15 November 2019
EMA/PDCO/523933/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

# Paediatric Committee (PDCO)

## Minutes for the meeting on 15-18 October 2019

Chair: Koenraad Norga – Vice-Chair: Sabine Scherer

**Health and safety information**

In accordance with the Agency's health and safety policy, delegates are to be briefed on health, safety and emergency information and procedures prior to the start of the meeting.

**Disclaimers**

Some of the information contained in these 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 these 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 (See 12.).

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.

Due to restricted involvement, the Chair Koenraad Norga deputised chairing the meeting to the newly elected Vice-Chair, Sabine Scherer, for the topic(s): 2.3.3, 2.3.29, 2.3.39, 3.3.9.

## 1.2. Adoption of agenda

The agenda for 15-18 October 2019 meeting was adopted and was published on the EMA website.

## 1.3. Adoption of the minutes

The minutes of the 17-20 September 2019 PDCO meeting were adopted and will be published on the EMA website.

# 2. Opinions

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

## 2.1. Opinions on Products

### 2.1.1. Remimazolam (as besylate) - EMEA-001880-PIP02-19

PAION Deutschland GmbH; Sedation during medical procedures / General anaesthesia and post-operative sedation up to 24h / Sedation in the intensive care unit (ICU) / Sedation for short procedures

Day 120 Opinion

Anaesthesiology

**Summary of Committee discussion:**

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO issued a positive opinion on the paediatric development plan after the Applicant clarified the few remaining issues at Day 90.
The use of the intranasal formulation in general anaesthesia is fully waived, as it would not be appropriate for this condition and it would result in no significant therapeutic benefit. The condition of sedation, including both procedural sedation and sedation in mechanically ventilated patients as proposed indications, covers children from birth to less than 18 years of age.

### 2.1.2. Narsoplimab - Orphan - EMEA-002479-PIP01-18

Omeros London Limited; Treatment in haematopoietic stem cell transplantation / Treatment of haematopoietic stem cell transplant associated thrombotic microangiopathy (HSCT-TMA)

Day 120 Opinion

Haematology-Hemostaseology

**Summary of Committee discussion:**

The PDCO at their October 2019 meeting adopted a PIP Opinion with a deferral.

### 2.1.3. Artesunate - Orphan - EMEA-002402-PIP02-18

ACE Pharmaceuticals BV; Plasmodia infections / Treatment of severe malaria caused by plasmodium falciparum in children aged 1 month to 18 years

Day 120 Opinion

Infectious Diseases

**Summary of Committee discussion:**

The PDCO agreed on a paediatric investigation plan for the condition 'treatment of severe malaria caused by *Plasmodium falciparum*', covering all paediatric population from birth to less than 18 years of age.

### 2.1.4. Iclaprim (mesylate) - EMEA-002391-PIP02-19

Hemex Germany GmbH; Infection with gram-positive bacteria

Day 120 Opinion

Infectious Diseases

**Summary of Committee discussion:**

Based on the assessment of this application and further discussions at the Paediatric Committee and considering the Applicant's feedback following the Day 90 discussion, the PDCO agreed with the proposed paediatric investigation plan and respective amendments. A deferral was agreed by the PDCO.

A positive Opinion was adopted for iclaprim (mesylate) for the treatment of acute bacterial skin and skin structure infections for all the subsets of the paediatric population.

### 2.1.5. Hydrocortisone (hemisuccinate) - EMEA-002305-PIP01-17

LABORATOIRE AGUETTANT; Prevention of bronchopulmonary dysplasia

Day 120 Opinion

Neonatology - Paediatric Intensive Care

**Summary of Committee discussion:**

Based on the assessment of this application, the PDCO adopted a positive Opinion for hydrocortisone (hemisuccinate) for the prevention of bronchopulmonary dysplasia (BPD).

### 2.1.6. Ganaxolone - EMEA-002341-PIP01-18

Marinus Pharmaceuticals Inc.; Cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder / Adjunctive treatment of seizures in paediatric patients aged 6 months to < 18 years old with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder

Day 120 Opinion

Neurology

**Summary of Committee discussion:**

The PDCO agreed on a PIP with a deferral for ganoxolone in the treatment of cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder.

### 2.1.7. Phenobarbital - EMEA-002532-PIP01-18

Proveca Limited; Epilepsy

Day 120 Opinion

Neurology

**Summary of Committee discussion:**

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

Committee and considering the Applicant's responses following the Day 90 discussion, the PDCO agreed with the proposed paediatric investigation plan. Overall, a positive Opinion was adopted.

### 2.1.8. Selpercatinib - Orphan - EMEA-002544-PIP01-18

Eli Lilly and Company Limited; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms) / Treatment of paediatric patients from ⩾6 months to <18 years of age with rearranged during transfection (RET)-altered, locally advanced or metastatic, solid tumours or primary central nervous system (CNS) tumours

Day 120 Opinion

Oncology

**Summary of Committee discussion:**

A positive Opinion for selpercatinib, with a deferral, for the condition of treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms) was agreed.

### 2.1.9. Crizotinib - EMEA-001493-PIP03-18

Pfizer Europe MA EEIG; Anaplastic lymphoma kinase (ALK)-positive inflammatory myofibroblastic tumour (IMT) / ALK-positive anaplastic large cell lymphoma (ALCL) / Treatment of paediatric patients with relapsed/refractory systemic ALK-positive ALCL / Treatment of paediatric patients with unresectable or relapsed/refractory ALK-positive IMT

Day 120 Opinion

Oncology

**Summary of Committee discussion:**

A positive Opinion, agreeing on a deferral, was adopted.

### 2.1.10. Iodine ($^{131}$I) murine IgG1 monoclonal antibody against B7-H3 - Orphan - EMEA-002101-PIP02-18

Y-mAbs Therapeutics A/S; Treatment of paediatric neuroblastoma patients with central nervous system (CNS) relapse as evidenced by CNS/leptomeningeal (LM) metastases

Day 120 Opinion

Oncology

**Summary of Committee discussion:**

During October 2019 PDCO plenary meeting, the PDCO adopted a positive Opinion for the PIP application for Iodine ($^{131}$I) murine IgG1 monoclonal antibody against B7-H3/CD276 for the treatment of paediatric neuroblastoma patients with central nervous system

(CNS)/ leptomeningeal (LM) metastases.

## 2.1.11. Ivosidenib - Orphan - EMEA-002247-PIP02-17

Agios Pharmaceuticals, Inc.; Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms), Treatment of malignant neoplasms of the central nervous system / Treatment of paediatric patients (2 to less than 18 years of age) with recurrent or progressive (R/P) malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms), including central nervous system tumours, with an isocitrate dehydrogenase-1 (IDH1) mutation

Day 120 Opinion

Oncology

**Summary of Committee discussion:**

The PDCO's views expressed at D90 were endorsed. The PDCO therefore adopted on its own motion a waiver for the entire paediatric population (from birth to less than 18 years of age) in the conditions 'treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms)' and 'treatment of malignant neoplasms of the central nervous system' based on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need in the paediatric population.
This was based on the consideration that studies that may be carried in paediatric patients with solid tumours harbouring isocitrate dehydrogenase (IDH) mutations are not expected to be able to collect sufficient data to establish a benefit/risk of the product in the paediatric population.
The PDCO emphasises that the granting of a waiver for the conditions mentioned above should not prevent the Applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

## 2.1.12. Larotrectinib - EMEA-001971-PIP03-18

Bayer AG; Treatment of malignant neoplasms of the central nervous system / Treatment of paediatric patients with a primary central nervous system (CNS) tumour with a neurotrophic tyrosine receptor kinase (NTRK) gene fusion

Day 120 Opinion

Oncology

**Summary of Committee discussion:**

The PDCO therefore recommended granting a paediatric investigation plan and a deferral for larotrectinib for the entire paediatric population from birth to less than 18 years of age in the condition 'Treatment of malignant neoplasms of the central nervous system'.

## 2.1.13. Marizomib - EMEA-002452-PIP01-18

Celgene Europe B.V.; Treatment of malignant glial tumors / Treatment of patients (paediatric) with diffuse intrinsic pontine glioma (DIPG) who have received radiation therapy

Day 120 Opinion

Oncology

**Summary of Committee discussion:**

Overall the PDCO agreed to a positive Opinion on a PIP with a deferral for marizomib in combination development with panobinostat for the treatment of malignant glial tumours.

