27 July 2018
EMA/PDCO/514093/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes of the meeting on 24-27 July 2018

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

24 July 2018, 14:00 - 19:30, room 3A

25 July 2018, 08:30 - 19:30, room 3A

26 July 2018, 08:30 - 19:00, room 3A

27 July 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 June 2018 PDCO were adopted and will be published on the EMA website.

2. Opinions

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

2.1. Opinions on Products

2.1.1. Anti-alpha synuclein monoclonal antibody - EMEA-002367-PIP01-18

Biogen Idec Limited; Treatment of Parkinson's disease

Day 30 opinion

Neurology

Summary of committee discussion:

The applicant has requested a full product-specific waiver for their product , which is developed for treatment of Parkinson's disease (PD) in adults.
Anti-alpha synuclein monoclonal antibody binds selectively to aggregated forms of alpha-synuclein (α-syn), which has a central role in the pathogenesis of PD. The proposed mode of action is to attenuate α-syn transmission from cell to cell in cultured neurons, and to diminish α-syn pathology and, potentially, slow disease progression.
However, while, PD and juvenile Parkinsonism (JP) both have a deficiency in nigrostriatal dopamine function, the underlying neuropathology in JP and adult PD is different: PD is defined by accumulations of alpha-synuclein (or, so called Lewy bodies) in the brain, whereas Lewy pathology is virtually absent in JP. Thus, alpha-synuclein is a sensible drug target in PD, whereas the various mechanisms behind the heterogeneous clinical phenotypes of JP appear not to be primarily alpha-synuclein-related. Consequently, anti-alpha synuclein monoclonal antibody is not expected to be efficacious in the paediatric patients with JP. The PDCO, therefore endorsed the applicant's request for a full waiver on the grounds, that the medicinal product is likely to be ineffective in all of the paediatric population.
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 anti-alpha synuclein monoclonal antibody for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of Parkinson's disease on the grounds, that the medicinal product is likely to be ineffective in all of the paediatric population.

2.1.2. Baricitinib - EMEA-001220-PIP03-16

Eli Lilly and Company Limited; Treatment of atopic dermatitis / Treatment of patients with moderate to severe atopic dermatitis

Day 120 opinion

Dermatology

Summary of committee discussion:

The PDCO members discussed the information provided by the applicant.
The PDCO adopted a positive opinion at Day 120.

2.1.3. Mirikizumab - EMEA-002208-PIP01-17

Eli Lilly and Company; 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 120 opinion

Dermatology / Gastroenterology-Hepatology

Summary of committee discussion:

The PDCO discussed the applicant's response to the Day 90 issues.
A positive opinion was adopted at Day 120.

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

The Medicines Company UK Ltd.; Treatment of elevated cholesterol

Day 120 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

At the PDCO July 2018 meeting the applicant – who requested to be heard in an OE – presented to the Committee the outstanding points after a number of changes had been made to the PIP after the Day 90 discussion.
The final condition agreed by the PDCO for this PIP to allow all the indications planned to be covered and in accordance with the agreed PIP will be 'treatment of elevated cholesterol' in analogy with previous PIPs agreed.
The studies of the PIP will be deferred to avoid delay of the availability of the medicine to the adult population given that studies in children will necessarily take longer to be concluded due to the rarity of the disease.

In conclusion, the PDCO adopted a positive opinion for inclisiran sodium and a deferral in 'treatment of elevated cholesterol'.

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

Shire Pharmaceuticals Ireland Limited; 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 120 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The applicant's responses to the Day 90 issues were acknowledged and a positive Opinion was adopted at Day 120.

2.1.6. 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 120 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO confirmed all the points discussed at Day 90 and agreed with the proposed plan from the applicant.
Thus, the PDCO adopted a positive Opinion at Day 120.

2.1.7. Ibalizumab - EMEA-002311-PIP01-17

Theratechnologies International Limited; 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 120 opinion

Infectious Diseases

Summary of committee discussion:

As it was already mentioned at Day 90, the Committee confirms that a positive opinion is adopted.

2.1.8. Onasemnogene abeparvovec - Orphan - EMEA-002168-PIP01-17

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

Day 120 opinion

Neurology

Summary of committee discussion:

The applicant responses to the questions sent at Day 90 were discussed.
The PDCO adopted a positive opinion on the agreement of a PIP.

