18 August 2017
EMA/PDCO/531408/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes of the meeting on 15-18 August 2017

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

15 August 2017, 14:00 - 19:00, room 3A

16 August 2017, 08:30 - 19:00, room 3A

17 August 2017, 08:30 - 19:00, room 3A

18 August 2017, 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.

1.3. Adoption of the minutes

The minutes of the July 2017 PDCO plenary meeting were adopted with amendments and will be published on the EMA website.

2. Opinions

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

2.1. Opinions on Products

2.1.1. Filgotinib - EMEA-001619-PIP04-17

Gilead Sciences International Ltd.; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis, and juvenile idiopathic arthritis)

Day 60 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

The applicant provided the requested clarifications to the draft opinion in line with the outcome of the Day 30 discussion. A positive opinion was adopted.

2.1.2. Influenza virus surface antigens (haemagglutinin) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin) of strain A (H1N1) / Influenza virus surface antigens (haemagglutinin) of strain B (Victoria lineage) - EMEA-002027-PIP02-17

Adimmune Corporation; Prevention of Influenza infection

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The applicant provided a response to the draft opinion on 31 July 2017.
As all issues raised at Day 30 were solved, the PDCO adopted a positive opinion on the paediatric plan proposed by the applicant for this egg-based quadrivalent inactivated influenza vaccine.

2.1.3. Ramucirumab - EMEA-002074-PIP01-16

Eli Lilly and Company Limited; Treatment of intestinal malignant neoplasm, Treatment of gastric cancer and gastro-oesophageal junction adenocarcinoma, Treatment of liver cancer, Treatment of urinary tract malignant neoplasm, Treatment of lung malignant neoplasm

Day 90 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the procedure for ramucirumab

The requestes for the product-specific waivers, which were considered already acceptable at the time of the first phase of the procedure, were maintained.
In summary, PDCO agreed with the applicant's request for the waivers and PDCO recommended granting a waiver for all subsets of the paediatric population (from birth to less than 18 years of age) in the following conditions:
- treatment of gastric cancer and gastro-oesophageal junction adenocarcinoma, treatment of intestinal malignant neoplasm and treatment of lung malignant neoplasm on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).
- treatment of liver cancer and treatment of urinary tract malignant neoplasm 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 subset(s).
The PDCO also concluded to adopt the Opinion at D90.

2.1.4. Recombinant human monoclonal antibody to GM-CSF - EMEA-001882-PIP02-16

GlaxoSmithKline Trading Services Limited; Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis) / Treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 1 year of age and older, Treatment of active polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years of age and older

Day 120 opinion

Immunology-Rheumatology-Transplantation

Summary of committee discussion:

Based on the assessment of this application the PDCO at their August 2017 meeting agreed a positive opinion for recombinant human monoclonal antibody to GM-CSF EMEA-001882-PIP02-16 for the condition treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis) including a deferral

2.1.5. tazobactam / ceftolozane - EMEA-001142-PIP02-16

Merck Sharp & Dohme (Europe), Inc.; Treatment of abdominal and gastrointestinal infections, Treatment of urinary tract infections, Treatment of pneumonia / Treatment of nosocomial pneumonia, Treatment of complicated intra-abdominal infections (cIAI). Treatment of complicated urinary tract infections (cUTI)

Day 120 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO adopted a positive opinion.

2.1.6. 5-(4-Fluoro-1-benzothiophen-2-yl)-8-methyl-1,9-dihydro-2H-[1,3]oxazolo[4,5-H][2,3]benzodiazepin-2-one - EMEA-002057-PIP01-16

Les Laboratoires Servier; Treatment of ischemic stroke to improve recovery

Day 120 opinion

Neurology

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the modified PIP proposal hence adopted a positive opinion.

2.1.7. Pyridopyrimidione SMN2 Splicing Modifier - EMEA-002070-PIP01-16

Roche Registration Limited; Treatment of spinal muscular atrophy

Day 120 opinion

Neurology

Summary of committee discussion:

The PDCO adopted a positive opinion on the agreement of a PIP and a deferral .

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

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

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed its view expressed on day 90 taking into account the applicant's clarifications and considered that all remaining issues were adequately resolved.

