16 October 2018
EMA/PDCO/644788/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Paediatric Committee (PDCO)

Minutes of the meeting on 18-21 September 2018

Chair: Dirk Mentzer – Vice-Chair: Koenraad Norga

18 September 2018, 14:00-19:00, room 3A

19 September 2018, 08:30- 19:00, room 3A

20 September 2018, 08:30- 19:00, room 3A

21 September 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 August 2018 PDCO were adopted and will be published on the EMA website.

2. Opinions

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

2.1. Opinions on Products

No items

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

Celgene Europe Ltd; Treatment of solid malignant tumours

Day 30 opinion

Oncology

Summary of committee discussion:

The completed studies were checked for compliance.
The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision P/0257/2018 of 14 August 2018.
The PDCO adopted on 21 September 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/0257/2018 of 14 August 2018).

2.2.2. Glycerol Phenylbutyrate - EMEA-C-000297-PIP02-12-M02

Horizon Pharma Ireland Limited; Treatment of Urea Cycle Disorders

Day 60 opinion

Endocrinology-Gynaecology-Fertility-Metabolism

Summary of committee discussion:

The completed study was checked for compliance.
The PDCO took note of preceding procedures and reports on partially completed compliance. These studies were considered compliant with the Agency's Decision (P/0068/2014) of 14 March 2014, during the previous partial compliance check on 25 April 2014, EMEA-C1-000297-PIP02-12-M01.
The PDCO adopted on 21 September 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/0191/2018).

2.2.3. Human normal immunoglobulin - EMEA-C-001797-PIP01-15-M01

Octapharma Pharmazeutika Produktionsges.m.b.H; Treatment of primary immunodeficiency

Day 60 opinion

Immunology-Rheumatology-Transplantation / Haematology-Hemostaseology

Summary of committee discussion:

The PDCO finalised on 19 September 2018 this full compliance check procedure.
A positive opinion was granted.

2.2.4. Lubiprostone - EMEA-C4-000245-PIP01-08-M05

Sucampo AG; Treatment of Constipation

Day 30 letter

Gastroenterology-Hepatology

Summary of committee discussion:

The PDCO discussed the completed studies and considered that these are compliant with the latest Agency's Decision (P/0175/2018) of 15 June 2018.
The PDCO finalised on D30 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. Ceftaroline fosamil - EMEA-C2-000769-PIP01-09-M08

Pfizer Limited; Treatment of community-acquired pneumonia

Day 30 letter

Infectious Diseases

Summary of committee discussion:

The PDCO considered the completed study compliant with the latest Agency's Decision (P/0176/2018) of 15 June 2018.
Compliance with the agreed non-clinical study and the clinical studies has been confirmed in a previous compliance procedure EMEA-C1-000769-PIP01-09-M04 (compliance report EMA/178405/2015).
The PDCO finalised on 21 September 2018 this partially completed compliance procedure.

2.2.6. Gilteritinib - EMEA-C1-002064-PIP01-16

Astellas Pharma Europe B.V.; Treatment of acute myeloid leukemia

Day 30 letter

Oncology / Haematology-Hemostaseology

Summary of committee discussion:

The initiation of the non-clinical study was checked for compliance. The study was started in accordance with the agreed PIP.
The initiation of the study was therefore considered compliant with the latest Agency's Decision (P/0006/2018) of 19 January 2018.
The PDCO finalised on 21 September 2018 this partially completed compliance procedure.

2.2.7. Ranibizumab - EMEA-C1-000527-PIP04-13-M01

Novartis Europharm Limited; Treatment of retinopathy of prematurity

Day 60 letter

Ophthalmology

Summary of committee discussion:

The PDCO discussed the completed study and considered that it is compliant with the latest Agency's Decision (P/0010/2017) of 31 January 2017.

The PDCO finalised on 21 September 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.

2.2.8. Onasemnogenum abeparvovecum - EMEA-C1-002168-PIP01-17

AveXis Netherlands BV; Spinal muscular atrophy type IV

Day 30 letter

Neurology

Summary of committee discussion:

The PDCO discussed the compliance request on 21 September 2018.
PDCO concluded that the study is compliant with the latest Agency's Decision (P/0272/2018) of 14 August 2018.