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

Newron Pharmaceuticals SpA; Treatment of Rett syndrome

Day 120 opinion

Neurology

Summary of committee discussion:

The PDCO considered all remaining issues resolved. The Committee adopted a positive opinion.

2.1.10. Afatinib - EMEA-001596-PIP02-17

Boehringer Ingelheim International GmbH; 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 120 opinion

Oncology

Summary of committee discussion:

The PDCO's views expressed at Day 90 were endorsed. The PDCO noted the clarifications provided by the applicant after Day 90.
In conclusion, the PDCO recommends granting a paediatric investigation plan for afatinib for children from birth to less than 18 years of age and a deferral for the conditions 'treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms)' and the 'treatment of malignant neoplasms of the central nervous system'.

2.1.11. Entrectinib - EMEA-002096-PIP01-16

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

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the application for entrectinib taking into account the applicant's responses provided after the Day 90 discussion.
All pending issues identified at Day 90 were considered solved and the PDCO recommended granting a paediatric investigation plan for entrectinib for children from birth to less than 18 years of age and a deferral for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms).

2.1.12. 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 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the application for ivosidenib taking into account the responses provided by the applicant after the Day 90 discussion. All pending issues identified at Day 90 were resolved satisfactorily.
In conclusion, the PDCO recommends granting a paediatric investigation plan for ivosidenib for children from 2 to less than 18 years of age and a deferral for the treatment of acute myeloid leukaemia.

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

Fennec Pharmaceuticals, Inc.; 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 120 opinion

Oncology / 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 proposed modified paediatric investigation plan. A positive opinion was therefore adopted.

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

TETEC AG; Treatment of cartilage disorders

Day 120 opinion

Other

Summary of committee discussion:

The PDCO re-discussed this product at Day 120 during the July 2018 plenary meeting. The PDCO confirmed all the points raised and discussed at Day 90. In addition, the PDCO considered the information provided by the applicant between Day 90 and Day 120. The PDCO adopted a positive Opinion at Day 120.

2.1.15. Palovarotene - EMEA-001662-PIP03-17

Clementia Pharmaceuticals Inc.; Treatment of Multiple Osteochondromas (MO)

Day 120 opinion

Other

Summary of committee discussion:

The PDCO re-discussed this procedure at Day 120 during the July 2018 plenary.
The PDCO confirmed the points raised and discussed at Day 90. The PDCO adopted a positive Opinion at Day 120.

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

Enzyvant Farber Ireland Ltd; Farber disease

Day 120 opinion

Other

Summary of committee discussion:

At its July 2018 meeting the PDCO noted the replies provided by the applicant on the outstanding minor points raised at Day 90 and agreed a positive opinion for recombinant human ceramidase in the Treatment of Farber disease.

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

Faron Pharmaceuticals Ltd; Treatment of Acute Respiratory Distress Syndrome

Day 120 opinion

Pneumology - Allergology

Summary of committee discussion:

At the end of the discussion, the PDCO agreed on a positive opinion for Interferon beta-1a for all subsets of the paediatric population (0 to 18 years of age) in the condition Treatment of Acute Respiratory Distress Syndrome.

2.1.18. Monovalent, recombinant, replication-incompetent human adenovirus serotype 26-vectored vaccine encoding the pre-fusion conformation-stabilised F protein derived from the RSV A2 strain - EMEA-002172-PIP02-17

Janssen-Cilag International NV; Prevention of lower respiratory tract disease caused by respiratory syncytial virus (RSV)

Day 120 opinion

Vaccines / Infectious Diseases

Summary of committee discussion:

The PDCO re-discussed the application taking into account the clarifications provided after the D90 discussion and the comments received on the draft opinion. All pending issues identified at Day 90 were resolved satisfactorily.
In conclusion, the PDCO recommends granting a paediatric investigation plan with a deferral for the prevention of lower respiratory tract disease caused by respiratory syncytial virus for the entire paediatric population.