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO adopted a positive opinion for (Z)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-4-(2-(of sulfamoylamino) ethylamino)-1,2,5-oxadiazole-3-carboximidamide in the condition of "treatment of all conditions included in the category of malignant neoplasms including Hodgkin lymphoma (except nervous system, haematopoietic and lymphoid tissue other than Hodgkin lymphoma)".

2.1.9. Autologous CD4+ and CD8+ T cells Expressing a CD19-Specific Chimeric Antigen Receptor (JCAR017) - EMEA-001995-PIP01-16

Celgene Europe Limited; Treatment of B-lymphoblastic leukemia/lymphoma, Treatment of mature B-cell neoplasms / Treatment of pediatric patients with relapsed or refractory CD19+ B-cell acute lymphoblastic leukemia, Treatment of pediatric patients with relapsed or refractory CD19+ B-NHL, including diffuse large B-cell lymphoma, Burkitt lymphoma, and primary mediastinal large B-cell lymphoma

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO discussed the procedure at Day 120 during the August 2017 plenary meeting. The PDCO adopted a positive Opinion at day 120.

2.1.10. Enasidenib - Orphan - EMEA-001798-PIP02-16

Celgene Europe Ltd; Treatment of Acute Myeloid Leukaemia / Treatment of patients aged 2 to 21 years old with relapsed or refractory IDH2- mutated AML after at least 2 prior induction attempts.

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO adopted a positive opinion on the PIP after reviewing the responses to the request of modification provided by the applicant, and after agreeing with the applicant further changes in the period between day 90 and day 120, in order to solve the few issues that had remained open after the applicant's responses.

2.1.11. Entospletinib - EMEA-002058-PIP01-16

Gilead Sciences International Ltd; Treatment of Acute myeloid leukemia

Day 120 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the procedure taking into account the responses provided after the D90 discussion and the comments received from the applicant on the draft opinion.

In conclusion, the PDCO recommends granting a paediatric investigation plan for entospletinib and a deferral.

2.1.12. Angiotensin II - EMEA-001912-PIP02-16

La Jolla Pharmaceutical Company; Catecholamine-resistant hypotension associated with distributive shock

Day 120 opinion

Other

Summary of committee discussion:

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agreed with the modified PIP proposal hence adopted a positive opinion.

2.1.13. Phenyl- and piperidin-containing derivative of amiloride - EMEA-002082-PIP01-16

Boehringer Ingelheim International GmbH; Treatment of cystic fibrosis / indicated to improve lung function and reduce pulmonary exacerbations for patients in all age groups with cystic fibrosis in conjunction with standard therapies.

Day 120 opinion

Pneumology - Allergology

Summary of committee discussion:

All remaining issues at Day 90 were resolved satisfactorily.

The PDCO adopted a positive opinion, including a deferral.

2.1.14. Amlodipine / Perindopril arginine / Bisoprolol fumarate - EMEA-002173-PIP01-17

Les Laboratoires Servier; Treatment of vascular hypertensive disorders, Treatment of ischaemic coronary artery disorders

Day 60 opinion

Cardiovascular Diseases

Summary of committee discussion:

The PDCO confirmed the Day 30 discussion at their August 2017 meeting
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 amlodipine / bisoprolol fumarate / perindopril arginine for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of hypertension, Treatment of ischaemic coronary artery disorders.

2.1.15. amlodipine besylate / hydrochlorothiazide / candesartan cilexetil - EMEA-002174-PIP01-17

Zentiva, k.s.; Treatment of essential hypertension

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 amlodipine (besylate) / candesartan (cilexetil) / hydrochlorothiazide for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of hypertension.

2.1.16. Lenalidomide - Orphan - EMEA-000371-PIP04-16

Celgene Europe Limited; treatment of mature b-cell neoplasms

Day 60 opinion

Oncology

Summary of committee discussion:

The PDCO re-discussed the requested product specific waiver for lenalidomide for the ‘treatment of mature B-cell neoplasms’ taking into consideration the additional justifications provided by the applicant after the D30 discussion, on 02 August 2017.