The PDCO finalised on 21 September 2018 this partially completed compliance procedure.

2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

2.3.1. Peanut Allergen Extract - EMEA-001481-PIP01-13-M03

DBV Technologies S.A; peanut allergy

Day 30 opinion

Pneumology - Allergology

Summary of committee discussion:

The PDCO discussed the modification request on 21 September 2018. Most of the requested changes are acceptable.
The PDCO adopted at Day 30 a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0286/2015 of 27 November 2015) as requested by the applicant.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

2.4. Opinions on Re-examinations

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

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

Gastroenterology-Hepatology

Summary of committee discussion:

The applicant requested re-examination of the opinion to defer study initiation. The PDCO concluded that deferring initiation of the paediatric study until efficacy data in adults is available was acceptable. Finally, given the current unmet need for the treatment of pouchitis in children, the Committee agreed to specify the initiation date of the paediatric study in the Opinion. A positive opinion was adopted.

2.4.2. 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

Infectious Diseases

Summary of committee discussion:

The PDCO at their September 2018 meeting discussed the re-examination of the opinion requested by the applicant relating to wording previously included. The changes requested by the applicant were supported. However, the PDCO made additional comments that need to be taken into consideration – where applicable - when the applicant comes back for compliance check and MA.
A positive opinion was adopted.

2.5. Opinions on Review of Granted Waivers

2.5.1. Clostridium botulinum neurotoxin type A (150 kD), free from complexing proteins-EMEA-001039-PIP03-17

Merz Pharmaceuticals GmbH; Treatment of hemifacial spasm

Neurology / Ophtamology

Summary of committee discussion:

The PDCO discussed this review of the product specific waiver opinion in the condition treatment of hemifacial spasm and agreed to extend the waiver to include the formulation solution for injection in pre-filled syringe. A positive opinion was adopted.

2.6. Finalisation and adoption of opinions

No items

2.7. Partial Compliance Checks completed by EMA

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

2.7.1. Tenofovir - EMEA-C4-000533-PIP01-08-M07

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

Day 30 letter

Infectious Diseases

Summary of committee discussion:

The completed studies were confirmed to be compliant as set out in the EMA's Decision (P/0262/2017 of 4/9/20170).

2.8. Revision of the PDCO opinions

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

AbbVie Ltd.; Lung carcinoma (small cell and non-small cell carcinoma)

For information

Oncology

Summary of committee discussion:

Due to an internal error in the pharmaceutical form the above opinion had to be revised and adopted again by the PDCO via written procedure on 16 September 2018. The pharmaceutical form "Powder for solution for injection" was corrected to "Powder for solution for infusion".

3. Discussion of applications

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. Small molecule Janus Kinase -1 inhibitor - EMEA-002312-PIP01-17

Moderate to severe atopic dermatitis

Day 90 discussion

Dermatology

3.1.2. Cenicriviroc - EMEA-001999-PIP02-17

NASH with Stage 2-3 fibrosis

Day 90 discussion

Gastroenterology-Hepatology

3.1.3. Human monoclonal IgG1 antibody against Tissue Factor Pathway Inhibitor - Orphan - EMEA-002285-PIP01-17

Pfizer Limited; Treatment of haemophilia B, Treatment of haemophilia A

Day 90 discussion

Haematology-Hemostaseology

3.1.4. Upadacitinib Hemihydrate - EMEA-001741-PIP04-17

Treatment of Atopic Dermatitis

Day 90 discussion

Immunology-Rheumatology-Transplantation / Dermatology

3.1.5. Brincidofovir - Orphan - EMEA-001904-PIP02-17

Chimerix UK Limited; Treatment of AdV in immunocompromised patients

Day 90 discussion

Infectious Diseases

3.1.6. Brincidofovir - Orphan - EMEA-001904-PIP03-18

Chimerix UK Limited; Treatment of smallpox

Day 90 discussion

Infectious Diseases

3.1.7. Eubacterial Spores, Purified Suspension, Encapsulated - EMEA-001970-PIP02-17

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

Day 90 discussion

Infectious Diseases

3.1.8. Evobrutinib - EMEA-002284-PIP01-17

Treatment of multiple sclerosis

Day 90 discussion

Neurology

3.1.9. Brigatinib - EMEA-002296-PIP01-17

Inflammatory Myofibroblastic Tumors (IMT), Non-small cell lung cancer (NSCLC), Anaplastic large cell lymphoma (ALCL) / Treatment of anaplastic lymphoma kinase (ALK) positive advanced non-small cell lung cancer (NSCLC), Treatment of paediatric patients ≥1 years of age with ALK+ unresectable or recurrent IMT, Treatment in combination with standard chemotherapy in paediatric patients ≥1 years of age with newly diagnosed ALK+ ALCL at high risk for recurrence

