21 January 2022
EMA/PDCO/64920/2022
Human Medicines Division

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

18-21 January 2022

Opinions on paediatric investigation plans

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

- Phospholipid esters from herring roe (HRO350), EMEA-003053-PIP01-21, from Arctic Bioscience, for the treatment of psoriasis;
- Efgartigimod alfa, EMEA-002597-PIP04-21, from argenx BV, for the treatment of immune thrombocytopenia;
- Recombinant humanized anti-blood dendritic cell antigen 2 (BDCA2) monoclonal antibody (BIIB059), EMEA-002555-PIP02-21, from Biogen Netherlands B.V., for the treatment of lupus erythematosus;
- Givinostat, EMEA-000551-PIP04-21, from Italfarmaco S.p.A., for the treatment of Duchenne muscular dystrophy;
- Acetyl-L-leucine ((s)-(acetylamino)-4-methylpentanoic acid), EMEA-002796-PIP01-20, from IntraBio Ltd., for the treatment of Niemann-Pick disease type C;
- Viltolarsen, EMEA-002853-PIP01-20, from NS Pharma, Inc., for the treatment of Duchenne muscular dystrophy;
- Zamtocabtagene autoleucel, EMEA-003009-PIP01-21, from Miltenyi Biomedicine GmbH, for the treatment of mature B cell neoplasms;
- Deutivacaftor / tezacaftor / (14S)-8-[3-(2-{dispiro[2.0.2^(4).1^(3)]heptan-7-yl}ethoxy)-1H-pyrazol-1-yl]-12,12-dimethyl-2lambda^(6)-thia-3,9,11,18,23-penta-azatetracyclo[17.3.1.1^(11,14).0^(5,10)]tetracosa-1(22),5,7,9,19(23),20-hexaene-2,2,4-trione calcium salt hydrate, EMEA-003052-PIP01-21, from Vertex Pharmaceuticals (Ireland) Limited, for the treatment of cystic fibrosis;
- Pyrrol-Hydroxyethylpyridin-3-ol derivative (MIJ821), EMEA-002946-PIP01-20, from Novartis Europharm Limited, for the treatment of major depressive disorder;

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

- Ralmitaront, EMEA-003003-PIP01-21, from Roche Registration GmbH, for the treatment of schizophrenia;
- L-carnitine / glucose / calcium chloride dihydrate / magnesium chloride hexahydrate / sodium lactate / sodium chloride, EMEA-003049-PIP01-21, from Iperboreal Pharma Srl, for the treatment of renal failure with carnitine deficiency;
- CpG 1018/Alum-adjuvanted recombinant SARS-CoV-2 Trimeric Spike (S) protein subunit vaccine (SCB-2019), EMEA-002987-PIP01-21, from Clover Biopharmaceuticals Ireland Limited, for the prevention of coronavirus disease 2019 (COVID-19);
- *Neisseria meningitidis* serogroup B fHbp subfamily B / *Neisseria meningitidis* serogroup B fHbp subfamily A / *Neisseria meningitidis* group Y polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group W-135 polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group C polysaccharide conjugated to tetanus toxoid carrier protein / *Neisseria meningitidis* group A polysaccharide conjugated to tetanus toxoid carrier protein, EMEA-002814-PIP02-21, from Pfizer Europe MA EEIG, for the invasive disease caused by *Neisseria meningitidis* group A, B, C, W and Y from 2 months of age;

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 0 opinions.