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

SmartGenRx Pty Ltd; Prevention of cardiovascular events

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed. Based on the assessment of this application the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for rosuvastatin calcium / indapamide hemihydrate / acetylsalicylic acid / perindopril tert-butylamine for all subsets of the paediatric population (0 to 18 years of age) in the condition of prevention of cardiovascular events on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

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

Kuhnil Pharm.CO.Ltd.; ICD10:E78.2

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 Omega-3-acid ethyl esters 90 / Rosuvastatin Calcium for all subsets of the paediatric population.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

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

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

Day 60 opinion

Neurology

Summary of committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed. The PDCO considered that taking into account the current unmet need in the paediatric ALS population, the potential benefit that arimoclomol citrate could bring to this population and the risk of off-label use, a waiver for the treatment of ALS cannot be granted.
The Committee adopted a positive opinion granting a product-specific waiver for 'Treatment of sporadic inclusion body myositis' and a negative opinion rejecting a product-specific waiver for 'Treatment of amyotrophic lateral sclerosis'.

2.1.22. Elotuzumab - EMEA-002377-PIP01-18

Bristol-Myers Squibb Pharma EEIG; Treatment of multiple myeloma

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this product at Day 60 during the July 2018 plenary meeting. The PDCO confirmed all the points raised and discussed at Day 30. Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the applicant's request for a waiver based on the grounds of lack of significant benefit because studies are not feasible. The PDCO recommends granting a waiver for elotuzumab for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of multiple myeloma.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

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

Trizell Ltd.; Treatment of mesothelioma

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed this product at Day 60 during the July 2018 plenary meeting. The PDCO took into consideration the information provided by the applicant after the Day 30 discussion. Thus, 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 based on the grounds of lack of significant benefit because studies are not feasible. The PDCO recommends granting a waiver for Nadofaragene firadenovec for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of mesothelioma.
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.

2.1.24. Tepotinib - EMEA-002345-PIP01-18

Merck KGaA; Treatment of lung malignant neoplasms

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO reviewed the conclusions reached at Day 30 together with the additional information submitted by the applicant. The conclusions reached at Day 30 were endorsed. A full waiver for the treatment of non-small cell lung carcinoma on the grounds that the disease does not occur in the paediatric population was agreed.

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

NTC srl; Prevention and treatment of inflammation and prevention of infection associated with cataract surgery

Day 60 opinion

Ophthalmology

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 Levofloxacin / Dexamethasone for all subsets of the paediatric population (0 to 18 years of age) in the condition of Prevention and treatment of inflammation and prevention of infection associated with cataract surgery.

2.1.26. Fasinumab - EMEA-002059-PIP01-16

Regeneron Ireland U.C.; Treatment of chronic pain

Day 60 opinion

Pain

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. The PDCO therefore recommends refusing a waiver for fasinumab for all subsets of the paediatric population in the condition of treatment of chronic pain.
A negative opinion was adopted.

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. 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 letter

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO finalised on 27 July 2018 this partially completed compliance procedure and confirmed the compliance of the PIP Studies according to the latest Agency's Decision (P/0067/2018) of 16 March 2018.

2.2.2. 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 letter

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0363/2017) of 1 December 2017.
Of note, EMA issued a corrigendum of Opinion EMEA-001741-PIP01-14-M01 in order to amend the pharmaceutical form 'tablet' and specify instead 'prolonged-release tablet'. The corrigendum was issued in parallel to this compliance check. The change in the pharmaceutical form has not impact on this interim compliance check.
The PDCO finalised on 27 July 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.

2.2.3. Amikacin (sulfate) / Amikacin - EMEA-C3-000525-PIP01-08-M04

Insmed Limited; Treatment of nontuberculous mycobacterial lung infection

Day 30 letter

Infectious Diseases / Pneumology - Allergology

Summary of committee discussion:

The PDCO discussed the completed study and considered that it is compliant with the latest Agency's Decision (P/0030/2015) of 30 January 2015. The PDCO finalised on 27 July 2018 this partially completed compliance procedure.

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

Zogenix International Ltd; Treatment of Dravet syndrome

Day 30 letter

Neurology

Summary of committee discussion:

The PDCO confirmed the compliance and adopted a positive outcome letter.

2.2.5. Galcanezumab - EMEA-C4-001860-PIP03-16-M01

Eli Lilly and Company Limited; Prevention of migraine headaches

Day 30 letter

Neurology

Summary of committee discussion:

The PDCO discussed the Study and concluded that it had been conducted in accordance with the PDCO opinion. Therefore a positive outcome letter was adopted by the PDCO at their July 2018 meeting.

