EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 July 2021
EMA/PDCO/433151/2021
Human Medicines Division

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

20-23 July 2021

Opinions on paediatric investigation plans

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

- Benralizumab, EMEA-001214-PIP05-19, from AstraZeneca AB, for the treatment of eosinophilic esophagitis;
- Cendakimab, EMEA-002640-PIP01-19, from Celgene Europe B.V., for the treatment of eosinophilic esophagitis;
- Concizumab, EMEA-002326-PIP04-20, from Novo Nordisk A/S, for the treatment of congenital haemophilia A and treatment of congenital haemophilia B;
- Tocilizumab, EMEA-000309-PIP07-21, from Roche Registration GmbH, for the treatment of coronavirus disease 2019 (COVID-19);
- Baricitinib, EMEA-001220-PIP08-20, from Eli Lilly and Company Limited, for the treatment of alopecia areata;
- Epcoritamab, EMEA-002907-PIP01-20, from AbbVie Ltd, for the treatment of mature B-cell malignancies;
- Ribitol, EMEA-002887-PIP01-20, from Premier Research Group S.L., for the treatment of Limb-Girdle Muscular Dystrophy;
- Ligelizumab, EMEA-001811-PIP03-20, from Novartis Europharm Limited, for the treatment of food allergy;
- Single chain urokinase plasminogen activator (scuPA), EMEA-002896-PIP01-20, from Lung Therapeutics, Inc., for the treatment of pleural effusion;
- Sodium chloride solution 4.2% (w/v) / 3,5-diamino-6-chloro-N-(N-(4-(4-(2-(hexyl((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl)amino)ethoxy)phenyl)butyl)-carbamimidoyl)pyrazine-2-carboxamide, EMEA-002935-PIP01-20, from Parion Sciences, Inc., for the treatment of Primary Ciliary Dyskinesia

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(PCD);

- Multivalent pneumococcal polysaccharide conjugate to carrier protein, EMEA-002780-PIP02-20, from Sanofi Pasteur, for the prevention of disease caused by Streptococcus pneumoniae;
- Casirivimab (REGN10933), EMEA-002964-PIP01-21, from Regeneron Ireland DAC; for the treatment of coronavirus disease 2019 (COVID-19) and prevention of coronavirus disease 2019 (COVID-19);
- Imdevimab (REGN10987), EMEA-002965-PIP01-21, from Regeneron Ireland DAC; for the treatment of coronavirus disease 2019 (COVID-19) and prevention of coronavirus disease 2019 (COVID-19);
- Efgartigimod alfa, EMEA-002597-PIP05-21, from argenx BV; for the treatment of myasthenia gravis;
- Azithromycin, EMEA-003021-PIP01-21, from Aspire Pharma Limited, for the prevention of bronchopulmonary dysplasia.

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:

- No item

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:

- Bisoprolol (fumarate) / amlodipine / indapamide / perindopril (arginine), EMEA-003015-PIP01-21, from Les Laboratoires Servier, for the treatment of hypertension;
- Prasterone / levonorgestrel / ethinylestradiol, EMEA-002960-PIP02-21, from Gedeon Richter Plc., for the treatment of hypoactive sexual desire disorder secondary to combined oral contraceptive use in women requiring contraception;
- Potassium bitartrate / citric acid / L-lactic acid, EMEA-002917-PIP01-20, from Evofem, Inc., for the prevention of urogenital Chlamydia trachomatis (CT) infection and Neisseria gonorrhoeae (GC) infection;
- Atezolizumab, EMEA-001638-PIP02-21, from Roche Registration GmbH, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, hematopoietic and lymphoid tissue neoplasms and melanoma);

- Selinexor, EMEA-002387-PIP02-21, from Karyopharm Europe GmbH, for the treatment of endometrial carcinoma;
- Prednisolone, EMEA-003004-PIP01-21, from Alfred E. Tiefenbacher (GmbH & Co. KG), for the treatment of prostate malignant neoplasms;
- Ociperlimab, EMEA-003028-PIP01-21, from BeiGene Ireland Limited, for the treatment of breast cancer, treatment of cervical cancer, treatment of endometrial carcinoma, treatment of gastric and gastroesophageal junction adenocarcinoma, treatment of head and neck epithelial malignant neoplasms, treatment of hepatocellular carcinoma, treatment of intestinal malignant neoplasms, treatment of lung cancer and treatment of oesophageal carcinoma;
- Florbetaben (18F), EMEA-001090-PIP02-21, from Life Molecular Imaging GmbH, for the diagnosis of cardiac amyloidosis;
- Ligelizumab, EMEA-001811-PIP04-21, from Novartis Europharm Limited, treatment of chronic inducible urticaria;