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:

- 2-{(3S)-7-fluoro-4-[(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-6-yl)carbonyl]-3,4-dihydro-2H-1,4-benzoxazin-3-yl}-N-methylacetamide (AZD9977) / Dapagliflozin, EMEA-003120-PIP01-21, from AstraZeneca AB, for the prevention of cardiovascular events in patients with chronic heart failure;
- Avexitide, EMEA-003125-PIP01-21, from EigerBio Europe Limited, for the treatment of postbariatric hypoglycaemia;
- Parsaclisib (as hydrochloride), EMEA-002696-PIP02-21, from Incyte Biosciences Distribution B.V., for the treatment of autoimmune haemolytic anaemia;
- Human normal immunoglobulin, EMEA-003121-PIP01-21, from Instituto Grifols, S.A., for the

treatment of post-polio syndrome;

- Tucatinib, EMEA-002242-PIP02-21, from Seagen B.V., for the treatment of all solid tumours;
- Cosibelimab, EMEA-003041-PIP01-21, from Checkpoint Therapeutics, Inc., for the treatment of cutaneous squamous cell carcinoma;
- Ceralasertib, EMEA-003127-PIP01-21, from AstraZeneca AB, for the treatment of lung carcinoma (small cell and non-small cell carcinoma);
- Sunvozertinib, EMEA-003132-PIP01-21, from Dizal (Jiangsu) Pharmaceutical Co., Ltd, for the treatment of non-small cell lung cancer;
- Nemtabrutinib, EMEA-003135-PIP01-21, from Merck Sharp & Dohme (Europe), Inc., for the treatment of mature B-cell malignancies;
- Tarlatamab, EMEA-003138-PIP01-21, from Amgen Europe BV, for the treatment of prostate malignant neoplasms and treatment of small cell lung cancer;
- (1S,3S)-3-({2-methyl-6-[1-methyl-5-({[methyl(propyl)carbamoyl]oxy}methyl)-1H-1,2,3-triazol-4-yl]pyridin-3-yl}oxy)cyclohexane-1-carboxylic acid (BMS-986278), EMEA-001649-PIP02-21, from Bristol-Myers Squibb Pharma EEIG, for the treatment of fibrosing interstitial lung diseases (ILD);
- Vimseltinib, EMEA-002802-PIP02-21, from Deciphera Pharmaceuticals, for the treatment of tenosynovial giant cell tumour;

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:

- Tralokinumab, EMEA-001900-PIP02-17-M06, from LEO Pharma A/S, for the treatment of atopic dermatitis;
- Delgocitinib, EMEA-002329-PIP02-20-M01, from LEO Pharma A/S, for the treatment of chronic hand eczema;
- Spesolimab, EMEA-002475-PIP02-19-M02, from Boehringer Ingelheim International GmbH, for the prevention of generalized pustular psoriasis and treatment of generalized pustular psoriasis;
- Pegvaliase, EMEA-001951-PIP01-16-M02, from BioMarin International Limited, for the treatment of hyperphenylalaninaemia;
- Dienogest / ethinyl estradiol, EMEA-002229-PIP01-17-M03, from Chemo Research, for the prevention of pregnancy;
- Guselkumab, EMEA-001523-PIP05-19-M01, from Janssen-Cilag International N.V., for the treatment of Crohn's disease;
- Mirikizumab, EMEA-002208-PIP01-17-M02, from Eli Lilly and Company, for the treatment of Crohn’s

disease and treatment of ulcerative colitis;

