO-convened PAWG - Research Toolkit for Paediatric Antiretroviral Drug and Formulation Development

PDCO member: Dirk Mentzer;

Summary of committee discussion:

The Committee discussed the WHO and Unitaid Research Toolkit for Paediatric Antiretroviral Drug and Formulation Development and in principle supported the initiative. Individual personal comments on the document will be sent by the end of the week.

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

Scope: Outcomes and action plan

Summary of committee discussion:

The Committee was informed about the progress made in the EMA/PDCO working groups and about the next steps towards the publication of the action plan on paediatrics.

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

The break-out session was cancelled.

11.1.2. Neonatology

Summary of committee discussion:

The break-out session was cancelled.

11.1.3. Inventory

Summary of committee discussion:

The break-out session was cancelled.

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 29 May-01 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	
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	
Alessandro Jenkner	Alternate	Italy	No interests declared	
Dina Apele-Freimane	Member	Latvia	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
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	
Doina Plesca	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Michal Odermarsky	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Fahimeda Ali	Expert - in person*	United Kindgom	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/