2.2.6. Lacosamide - EMEA-C-000402-PIP02-11-M05

UCB Pharma S.A.; Treatment of epilepsy with partial onset seizures

Day 30 opinion

Neurology

Summary of committee discussion:

The PDCO took note of preceding procedures and reports on partial compliance (EMEA-C1-000402-PIP02-11-M01 and EMEA-C2-000402-PIP02-11-M02).
The PDCO adopted on 27 July 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/0001/2018) of 08 January 2018.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. 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 60 opinion

Diagnostic

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 modification. A negative opinion has been adopted. The previously agreed PIP remains unchanged.

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

AstraZeneca AB; Treatment of Type 2 Diabetes

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 adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0247/2015 of 30/10/2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

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

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

Based on the overall review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed change could be accepted.
The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0214/2014 of 01/09/2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.4. 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)

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The PDCO discussed the applicant's responses to two outstanding issues from the Day 30 PDCO discussion in June for this modification request for Exenatide, a GLP-1 receptor agonist for the treatment of type 2 diabetes on 27 July 2018.
In conclusion, and 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 as set in

the Agency's latest decision (P/0244/2017 of 04/09/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.5. Recombinant human alpha-galactosidase A - Orphan - EMEA-001828-PIP01-15-M01

Protalix Ltd; Treatment of Fabry disease

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The applicant's response to the Day 30 issues was acknowledged.
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/0109/2016 of 15 April 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.6. 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 60 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The applicant submitted a request for modification of this PIP
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/0278/2016 of 07/10/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.7. 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 60 opinion

Gastroenterology-Hepatology

Summary of committee discussion:

The PDCO discussed the information provided by the applicant. The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0195/2014 of 8 August 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

Ablynx NV; Treatment of thrombotic thrombocytopenic purpura / Treatment of acquired thrombotic thrombocytopenic purpura

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

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

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0189/2016 of 15 July 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

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

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed. The applicant provided clarification after 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 and adopted a positive opinion.

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

Biotest AG; Treatment of congenital fibrinogen deficiency

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed change 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/0106/2017 of 11/04/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

Glaxo Group Limited; Treatment of systemic lupus erythematosus

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee 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/0063/2015 of 01/04/2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

Novimmune B.V; Treatment of Haemophagocytic Lymphohistiocytosis

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

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

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision P/0152/2018 of 18/5/2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

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

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

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

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision P/0151/2017 of 7/6/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.14. 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 60 opinion

Infectious Diseases

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 P/0206/2016 of 12/08/2016.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.15. 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 pediatric patients aged 3 to less than 18 years.

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed change to convert this PIP into a full product-specific waiver was acceptable.

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0012/2014 of 22 January 2014).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.16. 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 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO discussed at its July 2018 meeting the responses provided by the applicant. The PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0253/2017 of 21/7/2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

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

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO's view expressed at Day 30 was re-discussed and endorsed. The PDCO adopted a positive Opinion.

2.3.18. Autologous haematopoietic stem cells transduced with lentiviral vector Lenti-D encoding the human ATP-binding cassette, subfamily D, member 1 (ABCD1) cDNA - Orphan - EMEA-001244-PIP01-11-M02

bluebird bio France; Treatment of adrenoleukodystrophy

Day 60 opinion

Neurology

Summary of committee discussion:

The PDCO re-discussed the requested modification for autologous haematopoietic stem cells transduced with lentiviral vector Lenti-D encoding the human ATP-binding cassette, subfamily D, member 1 (ABCD1) cDNA, taking into account the clarifications provided by the applicant after the D30 discussion. All pending issues were considered solved.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP

as set in the Agency's latest decision (P/0329/2016 of 02 December 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

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

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

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 and the waiver extended to all subsets of the paediatric population.

The PDCO therefore adopted a favourable Opinion granting a product-specific waiver. The new PDCO opinion supersedes the previous PDCO Opinion.

2.3.21. 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 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the proposed modification for ponatinib taking into account the responses provided by the applicant after Day 30. All pending issues were considered solved.
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/0127/2017 of 05 May 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

Daiichi Sankyo Europe GmbH; Treatment of acute myeloid leukaemia / 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 60 opinion

Oncology

Summary of committee discussion:

The clarifications provided by the applicant after the Day 30 discussion were noted and the PDCO's view expressed at Day 30 endorsed including the acceptability of the deferral 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/0102/2018 of 16 March 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

Genzyme Europe B.V.; Treatment of Gaucher Disease Type 1 and Type 3 / Treatment of Gaucher Disease Type 2