Day 90 discussion

Oncology

3.1.10. Calcifediol - EMEA-002093-PIP02-17

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

Day 90 discussion

Uro-nephrology

3.1.11. Remimazolam (as besylate) - EMEA-001880-PIP01-18

Anaesthetic and allied procedures / ICU sedation, General anaesthesia, Procedural sedation

Day 30 discussion

Anaesthesiology

3.1.12. Ezetimibe / atorvastatin - EMEA-002410-PIP01-18

Treatment of hypercholesterolaemia

Day 30 discussion

Cardiovascular Diseases

3.1.13. Flurpiridaz F18 - EMEA-002413-PIP01-18

Coronary artery disease

Day 30 discussion

Cardiovascular Diseases

3.1.14. Glycopyrronium bromide - EMEA-002383-PIP01-18

Treatment of primary axillary hyperhidrosis

Day 30 discussion

Dermatology

3.1.15. Oxalobacter formigenes Strain HC-1 - Orphan - EMEA-000370-PIP02-18

OxThera AB; Treatment of Primary Hyperoxaluria

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Uro-nephrology

3.1.16. Dusquetide - EMEA-002306-PIP02-18

Treatment of Severe Oral Mucositis

Day 30 discussion

Gastroenterology-Hepatology

3.1.17. Adeno-associated viral vector serotype 5 containing a B domain deleted variant of human coagulation factor VIII gene - Orphan - EMEA-002427-PIP01-18

BioMarin International Limited; Treatment of patients with haemophilia A

Day 30 discussion

Haematology-Hemostaseology

3.1.18. Allogeneic CD34+ umbilical cord blood cells cultured ex vivo with Notch ligand Delta1 - Orphan - EMEA-002271-PIP01-17

Nohla Therapeutics, Inc.; Haematopoietic Stem Cell Transplantation (HSCT) / Patients with high risk haematologic malignancies undergoing myeloablative cord blood transplant (CBT)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.19. C1-esterase inhibitor human - Orphan - EMEA-002316-PIP02-18

CSL Behring GmbH; Treatment of antibody mediated rejection (AMR) in kidney transplantation

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.20. Ixekizumab - EMEA-001050-PIP02-18

Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis) / Children with juvenile idiopathic arthritis subtypes of enthesitis-related arthritis (including JoAS) and juvenile psoriatic arthritis

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.21. Sarilumab - EMEA-001045-PIP04-18

Treatment of muscular auto-immune disorder

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.1.22. Inolimomab - Orphan - EMEA-002372-PIP01-18

ElsaLys Biotech SA; Acute Graft versus Host Disease following heamatopoietic stem cell transplantation

Day 30 discussion

Immunology-Rheumatology-Transplantation / Oncology / Haematology-Hemostaseology

3.1.23. Entacapone / carbidopa monohydrate / levodopa - EMEA-002421-PIP01-18

Treatment of Parkinson's disease and Parkinsonism

Day 30 discussion

Neurology

3.1.24. Ganaxolone - EMEA-002341-PIP01-18

Treatment of Cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder / Adjunctive treatment of seizures in paediatric patients aged 2 to < 18 years old with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder

Day 30 discussion

Neurology

3.1.25. Alectinib hydrochloride - EMEA-002431-PIP01-18

Treatment of non-small cell lung cancer

Day 30 discussion

Oncology

3.1.26. Avadomide - Orphan - EMEA-002405-PIP01-18

Celgene Europe Limited; Treatment of mature B-cell neoplasms

Day 30 discussion

Oncology

3.1.27. Crizotinib - EMEA-001493-PIP02-18

Treatment of lung malignant neoplasms

Day 30 discussion

Oncology

3.1.28. Humanized IgG1 monoclonal antibody against GD2 (hu3F8) - EMEA-002346-PIP01-18

Treatment of neuroblastoma

Day 30 discussion

Oncology

3.1.29. Ipatasertib - EMEA-002396-PIP01-18

Treatment of prostate cancer, Treatment of breast cancer

Day 30 discussion

Oncology

3.1.30. Molibresib - EMEA-002406-PIP01-18

Treatment of malignant neoplasm of breast / Oestrogen receptor-positive breast cancer (ER+BC)