In conclusion, based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for lenalidomide for all subsets of the paediatric population (birth to less than 18 years of age) in the condition of treatment of mature b-cell neoplasms 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 subset(s)'.
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 such as acute myeloid leukaemia for which paediatric clinical trials are already ongoing. 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. Latanoprost / Netarsudil - EMEA-002175-PIP01-17

Aerie Pharmaceuticals Ireland Ltd; Treatment of Glaucoma

Day 60 opinion

Ophthalmology

Summary of committee discussion:

A positive opinion was adopted on D60.
Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the applicant's request for a waiver. The PDCO recommends granting a waiver for Latanoprost / Netarsudil for all subsets of the paediatric population (0 to 18 years of age) in the condition of Treatment of Glaucoma.

2.1.18. benralizumab - EMEA-001214-PIP02-17

AstraZeneca AB; chronic rhinosinusitis with nasal polyposis

Day 60 opinion

Oto-rhino-laryngology

Summary of committee discussion:

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

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. Damoctocog alfa pegol - EMEA-C-001229-PIP01-11-M03

Bayer AG; Treatment of hereditary Factor VIII deficiency

Day 30 letter

Haematology-Hemostaseology

Summary of committee discussion:

PDCO adopted on 15 August 2017 an opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0195/2017) of 10 July 2017.

2.2.2. doravirine - EMEA-C1-001676-PIP01-14-M01

Merck Sharp & Dohme (Europe), Inc.; Treatment of human immunodeficiency virus type 1 (HIV-1) infection

Day 60 letter

Infectious Diseases

Summary of committee discussion:

The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0115/2017) of 21 April 2017.
The PDCO finalised on 18 August 2017 this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be completed until this date.

2.2.3. lamivudine / tenofovir disoproxil funarate / doravirine - EMEA-C1-001695-PIP01-14-M01

Merck Sharp & Dohme (Europe), Inc.; Treatment of human immunodeficiency virus type 1 (HIV-1) infection

Day 60 letter

Infectious Diseases

Summary of committee discussion:

The PDCO discussed the completed studies at its August 2017 meeting and considered that these are compliant with the latest Agency's Decision (P/0116/2017) of 28 April 2017.
The PDCO finalised on 18 August 2017 this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be completed until this date.

2.2.4. Galcanezumab - EMEA-C1-001860-PIP04-16

Eli Lilly Nederland B.V.; Preventiont of cluster headache

Day 30 letter

Neurology

Summary of committee discussion:

The PDCO discussed the compliance request at its August 2017 meeting.
The PDCO finalised on 18 August 2017 this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be completed until this date.

2.2.5. Galcanezumab - EMEA-C2-001860-PIP03-16

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

Day 30 letter

Neurology

Summary of committee discussion:

The PDCO discussed the compliance request at its August 2017 meeting.
The PDCO finalised on 18 August 2017 this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be completed until this date.

2.2.6. Mexiletine hydrochloride - EMEA-C1-002012-PIP01-16

Lupin (Europe) Ltd; Treatment of myotonic disorders

Day 30 letter

Neurology

Summary of committee discussion:

The PDCO finalised on 15 August 2017 this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be initiated or completed until this date.

2.2.7. Autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 - EMEA-C1-001654-PIP01-14-M01

Novartis Europharm Limited; Treatment of B cell acute lymphoblastic leukaemia/ lymphoblastic lymphoma

Day 30 letter

Oncology

Summary of committee discussion:

The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0337/2016) of 02 December 2016.
The PDCO finalised on 18 August 2017 this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be completed until this date.

2.2.8. depatuxizumab mafodotin - EMEA-C1-001732-PIP02-15

AbbVie Ltd; Treatment of high-grade glioma

Day 30 letter

Oncology

Summary of committee discussion:

The PDCO finalised on 18 August 2017 this partially completed compliance procedure and confirmed the compliance of all those studies contained in the agreed paediatric investigation plan that were to be completed until this date.

2.2.9. entolimod - EMEA-C1-002020-PIP01-16

TMC Pharma Services Ltd.; Treatment of acute Radiation Syndrome

Day 30 letter

Other

Summary of committee discussion:

The PDCO discussed the completed studies and considered that these are not compliant with the latest Agency's Decision (P/0104/2017) of 11 April 2017.