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:

- Brodalumab, EMEA-001089-PIP02-13-M02, from LEO Pharma A/S, for the treatment of psoriasis;
- Rubidium Rb-82 Chloride, EMEA-000882-PIP03-11-M05, from Jubilant DraxImage Inc., dba Jubilant Radiopharma, for the visualisation of myocardial perfusion for diagnostic purposes;
- Recombinant parathyroid hormone: rhPTH (1-84), EMEA-001526-PIP01-13-M05, from Shire Pharmaceuticals Ireland Limited, for the treatment of hypoparathyroidism;
- Metreleptin, EMEA-001701-PIP01-14-M02, from Amryt Pharmaceuticals DAC, for the treatment of lipodystrophy;
- Avalglucosidase alfa, EMEA-001945-PIP01-16-M03, from Genzyme Europe B.V., for the treatment of Pompe disease;
- Dasiglucagon, EMEA-002233-PIP01-17-M01, from Zealand Pharma A/S, for the treatment of hypoglycaemia;
- Tolvaptan, EMEA-001231-PIP02-13-M08, from Otsuka Pharmaceutical Netherlands B.V., for the treatment of dilutional hyponatraemia and treatment of polycystic kidney disease;
- Dupilumab, EMEA-001501-PIP04-19-M01, from Regeneron Ireland DAC, for the treatment of eosinophilic esophagitis;
- Naldemedine, EMEA-001893-PIP01-15-M02, from Shionogi B.V., for the opioid-induced constipation;
- Pegylated-fibroblast growth factor 21 (BMS-986036), EMEA-002448-PIP01-18-M02, from Bristol-Myers Squibb International Corporation, for the treatment of non-alcoholic steatohepatitis (NASH);

- Fidanacogene elaparvovec, EMEA-002362-PIP02-19-M01, from Pfizer Europe MA EEIG, for the treatment of congenital factor IX deficiency (haemophilia B);
- Narsoplimab, EMEA-002479-PIP01-18-M01, from Omeros Ireland Limited, for the treatment in haematopoietic stem cell transplantation;
- Aztreonam / avibactam, EMEA-002283-PIP01-17-M02, from Pfizer Europe MA EEIG, for the treatment of infections caused by aerobic Gram-negative bacteria;
- Remdesivir, EMEA-002826-PIP01-20-M02, from Gilead Sciences International Ltd., for the coronavirus disease 2019 (COVID-19);
- Lacosamide, EMEA-000402-PIP03-17-M05, from UCB Pharma S.A., for the treatment of generalised epilepsy and epileptic syndromes;
- Bumetanide, EMEA-001303-PIP01-12-M04, from Les Laboratoires Servier, for the treatment of autism spectrum disorder;
- Solriamfetol, EMEA-002184-PIP01-17-M01, from Jazz Pharmaceuticals Ireland Limited, for the treatment of narcolepsy and treatment of obstructive sleep apnoea;
- Bosutinib, EMEA-000727-PIP01-09-M05, from Pfizer Europe MA EEIG, for the treatment of chronic myeloid leukemia;
- Selumetinib, EMEA-001585-PIP01-13-M05, from AstraZeneca AB, for the treatment of melanoma, treatment of neurofibromatosis type 1 and treatment of thyroid cancer;
- Pevonedistat, EMEA-002117-PIP01-17-M02, from Takeda Pharma A/S, for the treatment of acute myeloid leukaemia and treatment of myelodysplastic syndromes;
- Autologous tumor-infiltrating lymphocytes (LN-144/LN-145), EMEA-002776-PIP01-20-M01, from Iovance Biotherapeutics, Inc., for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms;
- Eliglustat, EMEA-000461-PIP02-11-M04, from Genzyme Europe B.V., for the treatment of Gaucher disease Type 1 and Type 3 and treatment of Gaucher disease Type 2;
- Human Thrombin / Human Fibrinogen, EMEA-001149-PIP01-11-M07, from Omrix Biopharmaceuticals N.V., for the treatment of cerebrospinal fluid leakage resulting from a surgical procedure and treatment of haemorrhage resulting from a surgical procedure;
- Bupropion HCl / naltrexone HCl, EMEA-001373-PIP01-12-M04, from Orexigen Therapeutics Ireland Limited, for the treatment of obesity;
- Patiromer calcium, EMEA-001720-PIP01-14-M02, from Vifor Fresenius Medical Care Renal Pharma France, for the treatment of hyperkalaemia;
- Mexiletine (hydrochloride), EMEA-002012-PIP01-16-M03, from Lupin Europe GmbH, for the treatment of myotonic disorders;
- Bupivacaine, EMEA-000877-PIP03-17-M03, from Pacira Ltd, for the postsurgical analgesia;
- Amikacin sulfate, EMEA-000525-PIP01-08-M07, from Insmed Netherlands B.V., for the treatment of Pseudomonas aeruginosa lung infection/colonisation in cystic fibrosis patients and treatment of nontuberculous mycobacterial (NTM) lung infection;
- Mometasone (furoate) / glycopyrronium bromide / indacaterol, EMEA-001812-PIP01-15-M01, from