Day 60 opinion

Other

Summary of committee discussion:

The PDCO at their July 2018 meeting noted the clarifications 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/0191/2015 of 17/7/2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

ReveraGen BioPharma Ltd; Treatment of Duchenne muscular dystrophy

Day 60 opinion

Other

Summary of committee discussion:

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

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0084/2018 of 26/1/2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

sanofi-aventis recherche & développement; Treatment of asthma

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

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

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0021/2017 of 3 February 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.26. 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 60 opinion

Pneumology - Allergology

Summary of committee discussion:

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

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0281/2016 of 4 November 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

Novartis Europharm Limited; Treatment of asthma

Day 60 opinion

Pneumology - Allergology

Summary of committee discussion:

The PDCO's views expressed on Day 30 were re-discussed taking into account the Applicant's clarifications, which were considered agreeable.
Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0057/2018 of 16 March 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

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

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 therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision. The new PDCO Opinion on the modified agreed PIP

supersedes the previous PDCO Opinion.

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

Gedeon Richter Plc.; F20 Treatment of schizophrenia

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 therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision. The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

Ferrer Internacional, S.A.; Bipolar disorder, Treatment of schizophrenia / For rapid control of agitation in patients with schizophrenia, For rapid control of agitation in patients with bipolar 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 therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision. The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

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

Shire Pharmaceutical Contracts Ltd; Treatment of hyperphosphataemia

Day 60 opinion

Uro-nephrology

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/0232/2016 of 09/09/2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.32. Omadacycline - EMEA-000560-PIP03-15-M01

Paratek UK Limited; Treatment of bacterial pneumonia

Day 30 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO endorsed the applicant's modification request and adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0168/2017 of 3 July 2017).
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.

No items

2.8. Revision of the PDCO opinions

2.8.1. 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 has re-discussed this application with particular attention to the previously missing information.

The PDCO therefore revised its previously adopted negative opinion and endorsed the proposed postponement of the completion dates. The revised positive opinion supersedes the previously adopted one.

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. EMEA-002350-PIP01-18

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

Day 60 discussion

Dermatology

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

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

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.3. Asciminib - EMEA-002347-PIP01-18

Treatment of Philadelphia positive Chronic Myelogenous Leukemia in chronic phase

Day 60 discussion

Haematology-Hemostaseology

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

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

Day 60 discussion

Haematology-Hemostaseology

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

Treatment of Systemic Lupus Erythematosus (SLE)

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.6. 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 60 discussion

Immunology-Rheumatology-Transplantation

3.1.7. Guselkumab - EMEA-001523-PIP03-18

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

Day 60 discussion

Immunology-Rheumatology-Transplantation

3.1.8. Rilpivirine - 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 60 discussion

Infectious Diseases

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

Prevention of nosocomial pneumonia caused by Staphylococcus aureus

Day 60 discussion

Infectious Diseases

3.1.10. 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 60 discussion

Oncology

3.1.11. Spartalizumab - EMEA-002351-PIP01-18

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

Day 60 discussion

Oncology

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

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

Day 60 discussion

Other

3.1.13. (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 60 discussion

Oto-rhino-laryngology

3.1.14. EMEA-002324-PIP01-17

Treatment of Cystic Fibrosis

Day 60 discussion

Pneumology - Allergology

3.1.15. EMEA-002191-PIP02-17

Treatment of Cystic Fibrosis

Day 60 discussion

Pneumology - Allergology

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

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

Day 60 discussion

Vaccines / Infectious Diseases

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

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

Day 60 discussion

Vaccines / Infectious Diseases

3.1.18. Indapamide / Perindopril arginine / Atorvastatin calcium trihydrate - EMEA-002395-PIP01-18

Treatment of Essential Hypertension, Treatment of Cardiovascular diseases, Prevention of Cardiovascular diseases, Treatment of Elevated Cholesterol

Day 30 discussion

Cardiovascular Diseases

3.1.19. EMEA-002378-PIP01-18

Treatment of acute heart failure

Day 30 discussion

Cardiovascular Diseases

3.1.20. EMEA-002363-PIP01-18

Treatment of transthyretin-mediated amyloidosis (ATTR amyloidosis) - cardiomyopathy amyloidosis, Treatment of transthyretin-mediated amyloidosis (ATTR amyloidosis) - polyneuropathy amyloidosis