The PDCO finalised on 16 August 2018 this partially completed compliance procedure.

2.2.10. asenapine (maleate) - EMEA-C-000228-PIP01-08-M04

N.V. Organon; Treatment of bipolar I disorder

Day 30 discussion

Psychiatry

Summary of committee discussion:

The PDCO confirmed that all the measures included in the PIP have been completed in compliance with the requirements. A positive opinion has been adopted.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Alirocumab - EMEA-001169-PIP01-11-M03

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

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

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/0102/2016 of 15 April 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.2. Naloxegol (as naloxegol oxalate) - EMEA-001146-PIP01-11-M03

Kyowa Kirin Pharmaceutical Development Limited; Treatment of opioid-induced constipation

Day 60 opinion

Gastroenterology-Hepatology

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.

2.3.3. Eltrombopag (eltrombopag olamine) - EMEA-000170-PIP03-13-M03

Novartis Europharm Limited; Bone Marrow Depression and Hypoplastic Anaemia / Treatment of cytopenias in paediatric patients with severe aplastic anaemia who are no receiving hematopoietic stem cell transplant

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/0007/2017 of 31/01/2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.4. Human thrombin / Human fibrinogen - EMEA-001340-PIP01-12-M03

Mallinckrodt Pharmaceuticals Ireland Ltd; Treatment of haemorrhage resulting from a surgical procedure / Supportive treatment where standard surgical techniques are insufficient for improvement of haemostasis

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

Additional clarifications were provided by the applicant on 4 August 2017.

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO therefore considered that only some of the proposed changes could be accepted. For these changes the PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0295/2016 of 4 November 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.5. roxadustat - EMEA-001557-PIP01-13-M01

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

Day 60 opinion

Haematology-Hemostaseology

Summary of committee discussion:

The PDCO view expressed at Day 30 was re-discussed and endorsed. The PDCO considered that most of the proposed changes could be accepted
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0020/2015 of 30 January 2015).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.6. Tenofovir alafenamide (as fumarate) - EMEA-001584-PIP01-13-M02

Gilead Sciences International Ltd.; Treatment of chronic hepatitis B / indicated for the treatment of chronic hepatitis B infection in paediatric patients aged 2 years and above.

Day 60 opinion

Infectious Diseases

Summary of committee discussion:

The PDCO discussed this application on D60. The applicant's responses to the D30 issues were acknowledged.

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO considered that some of the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0221/2016 of 12 August 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.7. avacopan - Orphan - EMEA-002023-PIP01-16-M01

ChemoCentryx, Ltd.; Treatment of ANCA-associated vasculitis

Day 30 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 on Day 30 a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0082/2017 of 22 May 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.3.8. L-asparaginase encapsulated in erythrocytes - Orphan - EMEA-000341-PIP02-09-M04

ERYTECH pharma S.A.; Treatment of acute lymphoblastic leukaemia

Day 30 opinion

Oncology

Summary of committee discussion:

The PDCO discussed the modification request during the August 2017 plenary meeting.

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/0188/2015 of 4 September 2015).

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

2.3.9. Japanese encephalitis vaccine (inactivated, adsorbed) - EMEA-000559-PIP01-09-M04

Valneva Austria GmbH; Prevention of Japanese encephalitis / Active immunization against Japanese encephalitis in children aged 2 months to <18 years

Day 30 opinion

Vaccines

Summary of committee discussion:

The PDCO discussed this modification on 18 August 2017.

Based on the review of the rationale submitted by the applicant for modifying the agreed paediatric investigation plan, the PDCO therefore 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/249/2011 of 25 October 2011).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.4. Opinions on Re-examinations

No items.

