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Human Medicines Division

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

22-25 March 2022

Opinions on paediatric investigation plans

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

- Ibutamoren mesylate, EMEA-003032-PIP01-21, from Lumos Pharma, Inc., for the treatment of growth hormone deficiency;
- Zinc gluconate / alisitol / retinyl palmitate, EMEA-002198-PIP01-21, from Vanessa Research Magyarorszag Kft, for the treatment of microvillus inclusion disease;
- Peptide derivative of glucagon-like-peptide 1 and glucagon with fatty acid side chain (BI 456906), EMEA-002942-PIP02-20, from Boehringer Ingelheim International GmbH, for the treatment of obesity;
- Mitapivat, EMEA-002684-PIP02-21, from Agios Netherlands B.V., for the treatment of thalassaemia;
- Deucravacitinib, EMEA-002350-PIP02-20, from Bristol-Myers Squibb International Corporation, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis);
- Adeno-associated viral vector serotype rh.10 expressing beta-galactosidase, EMEA-003020-PIP01-21, from Lysogene, for the treatment of GM1 gangliosidosis;
- Virus-like particle of SARS-CoV-2 spike protein (recombinant, adjuvant) (CoVLP), EMEA-003008-PIP01-21, from Medicago Inc., for the prevention of coronavirus disease 2019 (COVID-19);
- SARS-CoV-2 virus, beta-propiolactone inactivated, EMEA-003077-PIP01-21, from Valneva Austria GmbH, for the prevention of coronavirus disease 2019 (COVID-19);

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

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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:

- Atorvastatin / perindopril (arginine) / indapamide / amlodipine, EMEA-003173-PIP01-21, from Les Laboratoires Servier, for the treatment of hypertension;
- Dupilumab, EMEA-001501-PIP11-21, from Sanofi-Aventis Group, for the treatment of chronic pruritus of unknown origin;
- Anti-CD40L humanized monoclonal antibody (SAR441344), EMEA-002945-PIP02-21, from sanofi-aventis groupe, for the treatment of multiple sclerosis;
- Latozinemab, EMEA-002997-PIP02-22, from Alector, Inc., for the treatment of amyotrophic lateral sclerosis;
- Izaflortaucipir (18F), EMEA-003040-PIP02-21, from Life Molecular Imaging GmbH, for the diagnosis of Alzheimer's disease;
- Adeno-associated virus vector serotype 1 containing the human GRN gene, EMEA-003167-PIP01-21, from Passage Bio, Inc., for the treatment of frontotemporal dementia;
- Infigratinib, EMEA-002594-PIP03-21, from Helsinn Birex Pharmaceuticals Ltd., for the treatment of urothelial carcinoma;
- Sacituzumab govitecan, EMEA-002645-PIP03-21, from Gilead Sciences International Ltd., for the treatment of lung carcinoma (small cell and non-small cell carcinoma);
- Zandelisib, EMEA-003158-PIP01-21, from Kyowa Kirin Holdings B.V., for the treatment of mature B cell neoplasms;
- 3,4-dimethyl-N-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-1H-pyrazole-5-carboxamide, EMEA-003169-PIP01-21, from Cogent Biosciences, Inc, for the treatment of gastrointestinal stromal tumours;
- Human IgG4-based bispecific antibody binding to both B-cell maturation antigen (BCMA) and cluster of differentiation 3 (CD3) (REGN5458), EMEA-003175-PIP01-21, from Regeneron Ireland DAC, for the treatment of multiple myeloma;
- Pseudoephedrine / bilastine, EMEA-003164-PIP01-21, from FAES FARMA, S.A., for the treatment of allergic rhinitis;

- (2S) 4 [2 methoxyethyl [4 (5,6,7,8 tetrahydro 1,8 naphthyridin 2 yl)butyl] amino] 2 (quinazolin 4 ylamino)butanoic acid, EMEA-003159-PIP01-21, from Pliant Therapeutics Inc., for the treatment of idiopathic pulmonary fibrosis;