Day 30 discussion

Oncology

3.1.31. Pemigatinib - EMEA-002370-PIP01-18

Treatment of urothelial carcinoma, Treatment of cholangiocarcinoma

Day 30 discussion

Oncology

3.1.32. Aflibercept - EMEA-000236-PIP05-18

Treatment of retinopathy of prematurity (ROP)

Day 30 discussion

Ophthalmology

3.1.33. lentiviral vector containing the human ABCA4 gene for treatment of Stargardt's disease - Orphan - EMEA-002407-PIP01-18

Genzyme Europe B.V.; Treatment of inherited retinal disorders

Day 30 discussion

Ophthalmology

3.1.34. Triheptanoin - Orphan - EMEA-001920-PIP03-18

Ultragenyx Pharmaceutical Inc.; Glucose Transporter Type-1 Deficiency Syndrome

Day 30 discussion

Other

3.1.35. Ibuprofen - EMEA-002400-PIP01-18

Short-term symptomatic treatment of pain

Day 30 discussion

Pain

3.1.36. A fully human, IgG2 mAb - EMEA-002433-PIP01-18

Treatment of severe asthma in patients 6 year-olds and above as an add-on therapy of

standard of care

Day 30 discussion

Pneumology - Allergology

3.1.37. Dapagliflozin - EMEA-000694-PIP04-18

Treatment of N18 Chronic Kidney Disease

Day 30 discussion

Uro-nephrology

3.1.38. Recombinant Influenza Hemagglutinin-strain B (Yamagata lineage) / Recombinant Influenza Hemagglutinin-strain B (Victoria lineage) / Recombinant Influenza Hemagglutinin-strain A (H3N2 subtype) / Recombinant Influenza Hemagglutinin-strain A (H1N1 subtype) - EMEA-002418-PIP01-18

Prevention of influenza infection

Day 30 discussion

Vaccines

3.2. Discussions on Compliance Check

The following compliance checks have been put up for discussion and the members of the PDCO have been invited to comment on issues of possible non-compliance

3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

3.3.1. Enalapril maleate - EMEA-001706-PIP01-14-M02

Ethicare GmbH; Treatment of heart failure

Day 30 discussion

Cardiovascular Diseases

3.3.2. Tadalafil - EMEA-000452-PIP02-10-M05

Eli Lilly and Company Ltd; Benign prostatic hyperplasia, Pulmonary arterial hypertension / Treatment of Persistent Pulmonary Hypertension of the Newborn, Treatment of Pulmonary Arterial Hypertension

Day 30 discussion

Cardiovascular Diseases

3.3.3. Dabigatran etexilate mesilate - EMEA-000081-PIP01-07-M11

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

3.3.4. Edoxaban (tosylate) - EMEA-000788-PIP02-11-M08

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

3.3.5. Certolizumab pegol - EMEA-001071-PIP03-14-M01

UCB Pharma SA; Treatment of psoriasis / Treatment of moderate to severe chronic plaque psoriasis

Day 30 discussion

Dermatology

3.3.6. Lixisenatide - EMEA-000916-PIP01-10-M06

Sanofi-aventis R&D; Treatment of type 2 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.7. Migalstat hydrochloride - Orphan - EMEA-001194-PIP01-11-M03

Amicus Therapeutics UK Limited; Treatment of Fabry Disease

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

3.3.8. Tolvaptan - EMEA-001231-PIP02-13-M06

Otsuka Pharmaceutical Europe Ltd.; Polycystic Kidney Disease (PKD) / Treatment of progression of ADPKD, Treatment of progression of ARPKD

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Uro-nephrology

3.3.9. Apremilast - EMEA-000715-PIP05-13-M03

Celgene Europe Limited; Treatment of Behçet's Disease / Treatment of oral ulcers

associated with Behçet's Disease in children and adolescents from the age of 6 to less than 18 years