2.5. Finalisation and adoption of opinions

3. Discussion of applications

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

3.1. Discussions on Products D90-D60-D30

3.1.1. Crisaborole - EMEA-002065-PIP01-16

Mild to moderate atopic dermatitis

Day 90 discussion

Dermatology

3.1.2. Ligelizumab - EMEA-001811-PIP02-15

Treatment of chronic spontaneous urticaria

Day 90 discussion

Dermatology

3.1.3. (2S)-2-{[(2R)-2-[({[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-l]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino}butanoic acid - Orphan - EMEA-002054-PIP01-16

Albireo AB; Treatment of Progressive Familial Intrahepatic Cholestasis

Day 90 discussion

Gastroenterology-Hepatology

3.1.4. Iclaprim mesylate - EMEA-000345-PIP02-16

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

Day 90 discussion

Infectious Diseases

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

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

Day 90 discussion

Infectious Diseases

3.1.6. allopregnanolone - EMEA-002051-PIP01-16

Treatment of Status Epilepticus

Day 90 discussion

Neurology

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

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

Day 90 discussion

Oncology

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

Infant Bacterial Therapeutics AB; Prevention of necrotising enterocolitis

Day 90 discussion

Other / Neonatology - Paediatric Intensive Care / Gastroenterology-Hepatology

3.1.9. ivacaftor / tezacaftor - EMEA-002086-PIP01-16

Treatment of Cystic Fibrosis

Day 90 discussion

Pneumology - Allergology

3.1.10. Fluoromisonidazole (18F) - EMEA-001977-PIP04-17

Visualisation of tissue hypoxia in solid tumours for diagnostic purposes / Gliomas, Renal Cell Carcinoma, Sarcomas

Day 60 discussion

Diagnostic / Oncology

3.1.11. EMEA-002109-PIP01-16

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

Day 60 discussion

Gastroenterology-Hepatology

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

Novartis Europharm Limited; Treatment of sickle cell disease

Day 60 discussion

Haematology-Hemostaseology

3.1.13. EMEA-002184-PIP01-17

Treatment of excessive daytime sleepiness / Treatment of excessive daytime sleepiness in narcolepsy patients

Day 60 discussion

Neurology

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

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

Day 60 discussion

Neurology

3.1.15. Survival Motor Neuron Gene by Self-Complementary Adeno Associated Virus Serotype 9 - Orphan - EMEA-002168-PIP01-17

AveXis EU Limited; Spinal Muscular Atrophy

Day 60 discussion

Neurology

3.1.16. 16-base single-stranded PNA oligonucleotide linked to a 7 aminoacid peptide C214H290N114O57 - Orphan - EMEA-002119-PIP01-17

BIOGENERA SPA; Treatment of Neuroblastoma (NB) with MYCN expression/amplification

Day 60 discussion

Oncology

3.1.17. durvalumab - EMEA-002028-PIP01-16

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

Day 60 discussion

Oncology

3.1.18. Ixazomib - Orphan - EMEA-001410-PIP02-17

Takeda Pharm A/S; Treatment of Acute Lymphoblastic Leukaemia (ALL), Treatment of Multiple Myeloma (MM) / Treatment of adult patients with Newly Diagnosed Multiple Myeloma (NDMM), Treatment of paediatric patients diagnosed with relapsed precursor B-ALL or T-ALL

Day 60 discussion

Oncology

3.1.19. palbociclib - EMEA-002146-PIP01-17

Treatment of rhabdomyosarcoma, Treatment of Ewing sarcoma / treatment of refractory or recurrent rhabdomyosarcoma, treatment of refractory or recurrent Ewing sarcoma

Day 60 discussion

Oncology

3.1.20. tremelimumab - EMEA-002029-PIP01-16

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

Day 60 discussion

Oncology

3.1.21. sodium thiosulfate - EMEA-002147-PIP02-17

Platinum-induced ototoxic hearing loss / Reducing ototoxicity in patients > 1 month and <18 years of age receiving cisplatin chemotherapy for standard risk hepatoblastoma

Day 60 discussion

Oncology / Oto-rhino-laryngology

3.1.22. (R) - azasetron (as besylate) - Orphan - EMEA-002165-PIP01-17

Sensorion SA; Otoxicity, Prevention of cisplatin-Induced otoxicity

Day 60 discussion

Oto-rhino-laryngology

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

Essential hypertension / Treatment of essential hypertension as substitution therapy in adult

patients whose blood pressure is adequately controlled on the combination of amlodipine, irbesartan and hydrochlorothiazide, taken either as three single -component formulations or as a dual-component and a single component formulation