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:

- Remibrutinib, EMEA-002582-PIP01-19-M01, from Novartis Europharm Limited, for the treatment of chronic spontaneous urticaria;
- Human, recombinant, non-fucosylated IgG1k monoclonal antibody targeting OX-40 receptor on activated T cells, EMEA-002886-PIP01-20-M01, from Amgen Europe B.V., for the treatment of atopic dermatitis;
- Bis-choline tetrathiomolybdate, EMEA-002232-PIP02-19-M02, from Alexion Europe S.A.S., for the treatment of Wilson disease;
- Tirzepatide, EMEA-002360-PIP01-18-M02, from Eli Lilly and Company Ltd, for the treatment of type 2 diabetes mellitus;
- Tolvaptan, EMEA-001231-PIP02-13-M09, from Otsuka Pharmaceutical Netherlands B.V., for the treatment of dilutional hyponatraemia and treatment of polycystic kidney disease;
- Potassium sulphate / magnesium sulphate heptahydrate / sodium sulphate anhydrous, EMEA-000816-PIP02-10-M03, from IPSEN Consumer Healthcare, for the diagnosis of organic and/or functional bowel diseases;
- Odevixibat, EMEA-002054-PIP01-16-M03, from Albireo AB, for the treatment of progressive familial intrahepatic cholestasis;
- Luspatercept, EMEA-001521-PIP01-13-M06, from Bristol-Myers Squibb Pharma EEIG, for the treatment of beta-thalassaemia and treatment of myelodysplastic syndromes;
- Brincidofovir, EMEA-001904-PIP03-18-M02, from Chimerix IRL Limited, for the treatment of smallpox;
- Cefiderocol, EMEA-002133-PIP01-17-M02, from Shionogi B.V., for the treatment of infections due to aerobic gram-negative bacteria;
- Eslicarbazepine acetate, EMEA-000696-PIP02-10-M08, from BIAL - Portela & Ca, SA, for the treatment of epilepsy with partial onset seizures;
- Lenvatinib, EMEA-001119-PIP03-19-M02, from Eisai GmbH, for the treatment of all conditions included in the category of malignant neoplasms except haematopoietic and lymphoid tissue neoplasms, papillary thyroid cancer, follicular thyroid cancer and osteosarcoma;
- Cemiplimab, EMEA-002007-PIP02-17-M02, from Regeneron Ireland DAC, for the treatment of all

conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue);

- Venetoclax, EMEA-002018-PIP02-16-M05, from AbbVie Ltd, for the treatment of haematopoietic and lymphoid malignant neoplasms and treatment of solid tumour malignant neoplasms;
- Sonlicromanol, EMEA-002113-PIP01-16-M01, from Khondrion BV, for the treatment of mitochondrial respiratory chain/oxidative phosphorylation defects;
- Sufentanil (citrate) / ketamine (hydrochloride), EMEA-001739-PIP02-16-M01, from Cessatech A/S, for the treatment of acute pain;
- Regdanvimab, EMEA-002961-PIP01-21-M01, from Celltrion Healthcare Hungary Kft., for the treatment of coronavirus disease 2019 (COVID-19);
- Etranacogene dezaparvovec, EMEA-002722-PIP01-19-M01, from CSL Behring GmbH, for the treatment of haemophilia B;
- Dapagliflozin, EMEA-000694-PIP02-14-M03, from AstraZeneca AB, for the treatment of type 1 diabetes mellitus;

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

- Betibeglogene autotemcel, EMEA-001665-PIP01-14-M06, from bluebird bio (Netherlands) B.V., for the treatment of beta-thalassaemia;

Opinion on compliance check

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

- Treosulfan, EMEA-C-000883-PIP01-10-M05, from medac Gesellschaft für klinische Spezialpräparate mbH, for the conditioning treatment prior to haematopoietic progenitor cell transplantation;

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)