Day 30 discussion

Cardiovascular Diseases / Neurology

3.1.21. Dihomo-γ-linolenic acid (DGLA) - EMEA-002364-PIP01-18

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

Day 30 discussion

Dermatology

3.1.22. Dihomo-γ-linolenic acid (DGLA) - EMEA-002364-PIP02-18

Treatment of atopic dermatitis / Treatment of pruritus associated with mild to moderate atopic dermatitis, Treatment of mild to moderate atopic dermatitis

Day 30 discussion

Dermatology

3.1.23. Pyridoxal 5'-phosphate monohydrate - Orphan - EMEA-002404-PIP01-18

Medicure Pharma Europe Limited; Treatment of pyridox(am)ine 5'-phosphate oxidase (PNPO) deficiency

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.24. Tirzepatide - EMEA-002360-PIP01-18

Treatment of Type 2 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.1.25. Cell-free solution of lysed Escherichia coli culture, strain Laves - EMEA-002393-PIP01-18

Treatment of irritable bowel syndrome, Treatment of colitis (excluding infective)

Day 30 discussion

Gastroenterology-Hepatology

3.1.26. Ianalumab - EMEA-002338-PIP02-18

Primary Sjögren's Syndrome (pSS)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.27. Sarilumab - EMEA-001045-PIP02-18

Vasculitides

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.28. Iclaprim mesylate - EMEA-002391-PIP01-18

Infection with Gram-positive bacteria / Treatment of acute bacterial skin and skin structure infections caused by susceptible strains of Gram-positive bacteria

Day 30 discussion

Infectious Diseases

3.1.29. Oteseconazole - EMEA-002392-PIP01-18

Treatment of vulvovaginal candidiasis

Day 30 discussion

Infectious Diseases

3.1.30. A synthetic ribonucleic acid oligonucleotide directed against superoxide dismutase 1 (SOD1) messenger ribonucleic acid - Orphan - EMEA-002403-PIP01-18

Biogen Idec Ltd; Treatment of Amyotrophic lateral sclerosis

Day 30 discussion

Neurology

3.1.31. Ofatumumab - EMEA-002397-PIP01-18

Treatment of Multiple Sclerosis / Treatment of relapsing remitting multiple sclerosis

Day 30 discussion

Neurology

3.1.32. EMEA-002318-PIP01-18

Treatment of melanoma

Day 30 discussion

Oncology

3.1.33. Anti-FGFR2b humanised IgG1 monoclonal antibody (bemarituzumab) - EMEA-002401-PIP01-18

Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms) overexpressing FGFR2b

Day 30 discussion

Oncology

3.1.34. Autologous dendritic cells pulsed with allogeneic tumour cell lysate - Orphan - EMEA-002381-PIP01-18

Amphera BV; Treatment of malignant mesothelioma

Day 30 discussion

Oncology

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

Celgene Europe Limited; Treatment of mature B-cell neoplasms / Treatment of pediatric BCMA+ relapsed or refractory B non-Hodgkin lymphoma

Day 30 discussion

Oncology

3.1.36. Binimetinib - EMEA-001454-PIP05-18

Treatment of colorectal carcinoma

Day 30 discussion

Oncology

3.1.37. Brentuximab vedotin - Orphan - EMEA-000980-PIP04-18

Takeda Pharma A/S; Treatment of Mature T and NK neoplasms

Day 30 discussion

Oncology

3.1.38. Encorafenib - EMEA-001588-PIP03-18

Treatment of colorectal carcinoma

Day 30 discussion

Oncology

3.1.39. Pamiparib - EMEA-002389-PIP01-18

Gastric Neoplasms Malignant

Day 30 discussion

Oncology

3.1.40. Selinexor - Orphan - EMEA-002387-PIP01-18

Karyopharm Europe GmbH; Relapse/ Refractory Multiple myeloma

Day 30 discussion

Oncology

3.1.41. Diphtheria Toxin Interleukin-3 Fusion Protein; - Orphan - EMEA-002244-PIP02-18

Stemline Therapeutics, Inc.; Treatment of blastic plasmacytoid dendritic cell neoplasm

Day 30 discussion

Oncology

3.1.42. Telisotuzumab vedotin - EMEA-002361-PIP01-18

Lung carcinoma (small cell and non-small cell carcinoma)