Day 30 discussion

Cardiovascular Diseases

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

An adjuvant treatment of stable effort angina pectoris for Adults only

Day 30 discussion

Cardiovascular Diseases

3.1.25. Bimekizumab - EMEA-002189-PIP01-17

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

Day 30 discussion

Dermatology

3.1.26. Efpegsomatropin - EMEA-001227-PIP02-17

Treatment of growth hormone deficiency

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

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

E78.0 Pure hypercholesterolaemia, I25 Chronic ischaemic heart disease, E78.2 Mixed hyperlipidaemia

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Cardiovascular Diseases

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

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

Day 30 discussion

Gastroenterology-Hepatology

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

NASH / NASH with Fibrosis

Day 30 discussion

Gastroenterology-Hepatology

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

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

Day 30 discussion

Infectious Diseases

3.1.31. Pritelivir - EMEA-002180-PIP01-17

Topical treatment of recurrent herpes labialis

Day 30 discussion

Infectious Diseases

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

Premacure AB; Chronic lung disease of prematurity

Day 30 discussion

Neonatology - Paediatric Intensive Care

3.1.33. Lasmiditan - EMEA-002166-PIP01-17

Migraine with and without aura

Day 30 discussion

Neurology

3.1.34. capmatinib - EMEA-002203-PIP01-17

Treatment of lung malignant neoplasms

Day 30 discussion

Oncology

3.1.35. taselisib - EMEA-002210-PIP01-17

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

Day 30 discussion

Oncology

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

AbbVie Ltd; Treatment of breast cancer

Day 30 discussion

Oncology

3.1.37. Oxymetazoline HCL / Pilocarpine HCL - EMEA-002181-PIP01-17

Presbyopia

Day 30 discussion

Ophthalmology

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

Treatment of elevated cholesterol

Day 30 discussion

Other / Cardiovascular Diseases

3.1.39. Tanezumab - EMEA-001635-PIP03-17

Treatment of chronic pain

Day 30 discussion

Pain

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

Treatment of IgE-mediated cow's milk allergy

Day 30 discussion

Pneumology - Allergology

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

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

Day 30 discussion

Infectious Diseases

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

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

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

Day 30 discussion

Cardiovascular Diseases / Haematology-Hemostaseology

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

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

Day 30 discussion

Cardiovascular Diseases / Haematology-Hemostaseology

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

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

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

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

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

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

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

Roche Registration Limited; Anaemia associated with chronic kidney disease

Day 30 discussion

Haematology-Hemostaseology

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

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

Day 30 discussion

Haematology-Hemostaseology

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

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

Day 30 discussion

Immunology-Rheumatology-Transplantation

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

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

Day 30 discussion

Immunology-Rheumatology-Transplantation

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

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

Day 30 discussion

Immunology-Rheumatology-Transplantation

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

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

Day 30 discussion

Immunology-Rheumatology-Transplantation

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

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

Day 30 discussion

Infectious Diseases

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

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

Day 30 discussion

Infectious Diseases

3.3.13. Fostemsavir (tromethamine) - EMEA-001687-PIP01-14-M02

ViiV Healthcare UK Ltd; Treatment of human immunodeficiency virus (HIV-1) infection / Treatment of HIV-1 infection as part of a combination therapy in paediatric patients who have no more than 2 remaining available fully active antiretroviral therapies

Day 30 discussion

Infectious Diseases

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

Pfizer Limited; Duchenne Muscular Dystrophy

Day 30 discussion

Neurology

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

Novartis Europharm Limited; Prevention of migraine headaches

Day 30 discussion

Neurology

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

Teva GmbH; Prevention of migraine headaches

Day 30 discussion

Neurology

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

Pfizer Limited; Treatment of Acute Myloid Leukaemia

Day 30 discussion

Oncology

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

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

Day 30 discussion

Other

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

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

Day 30 discussion

Other / Oncology

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

Grünenthal GmbH; Treatment of chronic pain

Day 30 discussion

Pain

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

Chiesi Farmaceutici S.p.A.; COPD, Asthma / Maintenance therapy of asthma where use of a

combination product (inhaled corticosteroid and long-acting beta2-agonist) is appropriate: - patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting beta2-agonist or - patients already adequately controlled on both inhaled corticosteroids and long-acting beta2-agonists.