## 2.1.14. Zanubrutinib - EMEA-002354-PIP02-18

BeiGene Ireland, Ltd; Treatment of mature B-cell neoplasms excluding lymphoplasmacytic lymphoma (Waldenström's macroglobulinaemia) / Treatment of lymphoplasmacytic lymphoma (Waldenström's macroglobulinaemia) / Treatment of primary mediastinal B-cell lymphoma / Treatment of Burkitt lymphoma / Treatment of diffuse large B-cell lymphoma

Day 120 Opinion

Oncology

**Summary of Committee discussion:**

The PDCO's views expressed at D90 were endorsed and the Opinion finalised.
In summary, the PDCO recommended granting a paediatric investigation plan with a deferral in the condition 'treatment of mature B-cell neoplasms (excluding lymphoplasmacytic lymphoma)' and a waiver for the entire paediatric population from birth to less than 18 years of age for the condition 'treatment of lymphoplasmacytic lymphoma' on the grounds that the disease does not occur in the paediatric population.

## 2.1.15. Ketamine (hydrochloride) / sufentanil (citrate) - EMEA-001739-PIP02-16

Copenhagen University Hospital, Rigshospitalet; ICD10:R52 Treatment of pain

Day 120 Opinion

Pain

**Summary of Committee discussion:**

A positive opinion endorsing the PIP has therefore been adopted.

## 2.1.16. 3-[5-[(1R,2S)-2-(2,2-difluoropropanoylamino)-1-(2,3-dihydro-1,4-benzodioxin-6-yl)propoxy]indazol-1-yl]-N-[(3R)-tetrahydrofuran-3-yl]benzamide - EMEA-001976-PIP02-18

AstraZeneca AB; Asthma / Treatment to control persistent asthma

Day 120 Opinion

Pneumology – Allergology

**Summary of Committee discussion:**

In view of the agreement reached on the overall development, the PDCO agreed a positive Opinion for this PIP with a deferral.

### 2.1.17. Synthetic double-stranded siRNA oligonucleotide directed against lactate dehydrogenase A mRNA and containing four modified nucleosides which form a ligand cluster of four N-acetylgalactosamine residues - Orphan - EMEA-002493-PIP01-18

Dicerna EU Limited; The treatment of primary hyperoxaluria

Day 120 Opinion

Uro-nephrology

**Summary of Committee discussion:**

As the remaining minor issues were resolved between Day 90 and Day 120, a positive Opinion was adopted for this PIP for the treatment of primary hyperoxaluria (PH) in all paediatric age groups.

### 2.1.18. Ezetimibe / atorvastatin - EMEA-002649-PIP01-19

ELPEN Pharmaceutical Co. Inc; Treatment of hypercholesterolemia / The combination of atorvastatin and ezetimibe is indicated for the treatment of hypercholesterolemia as substitution therapy in adult patients adequately controlled with the individual substances given concurrently at the same dose level as in the fixed dose combination, but as separate products.

Day 60 Opinion

Cardiovascular Diseases

**Summary of Committee discussion:**

Based on the assessment of this application and the Day 30 plenary discussion, the PDCO agrees with the Applicant's request for a waiver. The PDCO recommends granting a waiver for ezetimibe / atorvastatin for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of 'treatment of hypercholesterolemia' due to lack of significant therapeutic benefit over other treatments.

### 2.1.19. Satoreotide trizoxetan - Orphan - EMEA-002632-PIP01-19

Ipsen Pharma; Diagnosis of small cell lung cancer / Diagnosis of neuroendocrine tumours / Diagnosis of breast cancer

Day 60 Opinion

Diagnostic / Oncology

**Summary of Committee discussion:**

In conclusion, based on the assessment of this application, the PDCO agrees with the

Applicant's request for a waiver and recommends granting a waiver for all subsets of the paediatric population (from birth to less than 18 years of age) in the conditions of 'diagnosis of neuroendocrine tumours (excluding neuroblastoma) on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible and of 'diagnosis of lung cancer' and 'diagnosis of breast cancer' on the ground that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).
The PDCO emphasises that the granting of a waiver for the conditions mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

## 2.1.20. (3S,7S)-22-(3-(((2-((5-(2-Carboxyethyl)-2-hydroxybenzyl)(carboxymethyl)amino)ethyl)(carboxymethyl)amino)methyl)-4-hydroxyphenyl)-5,13,20-trioxo-4,6,12,19-tetraazadocosane-1,3,7-tricarboxylic acid - EMEA-002622-PIP01-19

Advanced Nuclear Medicine Ingredients (ANMI); Diagnosis of biochemical recurrence of prostate cancer

Day 60 Opinion

Diagnostic / Uro-nephrology

**Summary of Committee discussion:**

Based on the assessment of this application the PDCO agrees with the Applicant's request for a waiver. The PDCO recommends granting a waiver for (3S,7S)-22-(3-(((2-((5-(2-Carboxyethyl)-2-hydroxybenzyl)(carboxymethyl)amino)ethyl)(carboxymethyl)amino)methyl)-4-hydroxyphenyl)-5,13,20-trioxo-4,6,12,19-tetraazadocosane-1,3,7-tricarboxylic acid for all subsets of the paediatric population (0 to 18 years of age) in the condition of Visualisation of prostate specific membrane antigen in prostate cancer.

## 2.1.21. $^{177}$Lu-satoreotide tetraxetan - Orphan - EMEA-002629-PIP01-19

Ipsen Pharma; Small cell lung cancer / Neuroendocrine tumours / Breast cancer

Day 60 Opinion

Oncology

**Summary of Committee discussion:**

The PDCO re-discussed this application in line with the conclusions made during the Day 30 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 $^{177}$Lu-Satoreotide tetraxetan for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'treatment lung cancer', 'treatment neuroendocrine tumours (excluding neuroblastoma)' and 'treatment breast cancer'.

The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. 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.

### 2.1.22. A fully humanized immunoglobulin G4 proline, alanine, alanine (IgG4 PAA) based bispecific antibody directed against cluster of differentiation 3 (CD3) receptor complex and G protein coupled receptor family C group 5 member D (GPRC5D) - EMEA-002615-PIP01-19

Janssen-Cilag International N.V.; Multiple myeloma

Day 60 Opinion

Oncology

**Summary of Committee discussion:**

The PDCO discussed this procedure at Day 60 during the October 2019 PDCO plenary meeting.
The PDCO recommends granting a waiver for a fully humanized immunoglobulin G4 proline, alanine, alanine (IgG4 PAA) based bispecific antibody directed against cluster of differentiation 3 (CD3) receptor complex and G Protein Coupled Receptor Family C Group 5 Member D (GPRC5D) for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'multiple myeloma'.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

### 2.1.23. Duvelisib - Orphan - EMEA-002587-PIP01-19

Verastem, Inc.; Treatment of chronic lymphocytic leukaemia /small lymphocytic lymphoma / Treatment of follicular lymphoma

Day 60 Opinion

Oncology

**Summary of Committee discussion:**

The PDCO re-discussed this application in line with the conclusion made at Day 30, agreeing to a broader condition wording for this waiver of treatment of mature b cell malignancies.
The PDCO recommends granting a waiver for duvelisib for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'treatment of mature b cell malignancies'.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population

are available even if a waiver has been granted in another condition.

### 2.1.24. Savolitinib - EMEA-002627-PIP01-19

AstraZeneca AB; Treatment of lung carcinoma (small cell and non-small cell carcinoma)

Day 60 Opinion

Oncology

**Summary of Committee discussion:**

The PDCO re-discussed the application in line with the outcome conclusion from the Day 30 discussion.
The PDCO recommends granting a waiver for savolitinib for all subsets of the paediatric population (0 to 18 years of age) in the condition of 'treatment of lung carcinoma'.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

### 2.1.25. Sitravatinib malate - EMEA-002633-PIP01-19

Mirati Therapeutics, Inc.; Treatment of non-small cell lung cancer

Day 60 Opinion

Oncology

**Summary of Committee discussion:**

The PDCO's view expressed at D30 was re-discussed. In conclusion, the Committee considered that a product specific waiver for sitravatinib and treatment of non-small cell lung cancer (NSCL) on the ground that the condition does not occur, or occur very rarely, in paediatric patients was agreeable. A positive opinion was adopted at D60.

### 2.1.26. Loxoprofen (sodium hydrate) - EMEA-002626-PIP01-19

Lead Chemical Co., Ltd; Local treatment of pain

Day 60 Opinion

Pain

**Summary of Committee discussion:**

Based on the assessment of this application and further discussions at the Paediatric Committee, the PDCO agrees with the Applicant's request for a waiver. The PDCO recommends granting a waiver for loxoprofen (sodium hydrate) for all subsets of the paediatric population (0 to 18 years of age) in the condition of treatment of pain on the ground of lack of significant therapeutic benefit over existing treatments.