- Etrasimod L-arginine, EMEA-002713-PIP01-19-M01, from Arena Pharmaceuticals, Inc., for the treatment of ulcerative colitis;
- Glutamine, EMEA-001996-PIP02-16-M01, from Emmaus Medical Europe Ltd., for the treatment of sickle cell disease;
- Efanesoctocog alfa, EMEA-002501-PIP01-18-M02, from Bioverativ Therapeutics, Inc., a Sanofi Company, for the treatment of haemophilia A;
- Imlifidase, EMEA-002183-PIP01-17-M01, from Hansa Biopharma AB, for the prevention of graft rejection following solid organ transplantation;
- Tenofovir disoproxil, EMEA-000533-PIP01-08-M11, from Gilead Sciences International Limited, for the treatment of chronic viral hepatitis B and treatment of human immunodeficiency virus (HIV-1) infection;
- Tedizolid phosphate, EMEA-001379-PIP01-12-M06, from Merck Sharp & Dohme (Europe), Inc., for the treatment of acute bacterial skin and skin structure infections;
- Fostemsavir (tromethamine), EMEA-001687-PIP01-14-M06, from ViiV Healthcare UK Ltd, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Ridinilazole (hydrate), EMEA-002250-PIP02-17-M01, from Summit Limited, for the treatment of *Clostridioides difficile* infection;
- Tixagevimab (AZD8895), EMEA-002900-PIP01-20-M01, from AstraZeneca AB, for the prevention or treatment of COVID-19;
- Cilgavimab (AZD1061), EMEA-002925-PIP01-20-M01, from AstraZeneca AB, for the prevention or treatment of COVID-19;
- Casirivimab, EMEA-002964-PIP01-21-M01, from Regeneron Ireland DAC, for the treatment of coronavirus disease 2019 (COVID-19) and prevention of coronavirus disease 2019 (COVID-19);
- Imdevimab, EMEA-002965-PIP01-21-M01, from Regeneron Ireland DAC, for the treatment of coronavirus disease 2019 (COVID-19) and prevention of coronavirus disease 2019 (COVID-19);
- Isoflurane, EMEA-002320-PIP01-17-M02, from Sedana Medical AB, for the sedation of mechanically ventilated patients;
- Eculizumab, EMEA-000876-PIP05-15-M05, from Alexion Europe SAS, for the treatment of myasthenia gravis;
- Eptinezumab, EMEA-002243-PIP01-17-M02, from H. Lundbeck A/S, for the prevention of migraine headaches;
- Delandistrogene moxeparvovec, EMEA-002677-PIP01-19-M01, from Roche Registration GmbH, for the treatment of Duchenne muscular dystrophy;
- Dinutuximab beta, EMEA-001314-PIP01-12-M01, from EUSA Pharma (Netherlands) BV, for the treatment of neuroblastoma;
- Ex vivo expanded autologous human corneal epithelium cells containing stem cells, EMEA-001082-PIP02-11-M03, from Holostem Terapie Avanzate S.r.l., for the treatment of limbal stem cell deficiency due to ocular burns;

- Vosoritide, EMEA-002033-PIP01-16-M02, from BioMarin International Limited, for the treatment of achondroplasia;
- Adrenaline (epinephrine), EMEA-002749-PIP01-19-M01, from ARS Pharmaceuticals IRL, Limited, for the treatment of allergic reactions;
- SARS CoV2 prefusion Spike delta TM (CoV2 preS dTM) protein, recombinant adjuvanted with AS03, EMEA-002915-PIP01-20-M01, from Sanofi Pasteur, for the prevention of coronavirus disease 2019 (COVID-19);
- Split influenza virus, inactivated containing antigens equivalent to the B-like strain (Yamagata lineage) / Split influenza virus, inactivated containing antigens equivalent to the B-like strain (Victoria lineage) / Split influenza virus, inactivated containing antigens equivalent to the A/H3N2-like strain / Split influenza virus, inactivated containing antigens equivalent to the A/H1N1-like strain, EMEA-002359-PIP01-18-M04, from Sanofi Pasteur, for the prevention of influenza infection;

The PDCO adopted opinions on the **refusal** of modifications to an agreed PIP for the following applications:

- Modified allergen extract of birch pollen, EMEA-000932-PIP01-10-M02, from ROXALL Medizin GmbH, for the treatment of allergic rhinitis / rhino-conjunctivitis;

Opinion on compliance check

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

- Nivolumab, EMEA-C-001407-PIP01-12-M03, from Bristol-Myers Squibb Pharma EEIG, for the treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue);
- Albutrepenonacog alfa, EMEA-C-001107-PIP01-10-M04, from CSL Behring GmbH, for the treatment of hereditary factor IX deficiency;

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)