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.10. Autologous CD34+ haematopoietic stem cells transduced ex vivo with EFS lentiviral vector encoding for the human ADA gene - Orphan - EMEA-001974-PIP01-16-M02

Orchard Therapeutics Limited; Treatment of severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID)

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.11. Filgotinib - EMEA-001619-PIP04-17-M01

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

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.12. Ixekizumab - EMEA-001050-PIP01-10-M04

Eli Lilly & Company Limited; Plaque psoriasis / Treatment of severe chronic plaque psoriasis in paediatric patients from the age of 6 years who are not adequately controlled by topical therapies

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.13. Secukinumab - EMEA-000380-PIP02-09-M04

Novartis Europharm Limited; Chronic Idiopathic Arthritis / Treatment of juvenile psoriatic arthritis, Treatment of enthesitis-related arthritis

Day 30 discussion

Immunology-Rheumatology-Transplantation

3.3.14. Avibactam / ceftazidime - EMEA-001313-PIP01-12-M08

Pfizer Limited; Treatment of bacterial infections / Treatment of complicated urinary tract infections / Treatment of complicated intra-abdominal infections, treatment of pneumonia, treatment of infections due to aerobic Gram-negative organisms

Day 30 discussion

Infectious Diseases

3.3.15. Letermovir - Orphan - EMEA-001631-PIP01-14-M03

Merck Sharp & Dohme (Europe), Inc.; Prevention of cytomegalovirus infection / Prevention of CMV viremia and/or disease in at-risk patients having undergone an allogeneic HSCT or SOT

Day 30 discussion

Infectious Diseases

3.3.16. Amikacin sulfate - Orphan - EMEA-000525-PIP01-08-M06

Insmed Limited; Treatment of Pseudomonas aeruginosa lung infection/colonisation in cystic fibrosis patients / Treatment of nontubercolous mycobacterial (NTM) lung infection

Day 30 discussion

Infectious Diseases / Pneumology - Allergology

3.3.17. Nanobody directed towards the fusion protein of human respiratory syncytial virus - EMEA-001553-PIP01-13-M02

Ablynx NV; Treatment of RSV lower respiratory tract infection

Day 30 discussion

Neonatology - Paediatric Intensive Care

3.3.18. D-Sorbitol / Naltrexone HCl / (RS)-Bacoflen - Orphan - EMEA-002164-PIP01-17-M01

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

Day 30 discussion

Neurology

3.3.19. Eculizumab - Orphan - EMEA-000876-PIP03-14-M02

Alexion Europe SAS; Treatment of paediatric patients with relapsing neuromyelitis optica spectrum disorders

Day 30 discussion

Neurology

3.3.20. Lasmiditan - EMEA-002166-PIP01-17-M01

Eli Lilly and Company Limited; Treatment of Migraine with and without aura

Day 30 discussion

Neurology

3.3.21. Risdiplam - EMEA-002070-PIP01-16-M02

Roche Registration GmbH; Treatment of spinal muscular atrophy

Day 30 discussion

Neurology

3.3.22. Daunorubicin (liposomal formulation) / cytarabine (liposomal formulation) - Orphan - EMEA-001858-PIP02-16-M02

JAZZ PHARMACEUTICALS IRELAND LIMITED; Treatment of acute myeloid leukaemia

Day 30 discussion

Oncology

3.3.23. Idasanutlin - Orphan - EMEA-001489-PIP01-13-M01

Roche Registration GmbH; Treatment of acute myeloid leukaemia, Treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue), Treatment of acute lymphoblastic leukaemia / Treatment of children with first relapse of, or with frontline-refractory acute myeloid leukaemia, Treatment of children with first relapse of, or with frontline-refractory acute lymphoblastic leukaemia, Treatment of children with a solid malignant tumour which is newly-diagnosed and metastatic, or refractory to first-line treatment

Day 30 discussion

Oncology

3.3.24. Idelalisib - EMEA-001350-PIP02-13-M04

Gilead Sciences International Ltd; Treatment of mature B-cell neoplasm / Treatment of children from 1 year to less than 18 years of age with a relapsed or refractory diffuse large B-cell lymphoma (DLBCL), mediastinal B-cell lymphoma (MBCL) or Burkitt lymphoma