Day 30 discussion

Oncology

3.1.43. Vinorelbine Tartrate - EMEA-002365-PIP01-18

Treatment of osteosarcomas, treatment of rhabdomyosarcoma, treatment of Ewing's sarcoma, treatment of non-rhabdomyosarcoma soft-tissue sarcomas / treatment of relapsed or refractory Ewing's sarcoma, treatment of relapsed or refractory rhabdomyosarcoma, treatment of relapsed or refractory osteosarcomas, treatment of relapsed or refractory non-rhabdomyosarcoma soft-tissue sarcomas

Day 30 discussion

Oncology

3.1.44. Eflapegrastim - EMEA-002385-PIP01-18

Treatment of Chemotherapy- Induced Neutropenia / Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Day 30 discussion

Oncology / Haematology-Hemostaseology

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

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

Day 30 discussion

Pneumology - Allergology

3.1.46. EMEA-002398-PIP01-18

Treatment of cystic fibrosis in individuals with cystic fibrosis who are homozygous for the F508del mutation and are receiving treatment with a CFTR modulator

Day 30 discussion

Pneumology - Allergology

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

Boehringer Ingelheim International GmbH; Treatment of fibrosing Interstitial Lung Diseases (ILD) in paediatric patients

Day 30 discussion

Pneumology - Allergology / Oncology

3.1.48. EMEA-002373-PIP01-18

Schizophrenia

Day 30 discussion

Psychiatry

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. Lamivudine (3TC) / Dolutegravir (DTG) - EMEA-C1-001940-PIP01-16-M01

ViiV Healthcare UK Limited; Treatment of human immunodeficiency virus (HIV-1) infection

Day 30 discussion

Infectious Diseases

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

No items.

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 18 September 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

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

6.1. Discussions on the applicability of class waiver for products

6.1.1. Trifluridine and Tipiracil Hydrochloride – EMEA-13-2018

Les Laboratoires Servier; The class of pyrimidine- and pyrimidine analogue-containing medicinal products for treatment of intestinal malignant neoplasms/ Treatment of adult patients with metastatic gastric cancer who have received at least two prior regimens

Summary of committee discussion:

The applicability of the class waiver as referred to in the Agency's Decision CW/0001/2015 to the planned therapeutic indication was confirmed. Other potential paediatric interests of this medicine suggested by PDCO: none identified at this stage.

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. Rivaroxaban - EMEA-000430-PIP01-08-M10

Bayer AG; Cardiovascular Diseases

Proposed indication: prevention of VTE risk in ambulatory cancer patients initiating systemic cancer therapy and at high risk for VTE

Summary of committee discussion:

The PDCO was of the view that the proposed indication "Prevention of VTE risk in ambulatory cancer patients initiating systemic cancer therapy and at high risk for VTE", falls under the scope of the above mentioned Decision, as the indication is considered to be covered by the waived condition "prevention of thromboembolic events" listed in the Agency's Decision.

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

9.1.1. August PDCO meeting- preparation of the written procedure

Scope: Adoption of timelines

Summary of committee discussion:

The timetable for the August written procedure was adopted with some changes.

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 June 2018 was presented to the PDCO members.
The members were also informed about 2 medicinal products, Mepsevii and Inovelon for which the CHMP adopted a positive opinion recommending a paediatric indication during their meeting in June 2018.

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

CHMP/PDCO joint session

Summary of committee discussion:

The experience from the first 1.5 years of the interaction was presented to both Committees.

9.2.3. Concept paper on the need for revision of the guideline on the investigation of medicinal products in the term and preterm neonate

Summary of committee discussion:

The Concept paper on the need for revision of the guideline on the investigation of medicinal products in the term and preterm neonate was adopted by CHMP during the ORGAM meeting in July. Final adoption of the document by the PDCO took place during the July PDCO plenary.

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

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

Summary of committee discussion:

The coordinator of the Newcastle CCLG (Children's Cancer and Leukaemia Group) Pharmacology Group presented the structure, aims and current projects of the network to the PDCO. The network, which specialises in paediatric oncology and related pharmacology, and which encompasses more than 20 collaborating centres, was formed in 2000 and runs stand-alone pharmacology trials sponsored by the Newcastle Hospitals NHS Foundation Trust, or larger national and European trials. Currently 8 active paediatric pharmacology trials are open for recruitment (75-100 patients recruited per year). Funding is received, among others, through ECMC (Experimental Cancer Medicine Centres) and Cancer Research UK centre grant for Newcastle Cancer Centre. Moreover, the network offers regular training courses to national research nurses. Recent publications related to patient welfare, e.g. blood volumes in paediatric clinical trials. The network had so far not been formally involved in discussions on PIPs. However, the network would be willing to provide the PDCO with consolidated network feedback (on non-confidential topics) if approached by the Committee.