## 2.1.27. Thiocolchicoside / diclofenac (sodium) - EMEA-002580-PIP01-19

WIN MEDICA S.A.; Acute low back pain / Treatment of acute low back pain in adults

Day 60 Opinion

Pain

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

## 2.1.28. Gefapixant (citrate) EMEA-002267-PIP02-19

Merck Sharp & Dohme (Europe), Inc.; R05 - Treatment of cough

Day 60 Opinion

Pneumology  Allergology

**Summary of Committee discussion:**

Based on the assessment of this application the PDCO agrees with the Applicant's request for a waiver. The PDCO recommends granting a waiver for gefapixant citrate salt for all subsets of the paediatric population (from birth to less than 18 years of age) in the condition of ‘treatment of unexplained or chronic refractory cough’ on the grounds that this condition does not occur in the paediatric population.
The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need. In principle according to the Paediatric Regulation, incentives for the development for use in the paediatric population are available even if a waiver has been granted in another condition.

## 2.1.29. Canakinumab - EMEA-000060-PIP07-19

Novartis Europharm Limited; Treatment of gout

Day 1 Opinion

Immunology – Rheumatology – Transplantation

**Summary of Committee discussion:**

The PDCO discussed the application for a waiver for the paediatric population from birth to less than 18 years of age for canakinumab, a human monoclonal anti-human interleukin-1 beta antibody, for the condition ‘treatment of gout’.

In conclusion, the PDCO agrees with the Applicant's request for a waiver and recommends granting a waiver for canakinumab for all subsets of the paediatric population (form to 18 years of age) in the condition of 'treatment of gout' 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).

### 2.1.30. Ritonavir / atazanavir (sulfate) - EMEA-002588-PIP01-19

Pharmaceutical Oriented Services Ltd; Treatment of human immunodeficiency virus (HIV-1) infection

Day 60 opinion

Infectious Diseases

**Summary of Committee discussion:**

In conclusion, the PDCO adopted a positive Opinion on the paediatric plan proposed by the Applicant including a deferral.

## 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. Asfotase alfa - EMEA-C-000987-PIP01-10-M04

Alexion Europe S.A.S.; Treatment of hypophosphatasia

Day 30 letter

Endocrinology-Gynaecology-Fertility-Metabolism

**Summary of Committee discussion:**

The PDCO took note of outcomes of preceding partial compliance check procedures: C1-000987-PIP01-10-M01 (withdrawn), C2-000987-PIP01-10-M02.
The PDCO adopted on 18/10/2019 an Opinion confirming the compliance of all studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0176/2019) of 15 May 2019.

### 2.2.2. Decitabine - EMEA-C-000555-PIP01-09-M06

Janssen-Cilag International NV; Treatment of acute myeloid leukaemia

Day 60 letter

Oncology

**Summary of Committee discussion:**

The PDCO took note of outcomes of the preceding partial compliance check procedure EMEA-C1-000555-PIP01-09-M01) of 15 July 2011.
The PDCO adopted on 18 October 2019 an Opinion confirming the compliance of all

studies in the agreed paediatric investigation plan as set out in the latest Agency's Decision (P/0234/2017) of 12 August 2017.

## 2.3. Opinions on Modification of an Agreed Paediatric Investigation Plan

### 2.3.1. Rubidium ($^{82}$Rb) chloride - EMEA-000882-PIP03-11-M04

Jubilant DraxImage Inc.; Visualization of myocardial perfusion for diagnostic purposes / rubidium chloride ($^{82}$Rb) injection is a radiopharmaceutical to be used in in positron-emission tomography (PET) imaging for the assessment of myocardial perfusion abnormalities

Day 60 Opinion

**Summary of Committee discussion:**

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

### 2.3.2. Chloroprocaine hydrochloride - EMEA-000639-PIP03-16-M01

Sintetica GmbH; Peripheral nerve block (local anaesthesia by perineural injection)

Day 60 Opinion

Anaesthesiology

**Summary of Committee discussion:**

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

### 2.3.3. Ambrisentan - Orphan - EMEA-000434-PIP01-08-M06

Glaxo Group Limited; Treatment of pulmonary arterial hypertension

Day 60 Opinion

Cardiovascular Diseases

**Summary of Committee discussion:**

The PDCO re-discussed the proposed modification taking into account the clarification provided by the Applicant after D30.
In summary, the PDCO adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0077/2019 of 22 March 2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

### 2.3.4. Aciclovir - EMEA-001066-PIP02-11-M03

VECTANS PHARMA; Herpes simplex labialis

Day 60 Opinion

Dermatology

**Summary of Committee discussion:**

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted to extend the scope of the waiver to cover all subsets of the paediatric population, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0166/2017 of 3 July 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

### 2.3.5. Bimekizumab - EMEA-002189-PIP01-17-M01

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

Day 60 Opinion

Dermatology

**Summary of Committee discussion:**

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, 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/0193/2018 of 17 July 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

### 2.3.6. Dupilumab - EMEA-001501-PIP01-13-M06

Regeneron Pharmaceuticals, Inc; Atopic dermatitis

Day 60 Opinion

Dermatology

**Summary of Committee discussion:**

Thus, 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/0158/2018 of 15 June 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.7. Volanesorsen - A phosphorothioate oligonucleotide targeted to apolipoprotein C-III - Orphan - EMEA-001915-PIP01-15-M01

Akcea Therapeutics; Familial chylomicronemia syndrome

Day 60 Opinion

Endocrinology-Gynaecology-Fertility-Metabolism

**Summary of Committee discussion:**

The PDCO discussed this procedure at Day 60 during the October 2019 PDCO plenary meeting.
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/0031/2017 of 30 January 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.8. Liraglutide - EMEA-000128-PIP02-09-M03

Novo Nordisk A/S; E66 Obesity / Treatment of obesity

Day 60 Opinion

Endocrinology-Gynaecology-Fertility-Metabolism

**Summary of Committee discussion:**

The applicant provided further information and clarifications between Day 30 and Day 60.
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/0154/2016 of 15 June 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.9. Lubiprostone - EMEA-000245-PIP01-08-M06

Sucampo AG; Chronic idiopathic 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 as set in the Agency's latest decision (P/0175/2018 of 15 June 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.10. Maralixibat chloride - Orphan - EMEA-001475-PIP03-17-M01

SFL Regulatory Services GmbH; Treatment of progressive familial intrahepatic cholestasis (PFIC)

Day 60 Opinion

Gastroenterology-Hepatology

**Summary of Committee discussion:**

The PDCO acknowledged the Applicant's response to the D30 report.
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/0024/2018 of 30 January 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.11. Naloxegol - EMEA-001146-PIP01-11-M05

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 as set in the Agency's latest decision.
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.12. Teduglutide - Orphan - EMEA-000482-PIP01-08-M05

Shire Pharmaceuticals Ireland Limited; ICD-9-CM Diagnosis 579.3 - Other and unspecified post-surgical non absorption - short bowel syndrome / Treatment of short bowel syndrome

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 as set in the Agency's latest decision (P/0351/2017 of 1 December 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.13. Avatrombopag (maleate) - EMEA-001136-PIP01-11-M01

Dova Pharmaceuticals Ireland Limited; Chronic immune thrombocytopenia / Treatment of thrombocytopenia in patients with chronic immune thrombocytopenia

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/0309/2011 of 20 December 2011).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.14. Crizanlizumab - Orphan - EMEA-002141-PIP01-17-M02

Novartis Europharm Limited; Treatment of sickle cell disease / Prevention of vaso-occlusive crises in patients with sickle cell disease

Day 60 Opinion

Haematology-Hemostaseology

**Summary of Committee discussion:**

The PDCO discussed the clarifications provided by the Applicant after D30 for crizanlizumab and treatment of sickle cell disease.
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/0060/2019 of 20 February 2019).