Day 30 discussion

Pneumology - Allergology

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

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

Day 30 discussion

Pneumology - Allergology

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

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

Day 30 discussion

Pneumology - Allergology

3.3.24. Brexpiprazole - EMEA-001185-PIP01-11-M04

Otsuka Europe Development and Commercialisation Ltd ; Schizophrenia / Treatment of schizophrenia in adolescents 13 to 17 years of age.

Day 30 discussion

Psychiatry

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

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

Day 30 discussion

Uro-nephrology / Neurology

3.3.26. 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 - EMEA-001782-PIP01-15-M01

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

Day 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 17 October 2017 for Nomination of Rapporteur and Peer reviewer

Summary of committee discussion:

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:

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

6.1.1. Intepirdine - EMEA-13-2017

Axovant Sciences Ltd.; All classes of medicinal products for treatment of Alzheimer's disease/Treatment of mild to moderate Alzheimer's disease

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 indications was confirmed.

6.1.2. Humanized recombinant IgG4 anti-human tau antibody - EMEA-14-2017

AbbVie Ltd; All classes of medicinal products for treatment of Alzheimer's disease/ Treatment of early Alzheimer's disease to delay disease progression.

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 indications was confirmed.

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

The members were also informed about 5 medicinal products, Symtuza, Verkazia, Humira, Sovaldi and Vimpat for which the CHMP adopted a positive opinion recommending a paediatric indication during their meeting in July 2017.

9.3. Coordination with EMA Working Parties / Working Groups / Drafting Groups

9.3.1. Non-clinical Working Group: D30 Products identified

PDCO member: Karen van Malderen

Summary of committee discussion:

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

9.3.2. Formulation Working Group

PDCO member: Brian Aylward

Summary of committee discussion:

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

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

PDCO member: Marianne Orholm, Maria Fernandez Cortizo

Summary of committee discussion:

The PDCO discussed the CMDh request to the Paediatric Committee related to Ozenoxacin.

A draft response will be prepared by the PDCO rapporteurs, circulated in the post-mail for comments of other PDCO members, and presented for adoption by the committee at next month meeting.

9.3.4. Report from workshop on personalised medicines held by EMA on 14 March 2017

Summary of committee discussion:

Report from workshop on personalised medicines was shared with PDCO for information.

9.3.5. Lactose of bovine origin-containing medicinal products

Pfizer Croatia d.o.o. (Solu-Medrol), various

PDCO member: Adriana Andric; Scope: Review of the benefit-risk balance following notification by Croatia of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Summary of committee discussion:

PDCO was informed on the review of the benefit-risk balance of medicinal products containing lactose of bovine origin, based on the pharmacovigilance data.

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

PDCO member: Sylvie Benchetrit;

Summary of committee discussion:

PDCO was invited for comments on the draft guideline on clinical investigation of medicinal products in the treatment of epileptic disorders.

9.4. Cooperation within the EU regulatory network

9.4.1. European Network of Paediatric Research (Enpr) – at European Medicines Agency (Enpr-EMA): Presentation of the the European Child & Adolescent Psychopharmacology Network (ECAPN)

Summary of committee discussion:

Alessandro Zuddas, the coordinator of the European Child and Adolescent Clinical Psychopharmacology Network (ECAPN) presented the network's main aims and initiatives to the PDCO. ECAPN is a network of currently 12 clinical centres specialised in child and adolescent psychiatry in the EU, many of which lead a national network of affiliated centres. It was established by members of the ECNP (European College of Neuropsychopharmacology) in order to facilitate the conduct of high-quality translational and clinical research in the field of paediatric psychopharmacology. The network aims to identify unmet paediatric needs in psychopharmacology, conducts collaborative industry-sponsored and academic trials, and develops strategies to improve state-of-the-art prescribing in practice.

As mentioned in the draft 10-year report on the implementation of the Paediatric Regulation the disease burden in the paediatric population in the EU is highest for mental and behavioural disorders (20% of total burden, based on disability-adjusted-life-years) but only 3% of agreed PIPs pertain to this therapeutic area. Alessandro Zuddas confirmed that the lack of authorised, effective medicines for many childhood disorders is a significant problem in the treatment of mental illnesses in the paediatric population. In addition to study proposals by industry, European collaborative efforts are needed to search for evidence-based approaches to prevent mental disorders with childhood/adolescence onset. Specific methodological issues of paediatric trials in this area include the enrolment of pathogenetically heterogeneous patients, limited generalisability and a high placebo effect, as well as a lack of validated biomarkers.