9.5. Cooperation with International Regulators

9.5.1. WHO-convened PAWG - Research Toolkit for Paediatric Antiretroviral Drug and Formulation Development – response to the WHO PAWG

PDCO member: Dirk Mentzer;

Summary of committee discussion:

The response to the open letter from PAWG to the PDCO, dated 28 May 2018, was endorsed by the Committee.

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. Update on relocation to Amsterdam

Summary of committee discussion:

The PDCO Committee was updated on the relocation status.

10.1.2. Training on paediatric requirements/legislations/initiatives in other regions – US

Summary of committee discussion:

The PDCO was informed about the legislative requirements related to paediatric drug development in the US.

10.1.3. Paediatric medicines Regulators' Network (PmRN) - WHO interactions – POSTPONED

10.1.4. Priority needs and plans for training 2018 – 2020

Summary of committee discussion:

The Committee was updated on the EU Network Training Centre, and specifically on the training available on paediatric topics in the EU NTC Learning Management System. In response to a request to consider priority areas for training in the future, various suggestions were given relating to training on (basic) modelling and simulation, methodology, PK/PD (paediatric aspects) and statistics. Training on the regulatory framework, particularly for new members, was considered important. Interest was also expressed in opportunities for learners to engage directly with experts in a specific area of expertise, possibly through webinars set up for such purpose. Further discussion will be organised between the EU NTC Secretariat, concerned EMA colleagues and interested PDCO members.

10.1.5. 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 that the action plan was being finalised taking into account the Agency's Business Continuity Planning (BCP) and that adoption and publication was planned for September.

10.1.6. Report from the SRLM Oslo meeting

Summary of committee discussion:

Feedback from the SRLM in Oslo was presented to the Committee.

10.1.7. Telematics strategy 2025

Summary of committee discussion:

The Concept paper outlining the content of the future EU Telematics strategy 2020 – 2025 was presented to the Committee.

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

Scientific and regulatory topics relevant for PIP were discussed.

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 paediatric inventory group continue working on a 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 24-27 July 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	No participation in final deliberations and voting on:	Belimumab - EMEA-000520-PIP02-13-M02, Retigabine - EMEA-000116-PIP01-07-M09, Mepolizumab - Orphan - EMEA-000069-PIP04-13-M02
Karen Van Malderen	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Suzana Mimica Matanovic	Alternate	Croatia	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	
Irja Lutsar	Member	Estonia	No interests declared	
Ann Marie Kaukonen	Member	Finland	No interests declared	
Pia Annunen	Alternate	Finland	No participation in discussion, final deliberations and voting on:	EMEA-002350-PIP01-18
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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Eleni Katsomiti	Member	Greece	No interests declared	
Ágnes Gyurasics	Member (CHMP member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	
Sara Galluzzo	Member	Italy	No interests declared	
Alessandro Jenkner	Alternate	Italy	No interests declared	
Dina Apele-Freimane	Member	Latvia	No restrictions applicable to this meeting	
Sigita Burokiene	Member	Lithuania	No interests declared	
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No interests declared	
Maaike van Dartel	Member	Netherlands	No interests declared	
Siri Wang	Member	Norway	No interests declared	
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	
Angeliki Siapkara	Member	United Kingdom	No interests declared	
Martina Riegl	Alternate	United Kingdom	No interests declared	
Fernando Cabanas	Member	Healthcare Professionals' Representative	No interests declared	
Riccardo Riccardi	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Catherine Cornu	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
Doina Plesca	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Günter Karl-Heinz Auerswald	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Michal Odermarsky	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Viviana Giannuzzi	Alternate	Patients' Organisation Representative	No restrictions applicable to this meeting	
Gareth Veal	Expert - in person*	EnprEMA	No restrictions applicable to this meeting	
Fahimeda Ali	Expert - in person*	United Kingdom	No interests declared	
Shiva Ramroop	Expert - in person*	United Kingdom	No interests declared	
Meeting run with support from relevant EMA staff				

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

13. Explanatory notes

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

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

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

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

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

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

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