### 2.3.15. Fitusiran - Synthetic double-stranded siRNA oligonucleotide directed against antithrombin mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues - Orphan - EMEA-001855-PIP01-15-M01

Genzyme Europe B.V.; Treatment of Haemophilia B, Treatment of Heamophilia A / Fitusiran is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in children aged ≥ 1 year with severe Haemophilia B, including patients who express neutralizing antibodies to exogenous factor IX substitution / Fitusiran is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in children aged ≥ 1 year with severe Haemophilia A including patients who express neutralizing antibodies to exogenous factor VIII substitution

Day 60 Opinion

Haematology-Hemostaseology

**Summary of Committee discussion:**

During the October 2019, the PDCO adopted a positive Opinion on the modification request for fitusiran (double-stranded small interfering ribonucleic acid (siRNA) directed against antithrombin (AT) mRNA) for the treatment of children from 1-18 years with Haemophilia A and Haemophilia B, with and without inhibitors.
In conclusion, based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0186/2019 of 15 May 2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

### 2.3.16. Vonicog alfa - EMEA-001164-PIP01-11-M03

Baxalta Innovations GmbH; Von Willebrand disease / Prevention and treatment of bleeding episodes and for surgical and invasive procedures in paediatric patients (less than 18 years of age) with von Willebrand disease

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/0225/2018 of 17 July 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.17. Apremilast - EMEA-000715-PIP02-11-M04

Celgene Europe B.V.; Treatment of juvenile idiopathic arthritis (JIA) / Treatment of juvenile psoriatic arthritis (JPsA)

Day 60 Opinion

Immunology-Rheumatology-Transplantation

**Summary of Committee discussion:**

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0080/2019 of 22 March 2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.18. Apremilast - EMEA-000715-PIP05-13-M04

Celgene Europe B.V.; Treatment of Behçet's disease / Treatment of oral ulcers associated with Behçet's disease

Day 60 Opinion

Immunology-Rheumatology-Transplantation

**Summary of Committee discussion:**

The PDCO discussed the clarifications provided by the Applicant on apremilast and treatment of Behcet's disease.

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/0398/2018 of 06 December 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.19. Avacopan - Orphan - EMEA-002023-PIP01-16-M03

ChemoCentryx Ireland Ltd.; Treatment of antineutrophil cytoplasmic antibody (ANCA) - associated vasculitis

Day 60 Opinion

Immunology-Rheumatology-Transplantation

**Summary of Committee discussion:**

The PDCO view expressed at Day 30 was re-discussed and endorsed.
The PDCO therefore adopted a negative Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0344/2017 of 23 November 2017).

## 2.3.20. Ibrutinib - Orphan - EMEA-001397-PIP04-17-M01

Janssen-Cilag International N.V.; Treatment of chronic graft versus host disease (cGVHD) / IMBRUVICA is indicated for the treatment of cGVHD in children 1 year of age and older

Day 60 Opinion

Immunology-Rheumatology-Transplantation

**Summary of Committee discussion:**

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0021/2019 of 03 January 2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.21. Itacitinib - Orphan - EMEA-002178-PIP01-17-M01

Incyte Biosciences Distribution B.V; Treatment of acute graft versus host disease (D89.810, ICD-10-CM) / Treatment of steroid naïve paediatric population with acute graft versus host disease after allogeneic hematopoietic stem cell transplantation

Day 60 Opinion

Immunology-Rheumatology-Transplantation

**Summary of Committee discussion:**

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO at the October 2019 PDCO plenary meeting 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/0208/2018 of 17 July 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.22. Rimiducid - Orphan - EMEA-001870-PIP01-15-M02

Beliicum Pharma Ltd; Treatment of  graft versus host disease / Treatment of graft versus host disease in paediatric patients who have received a mismatched, related, allogeneic haematopoietic stem cell transplantation together with rivogenlecleucel

Day 60 Opinion

Immunology-Rheumatology-Transplantation

**Summary of Committee discussion:**

The PDCO discussed the linked procedures EMEA-001869-PIP01-15-M02 and EMEA-001870-PIP01-15-M02 at Day 60 during the October 2019 PDCO plenary meeting.

Regarding PIP EMEA-001870-PIP01-15-M02, the PDCO confirmed all the conclusions

reached at Day 30. In addition, it took into consideration the clarifications the Applicant provided between Day 30 and Day 60.
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/0186/2018 of 17 July 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

### 2.3.23. Rivogenlecleucel - Orphan - EMEA-001869-PIP01-15-M02

Bellicum Pharma Ltd; Adjunctive treatment in haematopoietic stem cell transplantation / Treatment of immunodeficiency after mismatched, related, allogeneic transplantation in paediatric patients with malignant and non-malignant disorders amenable to haematopoietic stem cell transplantation

Day 60 Opinion

Immunology-Rheumatology-Transplantation

**Summary of Committee discussion:**

The PDCO discussed the linked procedures EMEA-001869-PIP01-15-M02 and EMEA-001870-PIP01-15-M02 at Day 60 during the October 2019 plenary meeting.

Regarding PIP EMEA-001869-PIP01-15-M02, the PDCO agreed that since rivogenlecleucel is now the recommended INN for this product, rivogenlecleucel will be used in the PIP Opinion.

The PDCO confirmed all the conclusions reached at Day 30. In addition, it took into consideration the clarifications the applicant provided between Day 30 and Day 60.
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/0194/2018 of 17 July 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

### 2.3.24. Daclatasvir - EMEA-001191-PIP01-11-M03

Bristol-Myers Squibb Pharma EEIG; Treatment of chronic viral hepatitis C

Day 60 Opinion

Infectious Diseases

**Summary of Committee discussion:**

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

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0311/2016 of 7 November 2016).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.25. Dalbavancin - EMEA-000016-PIP01-07-M07

Allergan Pharmaceuticals International Limited; Treatment of acute bacterial skin and skin structure infections (ABSSSI)

Day 60 Opinion

Infectious Diseases

**Summary of Committee discussion:**

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0113/2018 of 11/4/2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.26. Letermovir - Orphan - EMEA-001631-PIP01-14-M04

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

Day 60 Opinion

Infectious Diseases

**Summary of Committee discussion:**

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0385/2018 of 7 December 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.27. Zanamivir - EMEA-001318-PIP01-12-M03

GlaxoSmithKline Trading Services Limited; Treatment of influenza / Prevention of influenza / Treatment of influenza A and B virus infection / Prevention of influenza A and B virus infection

Day 60 Opinion

Infectious Diseases

**Summary of Committee discussion:**

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

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0212/2017 of 09 August 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.28. Fremanezumab - EMEA-001877-PIP01-15-M02

Teva GmbH; Prevention of migraine headaches

Day 60 Opinion

Neurology

**Summary of Committee discussion:**

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0308/2017 of 31 October 2017).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.29. Peginterferon beta-1a - EMEA-001129-PIP01-11-M04

Biogen Idec Ltd; Multiple sclerosis / Treatment of relapsing remitting forms of multiple sclerosis

Day 60 Opinion

Neurology

**Summary of Committee discussion:**

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0067/2019 of 22/03/2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.30. Abemaciclib - EMEA-002342-PIP01-18-M01

Eli Lilly and Company Limited; Ewing's Sarcoma (ES) / Treatment of relapsed/refractory Ewing sarcoma in children and young adults, in combination with irinotecan and temozolomide

Day 60 Opinion

Oncology

**Summary of Committee discussion:**

The PDCO discussed this procedure at Day 30 during the October 2019 PDCO plenary meeting.
The PDCO confirmed all the conclusions reached at Day 30 and took into consideration

the clarification provided by the Applicant between Day 30 and Day 60.

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/0124/2019 of 17 April 2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.31. Autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains - Orphan - EMEA-002369-PIP01-18-M01

Celgene Europe B.V.; Treatment of mature B-cell neoplasms / Treatment of paediatric patients with relapsed or refractory BCMA+ B-cell non-Hodgkin lymphoma

Day 60 Opinion

Oncology

**Summary of Committee discussion:**

The PDCO discussed this procedure at Day 60 during the October 2019 PDCO plenary meeting.
The PDCO confirmed all the conclusions reached at Day 30.

