



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

17 December 2021
EMA/PDCO/780344/2021
Human Medicines Division

PDCO monthly report of opinions on paediatric investigation plans and other activities

14-17 December 2021

Opinions on paediatric investigation plans

The Paediatric Committee (PDCO) adopted opinions agreeing paediatric investigation plans (PIPs) for the following medicines:

- Aficamten, EMEA-002958-PIP01-21, from Cytokinetics Inc., for the treatment of hypertrophic cardiomyopathy;
- Single strain of non-genetically modified *Prevotella histicola*, EMEA-002933-PIP01-20, from Evelo Biosciences, Inc., for the treatment of psoriasis;
- Ethinylestradiol / dienogest, EMEA-002229-PIP02-21, from Chemo Research, for the treatment of hirsutism associated with polycystic ovary syndrome;
- Poly(oxy-1,2-ethanediyl), alpha-hydro-omega-methoxy, ether with N-[[[2-[[[6-[[1-[3-[[3-(2,3-dihydroxypropoxy)propyl]amino]-3-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]thio]hexyl]amino]ethyl]amino]carbonyl]-2-methylalanyl-teriparatide (2:1) (TransCon PTH), EMEA-002955-PIP01-21, from Ascendis Pharma Bone Diseases A/S, for the treatment of hypoparathyroidism;
- Tildacerfont, EMEA-002970-PIP01-21, from Spruce Biosciences, Inc., for the treatment of congenital adrenal hyperplasia;
- 2-Amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-((1R,5S)-3-(tetrahydro-2H-pyran-4-yl)-3-azabicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide fumarate dihydrate (INCB000928), EMEA-002992-PIP01-21, from Incyte Biosciences Distribution B.V, for the treatment of fibrodysplasia ossificans progressiva;
- Benralizumab, EMEA-001214-PIP07-21, from AstraZeneca AB, for the treatment of eosinophilic gastritis/eosinophilic gastroenteritis;
- Izencitinib, EMEA-002757-PIP02-21, from Theravance Biopharma Ireland Limited, for the treatment of Crohn's disease;

Official address Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

An agency of the European Union



- Benralizumab, EMEA-001214-PIP04-19, from AstraZeneca AB, for the treatment of hypereosinophilic syndrome (HES);
- Alectinib, EMEA-002431-PIP02-21, from Roche Registration GmbH, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms);
- Ribociclib, EMEA-002765-PIP02-21, from Novartis Europharm Limited, for the treatment of neuroblastoma;
- Vorasidenib (as hemicitrate, hemihydrate salt), EMEA-002932-PIP02-21, from Les Laboratoires Servier (LLS), for the treatment of low grade glioma;
- Nirogacestat hydrobromide, EMEA-002971-PIP01-21, from SpringWorks Therapeutics, Inc, for the treatment of soft tissue sarcoma;
- ExPEC9V, EMEA-002996-PIP01-21, from Janssen-Cilag International NV, for the prevention of infections caused by extraintestinal pathogenic *Escherichia coli* (ExPEC);
- (1R,2S,5S)-N-((1S)-1-Cyano-2-((3S)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido)butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide, EMEA-003081-PIP01-21, from Pfizer Europe MA EEIG, for the treatment of coronavirus disease 2019 (COVID-19) and prevention of coronavirus disease 2019 (COVID-19);
- Derivative of 6-[2-(pyridin-2-yl)phenoxy]methyl}-1,2,3,4-tetrahydroisoquinoline, EMEA-003002-PIP01-21, from Boehringer Ingelheim International GmbH, for the treatment of chronic kidney disease;

The PDCO adopted an opinion(s) on the **refusal** of a PIP and a deferral, and on the granting of a product-specific waiver for:

- Insulin efsitora alfa, EMEA-003105-PIP01-21, from Eli Lilly and Company, for the treatment of type 1 diabetes mellitus and the treatment of type 2 diabetes mellitus.

For this medicine the PDCO granted a product-specific waiver on its own motion for all subsets of the paediatric population in the specified condition, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population and on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

A PIP sets out a programme for the development of a medicine in the paediatric population. The PIP aims to generate the necessary quality, safety and efficacy data through studies to support the authorisation of the medicine for use in children of all ages. These data have to be submitted to the European Medicines Agency, or national competent authorities, as part of an application for a marketing authorisation for a new medicine, or for one covered by a patent. In some cases, a PIP may include a waiver of the studies in one or more paediatric subsets, or a deferral.