Day 30 discussion

Oncology

3.3.25. Ixazomib - Orphan - EMEA-001410-PIP02-17-M01

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 30 discussion

Oncology

3.3.26. Lenvatinib - Orphan - EMEA-001119-PIP02-12-M04

Eisai Europe Ltd; Treatment of papillary thyroid carcinoma, Treatment of Osteosarcoma, Treatment of follicular thyroid carcinoma / Treatment of refractory or relapsed osteosarcoma in children and adolescents, Treatment of progressive, radioiodine-refractory differentiated thyroid cancer in children and adolescents

Day 30 discussion

Oncology

3.3.27. Dexamethasone / Povidone-Iodine - EMEA-001936-PIP01-16-M01

Shire Pharmaceuticals Ireland Ltd; Treatment of Infectious conjunctivitis (adenoviral and bacterial)

Day 30 discussion

Ophthalmology

3.3.28. Ex vivo expanded autologous human corneal epithelium cells containing stem cells - Orphan - EMEA-001082-PIP02-11-M02

Chiesi Farmaceutici S.p.A.; Treatment of limbal stem cell deficiency due to ocular burns

Day 30 discussion

Ophthalmology

3.3.29. Ketorolac trometamol / phenylephrine hydrochloride - EMEA-001256-PIP02-12-M02

Omeros Corporation; Lens therapeutic procedure

Day 30 discussion

Ophthalmology

3.3.30. Conestat alfa - EMEA-000367-PIP01-08-M08

Pharming Group N.V.; D84.1 Defects in the complement system esterase inhibitor (C1-INH) deficiency / Treatment of acute attacks of angioedema associated with hereditary C1 esterase inhibitor deficiency

Day 30 discussion

Other

3.3.31. Ivacaftor - Orphan - EMEA-000335-PIP01-08-M13

Vertex Pharmaceuticals (Europe) Limited; Treatment of Cystic Fibrosis

Day 30 discussion

Other

3.3.32. Palonosetron / fosnetupitant - EMEA-001198-PIP03-17-M01

Helsinn Birex Pharmaceuticals Limited; Prevention of Chemotherapy-Induced Nausea and Vomiting

Day 30 discussion

Other

3.3.33. Aluminium hydroxide adsorbed, de-pigmented glutaraldehyde polymerised, allergen extract of Betula alba pollen (birch pollen) - EMEA-000630-PIP02-09-M04

LETI Pharma GmbH; 30.1 Allergic rhinitis due to pollen, J30.2 Other seasonal allergic rhinitis, J30.3 Other allergic rhinitis, J30.4 Allergic rhinitis, unspecified H10.1 Acute allergic conjunctivitis / Treatment of patients with allergic rhinoconjunctivitis with or without intermittent allergic asthma due to sensitisation against tree pollens (Betula alba family), Treatment of patients with allergic rhinitis with or without intermittent allergic asthma due to sensitisation against tree pollens (Betula alba family)

Day 30 discussion

Pneumology - Allergology

3.3.34. Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extracts of birch, alder and hazel pollen - EMEA-000662-PIP02-09-M04

LETI Pharma GmbH; J 30.1 Allergic rhinitis due to pollen J 30.2 Other seasonal allergic rhinitis J 30.03 Other allergic rhinitis J 30.4 Allergic rhinitis, unspecified H10.1 Acute allergic conjunctivitis / Treatment of patients with allergic rhinitis with or without intermittent allergic asthma due to sensitisation against tree pollens (Betula alba family), Treatment of patients with allergic rhino-conjunctivitis with or without intermittent allergic asthma due to sensitisation against tree pollens (Betula alba family)

Day 30 discussion

Pneumology - Allergology

3.3.35. Peanut flour - EMEA-001734-PIP01-14-M03

Aimmune Therapeutics Inc; Peanut Allergy / Peanut oral immunotherapy for the reduction in clinical reactivity to accidental exposure in peanut children and adults

Day 30 discussion

Pneumology - Allergology

3.3.36. Tezepelumab - EMEA-001613-PIP01-14-M02

AstraZeneca AB; Treatment of asthma / Add-on maintenance treatment of patients with severe asthma aged 5 years and older