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0149/2019 of 17 April 2019).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.32. Pevonedistat - Orphan - EMEA-002117-PIP01-17-M01

Takeda Pharma A/S; Treatment of acute myeloid leukaemia (AML) / Treatment of myelodysplastic syndromes (MDS) / Treatment of paediatric patients with newly diagnosed high risk AML or relapsed or refractory (R/R) AML / Treatment of relapsed/refractory (R/R) myelodysplastic syndromes (MDS)

Day 60 Opinion

Oncology

**Summary of Committee discussion:**

The PDCO re-discussed the proposed modification taking into account the clarifications provided by the Applicant after D30.
In summary, 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/0054/2018 of 2 March 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

### 2.3.33. Ruxolitinib phosphate - EMEA-000901-PIP04-17-M01

Novartis Europharm Limited; Chronic graft versus host disease / Treatment of chronic graft versus host disease (GvHD) after allogeneic hematopoietic stem cell transplantation (alloSCT) in paediatric patients aged 28 days and above

Day 60 Opinion

Oncology

**Summary of Committee discussion:**

In conclusion, based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0061/2018 of 16 March 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

### 2.3.34. Inotuzumab ozogamicin - Orphan - EMEA-001429-PIP01-13-M03

Pfizer Europe MA EEIG; Treatment of acute lymphoblastic leukaemia / Treatment of relapsed or refractory B cell precursor acute lymphoblastic leukaemia

Day 60 Opinion

Oncology / Haematology-Hemostaseology

**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/0402/2017 of 19 December 2017).

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

### 2.3.35. Bilastine - EMEA-000347-PIP02-16-M01

Faes Farma S.A.; Treatment of allergic conjunctivitis

Day 60 Opinion

Ophthalmology

**Summary of Committee discussion:**

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

accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/009/2019 of 3 January 2019).s

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

## 2.3.36. Mexiletine hydrochloride - Orphan - EMEA-002012-PIP01-16-M02

Lupin Europe GmbH; Treatment of myotonic disorders

Day 60 Opinion

Other

**Summary of Committee discussion:**

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0210/2018 of 17 July 2018).
The new PDCO Opinion on the modified agreed PIP supersedes the previous PDCO Opinion.

## 2.3.37. Loxapine - EMEA-001115-PIP01-10-M07

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

Day 60 Opinion

Psychiatry

**Summary of Committee discussion:**

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

## 2.3.38. Lurasidone hydrochloride - EMEA-001230-PIP01-11-M05

AZIENDE CHIMICHE RIUNITE ANGELINI FRANCESCO - A.C.R.A.F. S.p.A.; Schizophrenia

Day 60 Opinion

Psychiatry

**Summary of Committee discussion:**

Based on the review of the rationale submitted by the Applicant for modifying the agreed paediatric investigation plan, the PDCO considered that the proposed changes could be accepted.
The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision.

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

## 2.3.39. Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1) - EMEA-001894-PIP01-15-M01

Seqirus GmbH; For the prevention of influenza caused by Influenza virus types A and B contained in the vaccine

Day 60 Opinion

Vaccines

**Summary of Committee discussion:**

The PDCO adopted by majority a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0303/2016 of 4 November 2016) and granted the extension of the waiver for the age subset from 6 months to less than 18 years of age on the grounds that the medicinal product does not represent a significant therapeutic benefit as the needs are already covered.

Twenty-three members voted in favour of the modification of the agreed PIP to extend the waiver to the entire paediatric population whilst six members had divergent views. The Norwegian PDCO member agreed with the Opinion.

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

## 2.3.40. Beclometasone dipropionate/ formoterol fumarate dihydrate/ glycopyrronium bromide - EMEA-001875-PIP02-18-M01

Chiesi Farmaceutici S.p.A.; Treatment of asthma / Regular treatment of asthma in patients not controlled with medium-high doses of inhaled corticosteroids and long-acting beta2-agonists

Day 0 Opinion

Pneumology-Allergology

**Summary of Committee discussion:**

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

The PDCO therefore adopted a favourable Opinion on the modification of the agreed PIP as set in the Agency's latest decision (P/0179/2019 of 15 May 2019).

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

### 2.3.41. Sodium thiosulfate - EMEA-002147-PIP02-17-M01

Fennec Pharmaceuticals, Inc.; Prevention of platinum-induced ototoxic hearing loss / Prevention of platinum-induced ototoxic hearing loss for standard risk hepatoblastoma (SR-HB) / Prevention of ototoxicity induced by cisplatin (CIS) chemotherapy in patients 1 month and <18 years of age with localized, non-metastatic, solid tumors

Day 1 Opinion

Oncology – Oto-rhino-laryngology

**Summary of Committee discussion:**

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

## 2.4. Opinions on Re-examinations

No items

## 2.5. Opinions on Review of Granted Waivers

No items

## 2.6. Finalisation and adoption of Opinions

No items

## 2.7. Partial Compliance Checks completed by EMA

The following partial compliance checks have concluded positively without PDCO discussion. The Committee has been informed in writing.

### 2.7.1. Vosoritide - EMEA-C1-002033-PIP01-16

BioMarin International Limited; Treatment of achondroplasia

Day 1 letter

Other

### 2.7.2. Durvalumab - EMEA-C1-002028-PIP01-16-M01

AstraZeneca AB; Treatment of malignant neoplasms of haematopoietic and lymphoid tissue

Day 1 letter

Oncology

### 2.7.3. Tremelimumab - EMEA-C1-002029-PIP01-16-M01

AstraZeneca AB; Treatment of malignant neoplasms of haematopoietic and lymphoid tissue

Day 1 letter

Oncology

### 2.7.4. Finerenone - EMEA-C1-001623-PIP01-14-M02

Bayer AG; Treatment of chronic kidney disease

Day 1 letter

Uro-nephrology

### 2.7.5. Ivacaftor / tezacaftor / N-(1,3-dimethyl-1H-pyrazole-4-sulfonyl)-6-[3-(3,3,3-trifluoro-2,2-dimethylpropoxy)-1H-pyrazol-1-yl]-2-[(4S)-2,2,4-trimethylpyrrolidin-1-yl]pyridine-3-carboxamide - EMEA-C1-002324-PIP01-17

Vertex Pharmaceuticals (Ireland) Limited; Treatment of cystic fibrosis

Day 1 letter

Other

### 2.7.6. Burosumab - Recombinant Human IgG1 monoclonal antibody targeting fibroblast growth factor 23 (FGF23) - EMEA-C3-001659-PIP01-15-M03

Kyowa Kirin Holdings B.V.; Treatment of X-linked hypophosphataemia; Indicated for the treatment of X-linked hypophosphataemia with radiographic evidence of bone disease in children 1 year of age and older and adolescents with growing skeletons

Day 1 letter

Other

### 2.7.7. Delamanid - EMEA-C1-001113-PIP01-10-M06

Otsuka Pharmaceutical Development & Commercialisation Europe GmbH; Treatment of multi drug resistant tuberculosis

Day 1 letter

Infectious Diseases

## 2.8. Revision of PDCO Opinions

No items

# 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. Abemaciclib - EMEA-002342-PIP02-18

High grade glioma (HGG), neuroblastoma (NBL) / Treatment of relapsed or refractory neuroblastoma in combination with irinotecan and temozolomide in paediatric patients / Treatment of newly diagnosed high grade glioma in combination with temozolomide in paediatric patients

Day 90 discussion

Oncology

### 3.1.2. EMEA-002616-PIP01-19

Treatment of atopic dermatitis

Day 60 discussion

Dermatology

### 3.1.3. EMEA-002582-PIP01-19

Treatment of chronic spontaneous urticaria

Day 60 discussion

Dermatology

### 3.1.4. Ruxolitinib - EMEA-002618-PIP01-19

Vitiligo

Day 60 discussion

Dermatology

### 3.1.5. Ladarixin - EMEA-002642-PIP01-19

Treatment of type 1 diabetes / Treatment of new-onset type 1 diabetes mellitus

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

### 3.1.6. Pegzilarginase - Orphan - EMEA-001925-PIP02-19

Aeglea BioTherapeutics, Inc.; Arginase 1 deficiency

Day 60 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

### 3.1.7. Benralizumab - EMEA-001214-PIP05-19

Treatment of eosinophilic esophagitis (EoE)

Day 60 discussion

Gastroenterology-Hepatology

### 3.1.8. Guselkumab - EMEA-001523-PIP04-19

Ulcerative colitis: ICD K51 / Treatment of ulcerative colitis

Day 60 discussion

Gastroenterology-Hepatology

### 3.1.9. Guselkumab - EMEA-001523-PIP05-19

Crohn's disease: ICD K50 / Treatment of Crohn's disease

Day 60 discussion

Gastroenterology-Hepatology

### 3.1.10. EMEA-002640-PIP01-19

Eosinophilic esophagitis / Treatment of eosinophilic esophagitis

Day 60 discussion

Gastroenterology-Hepatology

### 3.1.11. Relamorelin - EMEA-002323-PIP02-19

Gastroparesis

Day 60 discussion

Gastroenterology-Hepatology

### 3.1.12. Benralizumab - EMEA-001214-PIP04-19

Treatment of hypereosinophilic syndrome (HES)

Day 60 discussion

Haematology-Hemostaseology

### 3.1.13. EMEA-001312-PIP02-19

Prevention of acute graft-versus-host disease (GVHD)