In order to make best use of the important experience within the network it could be beneficial if companies consulted ECAPN early on during the development, even before a PIP strategy is discussed with the PDCO. It was pointed out though, that even if a consultation of ECAPN takes place after PIP agreement, there is the possibility for applicants to request modifications of the agreed plan in order to consider any network advice.

The network offered to the PDCO the possibility to provide a consolidated network expert opinion on general scientific questions (as opposed to individual expert opinion) within a 1-month timeframe.

9.5. Cooperation with International Regulators

None

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

None

9.7. PDCO work plan

None

9.8. Planning and reporting

9.8.1. Presentation regarding T cells expressing Chimeric Antigen Receptors (CAR-Ts) – postponed to PDCO September meeting - POSTPONED

Action: For discussion

10. Any other business

None

11. Breakout sessions

The breakout session were cancelled.

12. List of participants

List of participants including any restrictions with respect to involvement of members/alternates/ experts following evaluation of declared interests for the 15 – 18 August 2017 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Dirk Mentzer	Chair	Germany	No interests declared	
Karl-Heinz Huemer	Member	Austria	No interests declared	
Johanna Wernsperger	Alternate	Austria	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Adriana Andrić	Member	Croatia	No interests declared	
Suzana Mimica Matanovic	Alternate	Croatia	No interests declared	
Georgios Savva	Member	Cyprus	No interests declared	
Jaroslav Sterba	Member	Czech Republic	No interests declared	
Peter Szitanyi	Alternate	Czech Republic	No interests declared	
Marianne Orholm	Member	Denmark	No interests declared	
Kirstine Moll Harboe	Alternate	Denmark	No interests declared	
Ann Marie Kaukonen	Member	Finland	No interests declared	
Sylvie Benchetrit	Member via TC	France	No interests declared	
Dominique Ploin	Alternate	France	No interests declared	
Sabine Scherer	Member	Germany	No interests declared	
Immanuel Barth	Alternate	Germany	No interests declared	
Eleni Katsomiti	Member	Greece	No interests declared	
Ágnes Gyurasics	Member (CHMP member)	Hungary	No interests declared	
Brian Aylward	Member	Ireland	No interests declared	
Alessandro	Alternate	Italy	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jenkner				
Dina Apele-Freimane	Member	Latvia	No interests declared	
Goda Vaitkeviciene	Alternate	Lithuania	No interests declared	
Carola de Beaufort	Member (CHMP alternate)	Luxembourg	No interests declared	
Herbert Lenicker	Alternate	Malta	No interests declared	
Siri Wang	Member	Norway	No interests declared	
Ine Skottheim Rusten	Alternate	Norway	No interests declared	
Marek Migdal	Member	Poland	No interests declared	
Helena Fonseca	Member	Portugal	No interests declared	
Hugo Tavares	Alternate via TC	Portugal	No interests declared	
Dana Gabriela Marin	Member (CHMP alternate)	Romania	No interests declared	
Stefan Grosek	Member	Slovenia	No interests declared	
Fernando de Andrés Trelles	Member	Spain	No interests declared	
Maria Jesús Fernández Cortizo	Alternate	Spain	No interests declared	
Ninna Gullberg	Member	Sweden	No interests declared	
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	
Catherine Cornu	Alternate	Healthcare Professionals' Representative	No participation in final deliberations and voting on:	EMEA-000019-PIP08-12-M03
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Günter Karl-Heinz Auerswald	Member	Patients' Organisation Representative	No restrictions applicable to this meeting	
Paola Baiardi	Alternate	Patients' Organisation Representative	No participation in final deliberations and voting on:	EMEA-001882-PIP02-16
Dimitrios Athanasiou	Member	Patients' Organisation Representative	No interests declared	
Alessandro Zuddas Unica	Expert - in person*	EnprEMA		

* Experts were only evaluated against the product(s) they have been invited to talk about.

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/