Day 30 discussion

Pneumology - Allergology

3.3.37. Potassium hydrogen carbonate / Potassium citrate monohydrated - Orphan - EMEA-001357-PIP01-12-M02

Advicenne Pharma; Treatment of renal tubular acidosis

Day 30 discussion

Uro-nephrology

3.3.38. Cholera vaccine, live attenuated, oral (Strain CVD 103-HgR) - EMEA-001490-PIP01-13-M01

PaxVax Netherlands B.V.; Prevention of disease caused by V. cholerae serogroup O1

Day 30 discussion

Vaccines

3.3.39. Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1) - EMEA-001715-PIP01-14-M01

Seqirus Netherlands B.V.; Prevention of influenza

Day 30 discussion

Vaccines

3.3.40. Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1) - EMEA-002068-PIP01-16-M02

Seqirus UK Limited; Prevention of influenza

Day 30 discussion

Vaccines

3.3.41. Pneumococcal Polysaccharide Serotype 33F – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 23F – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 22F – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 19F – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 19A – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 18C – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 14 – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 9V – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 7F – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 6B – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 6A – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 5 – Diphtheria CRM197 Conjugate /

Pneumococcal Polysaccharide Serotype 4 – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 3 – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 1 – Diphtheria CRM197 Conjugate - EMEA-002215-PIP01-17-M01

Merck Sharp & Dohme (Europe), Inc.; Prevention of disease caused by Streptococcus pneumoniae / Active immunisation for the prevention of invasive disease, pneumonia and acute otitis media caused by Streptococcus pneumoniae in infants, children and adolescents from 6 weeks to less than 18 years of age.

Day 30 discussion

Vaccines

4. Nominations

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 04 December 2018 for Nomination of Rapporteur and Peer reviewer

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

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

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

4.3. Nominations for other activities

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

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. Duvelisib - EMEA-15-2018

Verastem Inc; The class of primarily alkylating medicinal products for treatment of

myeloproliferative neoplasms and mature B, T and NK cell neoplasms/ 1) Treatment of chronic lymphocytic leukaemia / small lymphocytic lymphoma, including patients with 17p deletion, who have received at least one prior therapy; 2) Treatment of follicular B cell non-Hodgkin lymphoma who have received at least two prior therapies

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. Octenidine dihydrochloride - EMEA-001384-PIP02-17

Schülke & Mayr GmbH; Prevention of oral soft tissue infections

Proposed indication: for temporary reduction of bacterial count in the oral cavity, for inhibition of plaque formation, in cases of insufficient oral hygiene capacity

7.1.2. Cemiplimab - EMEA-002007-PIP02-17

Regeneron Ireland U.C.; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue)

Proposed indications: Cemiplimab is indicated as the first-line treatment of unresectable, locally advanced, recurrent or metastatic non-small cell lung cancer, in patients whose tumors express PD-L1 >/= 50% of tumor cells; Cemiplimab in combination with ipilimumab and/or platinum-based doublet chemotherapy/ipilimumab, is indicated as the first-line treatment of unresectable, locally advanced, recurrent or metastatic non-small cell lung cancer, in patients whose tumors express PD-L1 >/= 50% of tumor cell; Cemiplimab, in combination with platinum-based doublet chemotherapy and/or ipilimumab/platinum-based doublet chemotherapy, is indicated as the first-line treatment of unresectable, locally advanced, recurrent or metastatic non-small cell lung cancer, in patients whose tumors express PD-L1 <50% of tumor cells

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

No items

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 August 2018, was presented to the PDCO members.

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

9.3.1. Non-clinical Working Group: D30 Products identified

PDCO member: Karen van Malderen

Summary of committee discussion:

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

9.3.2. Formulation Working Group

PDCO member: Brian Aylward

Summary of committee discussion:

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

9.3.3. Request for advice to CHMP and PDCO on orally inhaled products for children

Summary of committee discussion:

While the proposed approach, i.e. use of PK studies in the paediatric population, is considered agreeable in principle, concern with regard to its feasibility was raised as to whether it would also be accepted by parents and ethic committees.

A pilot period with re-assessment of its feasibility after a few years is suggested.