Day 60 discussion

Immunology-Rheumatology-Transplantation

### 3.1.14. Ravagalimab - EMEA-002617-PIP01-19

Ulcerative colitis

Day 60 discussion

Immunology-Rheumatology-Transplantation

### 3.1.15. The whole range of unmanipulated autologous mononuclear cells derived from human umbilical cord blood (Hau-UCB-mnc) - Orphan - EMEA-001799-PIP03-19

BrainRepair UG (haftungsbeschränkt); Periventricular leukomalacia (PVL) ICD-10-CM P91.2

Day 60 discussion

Neonatology - Paediatric Intensive Care

### 3.1.16. Cenobamate - EMEA-002563-PIP02-19

Treatment of epilepsy

Day 60 discussion

Neurology

### 3.1.17. Gaboxadol - Orphan - EMEA-002620-PIP01-19

Ovid Therapeutics; Angelman syndrome

Day 60 discussion

Neurology

### 3.1.18. Chimeric 2'-O-(2-methoxyethyl) modified antisense oligonucleotide - Orphan - EMEA-002546-PIP01-19

Roche Registration GmbH; Huntington’s disease

Day 60 discussion

Neurology

### 3.1.19. EMEA-002631-PIP01-19

Treatment of acute myeloid leukaemia

Day 60 discussion

Oncology

### 3.1.20. Autologous inactivated glioma cells - Orphan - EMEA-002661-PIP01-19

ERC Belgium; Recurrent high-grade glioma / Treatment of recurrent high-grade glioma

Day 60 discussion

Oncology

### 3.1.21. Autologous inactivated glioma cells - Orphan - EMEA-002662-PIP01-19

ERC Belgium; Recurrent high-grade glioma / Treatment of recurrent high-grade glioma

Day 60 discussion

Oncology

### 3.1.22. Autologous inactivated glioma cells - Orphan - EMEA-002663-PIP01-19

ERC Belgium; Recurrent high-grade glioma / Treatment of recurrent high-grade glioma

Day 60 discussion

Oncology

### 3.1.23. Autologous inactivated glioma cells - Orphan - EMEA-002664-PIP01-19

ERC Belgium; Recurrent high-grade glioma / Treatment of recurrent high-grade glioma

Day 60 discussion

Oncology

### 3.1.24. Sulindac / eflornithine hydrochloride monohydrate - Orphan - EMEA-001518-PIP03-19

CANCER PREVENTION PHARMA (IRELAND) LIMITED; Treatment of familial adenomatous polyposis

Day 60 discussion

Oncology

### 3.1.25. Temozolomide - EMEA-002634-PIP01-19

Treatment of malignant glioma / Children from the age of three years and adolescent patients with malignant glioma, such as glioblastoma multiforme or anaplastic astrocytoma, showing recurrence or progression after standard therapy, who have difficulty swallowing

Day 60 discussion

Oncology

### 3.1.26. Atropine - EMEA-002545-PIP01-19

Myopia

Day 60 discussion

Ophthalmology

### 3.1.27. Propranolol - EMEA-002625-PIP01-19

Retinopathy of prematurity

Day 60 discussion

Ophthalmology

### 3.1.28. Ondansetron - EMEA-002623-PIP01-19

Treatment of alcohol use disorder (AUD)

Day 60 discussion

Other / Neurology

### 3.1.29. EMEA-002639-PIP01-19

Cystic fibrosis / Treatment of cystic fibrosis in children from birth to <18 years

Day 60 discussion

Pneumology – Allergology

### 3.1.30. EMEA-002638-PIP01-19

Cystic fibrosis / Treatment of cystic fibrosis in children from birth to <18 years

Day 60 discussion

Pneumology – Allergology

### 3.1.31. EMEA-002641-PIP01-19

Prevention of pneumococcal disease caused by S. *pneumoniae* / For the active immunisation for the prevention of invasive pneumococcal diseases (IPD) caused by S. *pneumoniae* in infants, children and adolescents from 6 weeks to < 18 years of age

Day 60 discussion

Vaccines

### 3.1.32. Chloroprocaine - EMEA-000639-PIP04-19

Epidural block (extension of epidural anaesthesia in unplanned caesarean section)

Day 30 discussion

Anaesthesiology

### 3.1.33. Chloroprocaine - EMEA-000639-PIP05-19

Ocular surface anesthesia

Day 30 discussion

Anaesthesiology

### 3.1.34. Ethanol - EMEA-002672-PIP01-19

Treatment of primary hypertension

Day 30 discussion

Cardiovascular Diseases

### 3.1.35. Bis-choline tetrathiomolybdate - Orphan - EMEA-002232-PIP02-19

Alexion Europe S.A.S.; Wilson disease

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

### 3.1.36. Pegfilgrastim - EMEA-002671-PIP01-19

Treatment of chemotherapy-induced neutropenia and prevention of chemotherapy-

induced febrile neutropenia / Reduction in the duration of neutropenia and the incidence of febrile neutropenia in paediatric patients treated with cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukaemia and myelodysplastic syndromes)

Day 30 discussion

Haematology-Hemostaseology

### 3.1.37. Taniborbactam / cefepime - EMEA-002576-PIP01-19

Treatment of bacterial infections / Treatment of complicated urinary tract infections (cUTI) / Treatment of hospital acquired and ventilator acquired pneumonia (HAP/VAP) / Treatment of complicated intra-abdominal infections (CIAI)

Day 30 discussion

Infectious Diseases

### 3.1.38. Masitinib mesylate - Orphan - EMEA-001266-PIP04-19

AB Science; Treatment of amyotrophic lateral sclerosis

Day 30 discussion

Neurology

### 3.1.39. Rozanolixizumab - Orphan - EMEA-002681-PIP01-19

UCB Pharma S.A.; Treatment of myasthenia gravis

Day 30 discussion

Neurologys

### 3.1.40. EMEA-002635-PIP01-19

Treatment of advanced or metastatic malignancies harbouring anaplastic lymphoma kinase (ALK) ROS1, or NTRK1-3 alterations

Day 30 discussion

Oncology

### 3.1.41. EMEA-001862-PIP02-19

Treatment of mantle cell lymphoma

Day 30 discussion

Oncology

### 3.1.42. Cyclophosphamide - EMEA-002644-PIP01-19

Treatment of malignant disease / Cyclophosphamide is a cytotoxic drug for the treatment of malignant disease in children. As a single agent, it has successfully produced an objective remission in a wide range of malignant conditions / Cyclophosphamide is also frequently used in combination with other cytotoxic drugs, radiotherapy or surgery

Day 30 discussion

Oncology

### 3.1.43. Iberdomide - EMEA-002636-PIP01-19

Treatment of mature B-cell neoplasms

Day 30 discussion

Oncology

### 3.1.44. Imatinib - EMEA-002643-PIP01-19

Treatment of newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) integrated with chemotherapy / Treatment of chronic myelogenous leukaemia: Philadelphia chromosome (Ph1) positive with crisis of blast cells / Paediatric patients with newly diagnosed Philadelphia chromosome (bcr-abl) positive (Ph+) chronic myeloid leukaemia (CML) for whom bone marrow transplantation is not considered as the first line of treatment / Paediatric patients with Ph+ CML in chronic phase after failure of interferon-alpha therapy or in accelerated phase or blast crisis / Paediatric patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) integrated with chemotherapy

Day 30 discussion

Oncology

### 3.1.45. Lenvatinib - EMEA-001119-PIP03-19

Treatment of all conditions included in the category of malignant neoplasms except haematopoietic and lymphoid tissue

Day 30 discussion

Oncology

### 3.1.46. Sacituzumab govitecan - EMEA-002645-PIP01-19

Refractory/relapsed triple-negative breast cancer (TNBC)

Day 30 discussion

Oncology

### 3.1.47. EMEA-002606-PIP02-19

Treatment of multiple myeloma

Day 30 discussion

Oncology / Haematology-Hemostaseology

### 3.1.48. EMEA-002656-PIP01-19

Chikungunya disease

Day 30 discussion

Vaccines

### 3.1.49. Aztreonam / avibactam sodium - EMEA-002283-PIP01-17

Infections caused by Gram-negative bacteria, including those that produce metallo-β-lactamases, for which there are limited or no treatment options / For the treatment of complicated urinary tract infections / For the treatment of ventilator associated pneumonia / For the treatment of complicated intra-abdominal infections / For the treatment of hospital-acquired pneumonia