Adoption of an opinion following re-examination

The PDCO adopted opinions for the following products:

- Following the re-examination of the positive opinion on a modification to an agreed PIP adopted on 15 October 2021 for glycopyrronium bromide, EMEA-002383-PIP01-18-M01, from Dr. August Wolff GmbH & Co. KG - Arzneimittel, for the treatment of hyperhidrosis, the PDCO adopted a revised positive opinion and agreed to the changes regarding the measures and the timelines of the

paediatric investigation plan and the timelines of the deferral in the scope set out in the Annex I of the opinion;

- Following the re-examination of the positive opinion on a modification to an agreed PIP adopted on 15 October 2021 for ravulizumab, EMEA-001943-PIP04-20, from Alexion Europe SAS, for the treatment of neuromyelitis optica spectrum disorders, the PDCO recommended to maintain its opinion and agreed a paediatric investigation plan in accordance with Article 17(1) of said Regulation; granted a deferral in accordance with Article 21 of said Regulation and granted a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

A re-examination of the opinion can be requested by the applicant within 30 days following receipt of the opinion of the PDCO. The grounds for the re-examination should be based only on the original information and scientific data provided in the application that were previously available to the PDCO and on which the initial opinion was based. This may include new analysis of the same data or minor protocol amendments to a previously proposed study. Significant changes to the previous plan cannot be part of the re-examination process.

Opinions on product-specific waivers

The PDCO adopted positive opinions for product-specific waivers, recommending that the obligation to submit data obtained through clinical studies with children be waived in all subsets of the paediatric population, for the following medicines:

- Acetylsalicylic acid / rosuvastatin calcium, EMEA-002239-PIP02-21, from Lanova Farmaceutici SRL, for the prevention of cardiovascular events;
- Colchicine, EMEA-003101-PIP01-21, from Pharmascience International Limited, for the prevention of cardiovascular events;
- Derivative of pyrrolopyrimidine, EMEA-003109-PIP01-21, from AstraZeneca AB, for the prevention of cardiovascular events in patients with heart failure;
- Fostamatinib, EMEA-001196-PIP03-21, from Instituto Grifols, S.A., for the treatment of autoimmune haemolytic anaemia;
- Gantenerumab, EMEA-003107-PIP01-21, from Roche Registration GmbH, for the prevention of Alzheimer's disease;
- Pembrolizumab / favezelimab, EMEA-003104-PIP01-21, from Merck, Sharp & Dohme (Europe) Inc, for the treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue neoplasms and melanoma) and treatment of malignant neoplasms of the central nervous system;
- Aumolertinib, EMEA-003106-PIP01-21, from SFL Pharmaceuticals Deutschland GmbH, for the treatment of lung cancer;

The PDCO adopted 0 opinions on the **refusal** of a request for waiver.

Waivers can be issued if there is evidence that the medicine concerned is likely to be ineffective or unsafe in the paediatric population, or that the disease or condition targeted occurs only in adult populations, or that the medicine, or the performance of trials, does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

Opinions on modifications to an agreed PIP

The PDCO also adopts, every month, opinions on modifications to an agreed PIP, which can be requested by the applicant when the plan is no longer appropriate or when there are difficulties that render the plan unworkable. The PDCO adopted positive opinions, agreeing change(s), for the following products:

- Dupilumab, EMEA-001501-PIP02-13-M07, from sanofi-aventis groupe, for the treatment of asthma;
- Vadadustat, EMEA-001944-PIP01-16-M03, from Otsuka Pharmaceutical Development & Commercialisation Europe GmbH, for the treatment of anaemia due to chronic disorders;
- Mitapivat, EMEA-002684-PIP01-19-M01, from Agios Netherlands B.V., for the treatment of pyruvate kinase deficiency;
- Baricitinib, EMEA-001220-PIP01-11-M06, from Eli Lilly and Company Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Allogeneic bone marrow derived mesenchymal stromal cells, ex-vivo expanded, EMEA-002706-PIP01-19-M01, from medac Gesellschaft für klinische Spezialpräparate mbH, for the treatment of acute graft-versus-host disease;
- Avibactam / ceftazidime, EMEA-001313-PIP01-12-M11, from Pfizer Europe MA EEIG, for the treatment of infections due to aerobic Gram-negative organisms, treatment of intra-abdominal infections, treatment of pneumonia and treatment of urinary tract infections;
- Cabotegravir, EMEA-001418-PIP01-13-M04, from ViiV Healthcare UK Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Atazanavir (sulphate) / cobicistat, EMEA-001465-PIP01-13-M04, from Bristol-Myers Squibb Pharma EEIG, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Brivaracetam, EMEA-000332-PIP02-17-M03, from UCB Pharma S.A., for the treatment of neonatal seizures and treatment of paediatric epilepsy syndromes;
- Onasemnogene abeparvovec, EMEA-002168-PIP01-17-M04, from Novartis Gene Therapy EU Limited, for the treatment of spinal muscular atrophy;
- Phenobarbital, EMEA-002532-PIP01-18-M02, from Proveca Pharma Limited, for the treatment of epilepsy;
- Talimogene laherparepvec, EMEA-001251-PIP01-11-M05, from Amgen Europe B.V., for the treatment of melanoma;
- Gemtuzumab ozogamicin, EMEA-001733-PIP02-15-M02, from Pfizer Europe MA EEIG, for the treatment of acute myeloid leukaemia;
- Avapritinib, EMEA-002358-PIP02-18-M02, from Blueprint Medicines (Netherlands) B.V., for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms);
- Cysteamine (hydrochloride), EMEA-000322-PIP01-08-M06, from Recordati Rare Diseases SARL, for the treatment of corneal cystine crystal deposits in cystinosis;
- Lanadelumab, EMEA-001864-PIP01-15-M06, from Takeda Pharmaceuticals International AG Ireland Branch, for the prevention of hereditary angioedema attacks;

- Budesonide / glycopyrronium bromide / formoterol fumarate dihydrate, EMEA-002063-PIP01-16-M01, from AstraZeneca AB, for the treatment of asthma;
- Dexmedetomidine (hydrochloride), EMEA-002758-PIP01-19-M01, from BioXcel Therapeutics, Inc., for the treatment of bipolar disorder and treatment of schizophrenia;

Opinion on compliance check

The PDCO adopted positive opinions on (full) compliance check for:

- Simeticone / macrogol 4000 / potassium chloride / sodium sulphate, anhydrous / sodium chloride / citric acid, anhydrous / sodium citrate, EMEA-C-001356-PIP02-12-M04, from Alfasigma S.p.A., for the bowel cleansing prior to clinical procedures;
- Peramivir, EMEA-C-001856-PIP02-16-M02, from BioCryst Ireland Limited, for the treatment of influenza;
- Pneumococcal polysaccharide serotype 1 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 3 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 4 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 5 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 6A – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 6B – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 7F – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 9V – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 14 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 18C – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 19A – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 19F – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 22F – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 23F – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 33F – diphtheria CRM197 conjugate (15-valent pneumococcal polysaccharide conjugate vaccine [V114]), EMEA-C-002215-PIP01-17-M03, from Merck Sharp & Dohme (Europe), Inc., for the prevention of disease caused by *Streptococcus pneumoniae*;

A compliance check is performed to verify that all the measures agreed in a PIP and reflected in the Agency's decision have been conducted in accordance with the decision, including the agreed timelines. Full compliance with all studies/measures contained in the PIP is one of several prerequisites for obtaining the rewards and incentives provided for in Articles 36 to 38 of the Paediatric Regulation.

Before the submission of a request for a compliance check, applicants are encouraged to consult the [Agency's Procedural](#) advice for validation of a new marketing authorisation application or extension/variation application and compliance check with an agreed PIP.

Notes:

1. As of 26 January 2009, pharmaceutical companies that submit an application for a marketing authorisation for a medicinal product, or those that submit an application for an extension of indication, a new route of administration, or a new pharmaceutical form of a medicinal product already authorised in the European Union, have to provide either the results of studies in children conducted in accordance with an approved PIP, or an Agency's decision on a waiver or on a deferral.
2. Opinions of the Paediatric Committee (PDCO) on PIPs and waivers lead to Agency's decisions within the timeframe laid down by the [Paediatric Regulation](#) (Regulation (EC) No 1901/2006, as amended). The decisions can be found on the Agency's website at:
https://www.ema.europa.eu/en/medicines/ema_group_types/ema_pip

Enquiries to: [AskEMA](https://www.ema.europa.eu/en/about-us/contact/send-question-european-medicines-agency) (<https://www.ema.europa.eu/en/about-us/contact/send-question-european-medicines-agency>)