9.3.4. PDCO Response to the RDG letter on the revision of the OIP GL

PDCO members: Sabine Scherer, Eva Agurell

Summary of committee discussion:

The PDCO adopted the letter.

9.4. Cooperation within the EU regulatory network

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

No items

9.5. Cooperation with International Regulators

No items

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

No items

9.7. PDCO work plan

No items

9.8. Planning and reporting

No items

10. Any other business

10.1.1. Regulatory Science Engagement Plan to 2025

Scope: presentation of EMA's regulatory science engagement plan

Summary of committee discussion:

The PDCO noted the information.

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

Scope: Outcomes and action plan

Summary of committee discussion:

The PDCO adopted an action plan to further improve the implementation of the Paediatric Regulation.

10.1.3. Paediatric addendum to anti-cancer guideline: proposal for way forward

Summary of committee discussion:

A proposal for a way forward on the paediatric addendum to anti-cancer guideline was presented to the PDCO and it was agreed by the Committee.

10.1.4. Report from the paediatric strategy forum for medicinal product development of checkpoint inhibitors for use in combination therapy in paediatric patients

Summary of committee discussion:

Feedback from the paediatric strategy forum was presented to the Committee.

10.1.5. Joint CHMP & PDCO Strategic Review & Learning Meeting Vienna, Austria, 26-28 September 2018

Summary of committee discussion:

The PDCO was further updated on the program and PDCO topics.

10.1.6. Workshop on Allergen Immunotherapy (AIT) for Children, 26 June 2018

Scope: Adoption of the minutes

Summary of committee discussion:

The PDCO adopted the minutes of the workshop.

11. Breakout sessions

11.1.1. Paediatric oncology

Summary of committee discussion:

The group shares their views on the paediatric strategy forum for medicinal product development of checkpoint inhibitors for use in combination therapy in paediatric patients held in September, including possible implications for the PIPs.

11.1.2. Neonatology

Summary of committee discussion:

The neonatal group discussed input for a scientific advice related procedure. Furthermore aspects around the publication of the Concept paper for public consultation to revise the neonatal guideline were discussed. The information of the opportunity to provide input should be distributed to as many stakeholders as possible.

11.1.3. Inventory

Summary of committee discussion:

The inventory group continue discussion on the assessment of unmet needs for products discussed by the PDCO.

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 September 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:	Molibresib - EMEA-002406-PIP01-18
Karen Van Malderen	Alternate	Belgium	No interests declared	
Dimitar Roussinov	Member	Bulgaria	No restrictions applicable to this meeting	
Adriana Andrić	Member	Croatia	No interests declared	
Georgios Savva	Member	Cyprus	No interests declared	
Jaroslav Sterba	Member	Czech Republic	No interests declared	
Kirstine Moll Harboe	Member	Denmark	No interests declared	
Mona Ring Gatke	Alternate	Denmark	No interests declared	
Irja Lutsar	Member	Estonia	No interests declared	
Jana Lass	Alternate	Estonia	No interests declared	
Ann Marie Kaukonen	Member	Finland	No interests declared	
Pia Annunen	Alternate	Finland	No restrictions applicable to this meeting	
Sylvie Benchetrit	Member	France	No interests declared	
Dominique Ploin	Alternate	France	No interests declared	
Sabine Scherer	Member	Germany	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Yuansheng Sun	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	
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	
Goda Vaitkeviciene	Alternate	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	Member	Spain	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Andrés Trelles				
Maria Jesús Fernández Cortizo	Alternate	Spain	No interests declared	
Eva Agurell	Alternate	Sweden	No interests declared	
Angeliki Siapkara	Member	United Kingdom	No interests declared	
Martina Riegl	Alternate	United Kingdom	No interests declared	
Fernando Cabanas	Member	Healthcare Professionals' Representative	No interests declared	
Francesca Rocchi	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Catherine Cornu	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Johannes Taminiau	Member	Healthcare Professionals' Representative	No interests declared	
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	
Marie Louise Schougaard Christiansen	Expert - in person*	Denmark	No interests declared	
Juliana Min	Expert - in person*	United Kingdom	No interests declared	
Homera Fahimeda Binte Ali	Expert - in person*	United Kingdom	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Immanuel Barth	Expert - via telephone*	Germany	No interests declared	
Eleni Gaki	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/