Day 90 discussion

Infectious Diseases

## 3.2. Discussions on Compliance Check

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

### 3.2.1. Valoctocogene roxaparvovec - EMEA-C1-002427-PIP01-18

BioMarin International Ltd.; Treatment of congenital haemophilia A

Day 30 discussion

Haematology-Hemostaseology

### 3.2.2. Baloxavir marboxil - EMEA-C1-002440-PIP01-18

Roche Registration GmbH; Treatment of influenza

Day 30 discussion

Infectious Diseases

### 3.2.3. Lasmiditan - EMEA-C1-002166-PIP01-17-M02

Eli Lilly and Company Limited; Treatment of migraine headache

Day 30 discussion

Neurology

### 3.2.4. Ragweed pollen extract (ambrosia artemisiifolia) - EMEA-C-001881-PIP01-15

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

Day 30 discussion

Pneumology – Allergology

### 3.2.5. Potassium hydrogen carbonate / Potassium citrate monohydrated - EMEA-C-001357-PIP01-12-M02

ADVICENNE; Treatment of renal tubular acidosis

Day 30 discussion

Uro-nephrology

## 3.3. Discussions on Modification of an Agreed Paediatric Investigation Plan

### 3.3.1. Edoxaban - EMEA-000788-PIP02-11-M09

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

### 3.3.2. Small molecule Janus Kinase -1 inhibitor - EMEA-002312-PIP01-17-M01

Pfizer Europe MA EEIG; Moderate to severe atopic dermatitis

Day 30 discussion

Dermatology

### 3.3.3. Exenatide - EMEA-000689-PIP01-09-M09

AstraZeneca AB; Non-insulin dependent diabetes mellitus (excluding treatment with thiazolidinediones) / Non-insulin dependent diabetes mellitus (treatment including

thiazolidinediones) / Non-insulin dependent diabetes mellitus - in combination with insulin (with or without oral antidiabetics) / Treatment of type 2 diabetes mellitus

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism

### 3.3.4. Tolvaptan - EMEA-001231-PIP02-13-M07

Otsuka Pharmaceutical Netherlands B.V.; Polycystic kidney disease (PKD) / Treatment of progression of autosomal dominant polycystic kidney disease (ADPKD)

Day 30 discussion

Endocrinology-Gynaecology-Fertility-Metabolism / Uro-nephrology

### 3.3.5. Ozanimod hydrochloride - EMEA-001710-PIP03-17-M01

Celgene Europe B.V.; Treatment of ulcerative colitis / Treatment of moderate to severely active ulcerative colitis

Day 30 discussion

Gastroenterology-Hepatology

### 3.3.6. Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human betaA-T87Q-globin gene - Orphan - EMEA-001665-PIP01-14-M03

bluebird bio (Netherlands) B.V.; Treatment of β-thalassaemia / Treatment of β--thalassaemia major and severe intermedia

Day 30 discussion

Haematology-Hemostaseology

### 3.3.7. Human cell line recombinant human Factor VIII (human-cl rhFVIII) / Human coagulation factor VIII (rDNA) - EMEA-001024-PIP01-10-M02

Octapharma Pharmazeutika Produktionsges.m.b.H; D66: Hereditary factor VIII deficiency, haemophilia A / Haemophilia A

Day 30 discussion

Haematology-Hemostaseology

### 3.3.8. Luspatercept - Orphan - EMEA-001521-PIP01-13-M04

Celgene Europe B.V.; Anaemias due to chronic disorders / Treatment of anaemia in patients with beta-thalassemia intermedia and major

Day 30 discussion

Haematology-Hemostaseology

### 3.3.9. Belimumab - EMEA-000520-PIP02-13-M03

Glaxo Group Limited; Systemic lupus erythematosus / Treatment of systemic lupus erythematosus

Day 30 discussion

Immunology-Rheumatology-Transplantation

### 3.3.10. Voxilaprevir / velpatasvir / sofosbuvir - EMEA-001822-PIP01-15-M01

Gilead Sciences Ireland UC; Treatment of chronic hepatitis C / Treatment of chronic hepatitis C in adolescents and children 12 years of age and older

Day 30 discussion

Infectious Diseases

### 3.3.11. Daclizumab - EMEA-001349-PIP01-12-M03

Biogen Idec Ltd; Multiple sclerosis / Treatment of relapsing remitting forms of multiple sclerosis

Day 30 discussion

Neurology

### 3.3.12. Avapritinib - Orphan - EMEA-002358-PIP02-18-M01

Blueprint Medicines (Netherlands) B.V.; Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms) / Treatment of paediatric patients from 2 to less than 18 years of age with relapsed/refractory solid tumour harbouring mutations in either KIT or PDGFR-alpha

Day 30 discussion

Oncology

### 3.3.13. Brigatinib - EMEA-002296-PIP01-17-M01

Takeda Pharm A/S; 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 30 discussion

Oncology

### 3.3.14. Lumacaftor / ivacaftor - EMEA-001582-PIP01-13-M09

Vertex Pharmaceuticals (Europe) Ltd; Cystic fibrosis / Treatment of cystic fibrosis

Day 30 discussion

Other

### 3.3.15. Selexipag - EMEA-000997-PIP01-10-M03

Janssen Cilag International NV; Pulmonary arterial hypertension / Treatment of pulmonary arterial hypertension

Day 30 discussion

Other

### 3.3.16. Dupilumab - EMEA-001501-PIP02-13-M04

sanofi-aventis recherche & développement; Treatment of asthma

Day 30 discussion

Pneumology – Allergology

### 3.3.17. Tezepelumab - EMEA-001613-PIP01-14-M04

AstraZeneca AB; Treatment of asthma / Tezepelumab is indicated as add-on maintenance treatment of patients with severe asthma aged 5 years and older

Day 30 discussion

Pneumology – Allergology

### 3.3.18. Agomelatine - EMEA-001181-PIP01-11-M05

Les Laboratoires Servier; Major depressive episodes

Day 30 discussion

Psychiatry

### 3.3.19. Lumasiran sodium - Orphan - EMEA-002079-PIP01-16-M01

Alnylam UK Limited; Treatment of primary hyperoxaluria type 1

Day 30 discussion

Uro-nephrology

### 3.3.20. Daprodustat - EMEA-001452-PIP01-13-M02

Alexandra West; Treatment of anaemia associated with chronic renal disease

Day 30 discussion

Uro-nephrology / Haematology-Hemostaseology

# 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 for Nomination of Rapporteur and Peer reviewer

No items

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

**Summary of committee discussion:**

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

## 4.3. Nominations for other activities

**Summary of committee discussion:**

The PDCO approved the lists of Rapporteurs and Peer Reviewers.

# 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.

## 5.1. New Scientific Advice

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

## 5.2. Ongoing Scientific Advice

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

## 5.3. Final Scientific Advice (Reports and Scientific Advice letters)

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. Elacestrant – EMEA-14-2019

Radius International, Limited; The classes of oestrogen receptor modulator medicinal products for treatment of breast malignant neoplasms / Treatment of advanced/metastatic oestrogen receptor (ER)+ breast cancer

**Action:** For adoption

# 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

No items

# 8. Annual reports on deferrals

Note: The annual reports on deferrals to be noted by the members of the PDCO are flagged in the Annex B.

# 9. Organisational, regulatory and methodological matters

## 9.1. Mandate and organisation of the PDCO

### 9.1.1. PDCO Vice-Chairperson - election

**Summary of Committee discussion:**

Following the election of Koenraad Norga as the new Chairperson in July 2019 with a mandate starting on 14 September 2019 (see PDCO minutes July 2019) as well as the elections organised in September 2019 to elect the new Vice- Chairperson (see PDCO minutes September 2019), the PDCO proceeded with a second election of the vice-Chairperson as per the principles discussed in September 2019. The election of a new vice-Chairperson took place on 16 October 2019. The EMA Secretariat reminded the PDCO members of the Rules of Procedure (EMA/348440/2008 Rev.1) pertaining to the election of the Vice-Chairperson as well as the election process. Candidate(s) addressed the PDCO.

The election took place in the presence of 30 PDCO members out of which 29 were eligible to vote[1]. Sabine Scherer, PDCO member for Germany, was elected as PDCO Vice-Chair. Her mandate started immediately on 16 October 2019 for a term of three years, which may be renewed once. The newly elected Vice-Chair thanked the Committee.

## 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 informed about the final CHMP Opinions on medicinal products with recommended paediatric indications adopted in September 2019. These included Benlysta (belimumab).

The list of procedures with paediatric indications to be evaluated by the CHMP, starting in September 2019, 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 (NcWG) evaluation and discussion.

### 9.3.2. Formulation Working Group

PDCO member: Brian Aylward

**Summary of Committee discussion:**

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

### 9.3.3. Extrapolation: case studies under assessment

MSWP Chair: Kristin Karlsson;

**Summary of Committee discussion:**

Case examples were presented to the Committee on procedures under assessment using extrapolation.