Novartis Europharm Limited, for the treatment of asthma;

- Berotralstat, EMEA-002449-PIP02-18-M01, from BioCryst Ireland Limited, for the treatment of hereditary angioedema;
- Recombinant *Clostridioides difficile* Toxoids A and B, EMEA-002112-PIP01-16-M01, from Pfizer Europe MA EEIG, for the prevention of Clostridioides difficile infection;
- Pneumococcal Polysaccharide Serotype 33F - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 23F - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 22F - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 19F - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 19A - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 18C - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 14 - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 9V - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 7F - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 6B - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 6A - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 5 - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 4 - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 3 - Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 1 - Diphtheria CRM197 Conjugate, EMEA-002215-PIP01-17-M03, from Merck Sharp & Dohme (Europe), Inc., for the prevention of disease caused by Streptococcus pneumoniae;
- Pneumococcal polyssacharide serotype 33F conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 23F conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 22F conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 19F conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 19A conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 18C conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 15B conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 14 conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 12F conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 11A conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 10A conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 9V conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 8 conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 7F conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 6B conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 6A conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 5 conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 4 conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 3 conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate / Pneumococcal polyssacharide serotype 1 conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate, EMEA-002330-PIP01-18-M01, from Pfizer Europe MA EEIG, for the disease caused by Streptococcus pneumoniae;

- Entrectinib, EMEA-002096-PIP01-16-M03, from Roche Registration GmbH, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms);
- Rezafungin acetate, EMEA-002319-PIP01-17-M01, from Mundipharma Corporation (Ireland) Limited, for the treatment of invasive candidiasis;

Opinion on compliance check

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

- Tadalafil, EMEA-C-000452-PIP02-10-M06, from Eli Lilly and Company Limited, for the treatment of pulmonary arterial hypertension;
- Octocog alfa, EMEA-C-001064-PIP01-10-M03, from Bayer AG, for the treatment of hereditary Factor VIII deficiency;
- Turoctocog alfa pegol - EMEA-C-001174-PIP02-12-M02, from Novo Nordisk A/S; for the treatment of hereditary Factor VIII 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.

Withdrawals

The PDCO noted that 6 applications were withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure).

Other matters

The PDCO welcomed the re-nomination from Bulgaria, Dimitar Roussinov.

The next meeting of the PDCO will be held on 7-10 September 2021.

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. PDCO opinions on PIPs and waivers are transformed into 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
3. More information about the PDCO and the Paediatric Regulation is available in the Regulatory section of the Agency's website: _https://www.ema.europa.eu/en/committees/paediatric-committee-pdco
4. This meeting report, together with other information on the work of the Agency's, can be found on the Agency's website: http://www.ema.europa.eu

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