[1] Icelandic and Norwegian members do not vote for the PDCO Chairperson election as per the Rules of Procedure of the Paediatric Committee (PDCO). At the current meeting, there was no PDCO representative from Iceland.

### 9.3.4. Extrapolation: Discussion of draft extrapolation guidance template

**Summary of Committee discussion:**

The Committee discussed a draft guidance document aiming at a structured approach to using extrapolation in paediatric drug development.

### 9.3.5. Scientific advice working party (SAWP) – nomination of a PDCO representative

**Summary of Committee discussion:**

Further to the call open at the September 2019 PDCO plenary meeting (see PDCO minutes September 2019) for the PDCO to nominate a PDCO representative at SAWP, the PDCO completed the nomination process.

## 9.4. Cooperation within the EU regulatory network

### 9.4.1. European Network of Paediatric Research (Enpr) - European Medicines Agency (EMA): Report on face-to-face meeting

PDCO member: Marek Migdal, Angeliki Siapkara

**Summary of Committee discussion:**

The PDCO was informed about the discussions and outcomes of this year's meeting of the members and coordinating group of Enpr-EMA which took place on 14 October 2019.

## 9.5. Cooperation with International Regulators

### 9.5.1. Report from the Paediatric Cluster Teleconference

**Summary of Committee discussion:**

The Committee was informed about the discussions at the Paediatric Cluster teleconferences taking place on 24 September 2019 and 04 October 2019.

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

### 9.6.1. Fifth Accelerate Paediatric Strategy Forum for Medicinal Product Development of Epigenetic Modifiers in Children

**Summary of Committee discussion:**

The Committee was informed about the upcoming 5th Accelerate Strategy Forum and colleagues invited to express their interest to participate.

## 9.7. PDCO work plan

### 9.7.1. PDCO Work Plan 2020 proposal

PDCO member: Koenraad Norga;

**Summary of Committee discussion:**

The timelines for drafting and adopting the Work Plan 2020 were presented to the Committee and a call for topics was raised.

## 9.8. Planning and reporting

No items

# 10. Any other business

### 10.1.1. Update on EMA relocation

**Summary of Committee discussion:**

Following the update in September 2019 on the planned timelines for the new permanent EMA headquarters in Amsterdam, the Netherlands (for further background, see PDCO minutes September 2019), the PDCO was updated on further practical information relating to the new EMA building.

# 11. Breakout sessions

### 11.1.1. Paediatric oncology

**Summary of Committee discussion:**

The group discussed upcoming events and ongoing PIPs regarding paediatric oncology.

### 11.1.2. Neonatology

**Summary of Committee discussion:**

The Neonatology breakout session discussed ongoing PIPs and Scientific Advices involving neonates.

### 11.1.3. Inventory

**Summary of Committee discussion:**

The paediatric inventory group reconvened on the margins of the PDCO plenary meeting to continue discussion on assessment of unmet needs.

# 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 September 2019 meeting

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Koenraad Norga | Chair | Belgium | When chairing the meeting:<br>To be replaced for discussions, final deliberations and voting<br><br>When not chairing the meeting: No participation in final deliberations and voting | Ambrisentan - Orphan - EMEA-000434-PIP01-08-M06;<br><br>Zanamivir - EMEA-001318-PIP01-12-M03;<br><br>Rolapitant - EMEA-001768-PIP02-15-M02;<br><br>Belimumab - EMEA-000520-PIP02-13-M03 |
| Karl-Heinz Huemer | Member | Austria | No interests declared | N/A |
| Johanna Wernsperger | Alternate | Austria | No interests declared | N/A |
| Karen Van Malderen | Alternate | Belgium | No interests declared | N/A |
| Dimitar Roussinov | Member | Bulgaria | No restrictions applicable to this meeting | None |
| Georgios Savva | Member | Cyprus | No interests declared | N/A |
| Tereza Bazantova | Member | Czech Republic | No interests declared | N/A |
| Kirstine Moll Harboe | Member | Denmark | No interests declared | N/A |
| Jana Lass | Alternate | Estonia | No interests declared | N/A |
| Ann Marie Totterman | Member | Finland | No interests declared | N/A |
| Pia Annunen | Alternate | Finland | No participation in discussion, final deliberations and voting on: | Daclatasvir - EMEA-001191-PIP01-11-M03 - Treatment of chronic viral hepatitis C - Bristol-Myers Squibb Pharma EEIG |
| Sylvie Benchetrit | Member | France | No interests declared | N/A |
| Dominique Ploin | Alternate | France | No interests declared | N/A |
| Sabine Scherer | Member | Germany | No interests declared | N/A |
| Yuansheng Sun | Alternate | Germany | No interests declared | N/A |
| Eleni Katsomiti | Member | Greece | No interests declared | N/A |
| Anastasia | Alternate | Greece | No interests declared | N/A |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Mountaki | | | | |
| Ágnes Gyurasics | Member (CHMP member) | Hungary | No interests declared | N/A |
| Brian Aylward | Member | Ireland | No interests declared | N/A |
| Sara Galluzzo | Member | Italy | No interests declared | N/A |
| Dina Apele-Freimane | Member | Latvia | No restrictions applicable to this meeting | None |
| Sigita Burokiene | Member | Lithuania | No interests declared | N/A |
| Herbert Lenicker | Alternate | Malta | No interests declared | N/A |
| Roel Bolt | Member | Netherlands | No interests declared | N/A |
| Maaike van Dartel | Alternate | Netherlands | No interests declared | N/A |
| Siri Wang | Member | Norway | No interests declared | N/A |
| Anette Solli Karlsen | Alternate | Norway | No interests declared | N/A |
| Marek Migdal | Member | Poland | No interests declared | N/A |
| Helena Fonseca | Member | Portugal | No interests declared | N/A |
| Hugo Tavares | Alternate | Portugal | No interests declared | N/A |
| Dana Gabriela Marin | Member (CHMP alternate) | Romania | No interests declared | N/A |
| Peter Sisovsky | Member | Slovakia | No interests declared | N/A |
| Peter Szitanyi | Alternate | Slovakia | No interests declared | N/A |
| Stefan Grosek | Member | Slovenia | No interests declared | N/A |
| Fernando de Andrés Trelles | Member | Spain | No interests declared | N/A |
| Maria Jesus Fernández Cortizo | Alternate | Spain | No interests declared | N/A |
| Ninna Gullberg | Member | Sweden | No interests declared | N/A |
| Eva Agurell | Alternate | Sweden | No interests declared | N/A |
| Angeliki Siapkara | Member | United Kingdom | No interests declared | N/A |
| Martina Riegl | Alternate | United Kingdom | No interests declared | N/A |
| Fernando Cabanas | Member | Healthcare Professionals' Representative | No restrictions applicable to this meeting | None |
| Jorrit | Alternate | Healthcare | No interests declared | N/A |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Gerritsen | | Professionals' Representative | | |
| Francesca Rocchi | Member | Healthcare Professionals' Representative | No restrictions applicable to this meeting | N/A |
| Catherine Cornu | Alternate | Healthcare Professionals' Representative | No participation in discussion, final deliberations and voting on: | Lumasiran sodium - Orphan - EMEA-002079-PIP01-16-M01 - Treatment of primary hyperoxaluria Type 1 - Alnylam UK Limited; |
| Johannes Taminiau | Member | Healthcare Professionals' Representative | No interests declared | N/A |
| Doina Plesca | Alternate | Healthcare Professionals' Representative | No restrictions applicable to this meeting | N/A |
| Günter Karl-Heinz Auerswald | Member | Patients' Organisation Representative | No restrictions applicable to this meeting | N/A |
| Paola Baiardi | Alternate | Patients' Organisation Representative | No restrictions applicable to this meeting | N/A |
| Michal Odermarsky | Member | Patients' Organisation Representative | No restrictions applicable to this meeting | N/A |
| Dimitrios Athanasiou | Member | Patients' Organisation Representative | No interests declared | N/A |
| Kristin Karlsson | Expert - in person* | MSWP Chair | | Edoxaban (tosylate) - EMEA-000788-PIP02-11-M09 |
| Maria Estela Moreno Martin | Expert - in person* | ES Expert | | N/A |
| Helena Back | Expert - in person* | SE Expert | | N/A |
| Marina Senek | Expert - in person* | SE Expert | | N/A |
| Katriina Tarkiainen | Expert - via telephone* | FI Expert | | N/A |

* 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/