EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Human Medicines Division

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

20-23 April 2021

Opinions on paediatric investigation plans

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

- 3,4-Dimethoxy-N-methylbenzohydroxamic acid / Deferoxamine mesylate / Alpha-ketoglutaric acid / Arginine / Alanine / Glycine / Aspartic acid / Tryptophan / N-acetyl-histidine (monohydrate) / Histidine / Calcium chloride (dihydrate) / Magnesium chloride (hexahydrate) / Potassium chloride / Sodium chloride, EMEA-002735-PIP01-19, from Dr. Franz Köhler Chemie GmbH, for cardioplegia;
- Sotatercept, EMEA-002756-PIP01-19, from Acceleron Pharma, for the treatment of pulmonary arterial hypertension;
- Human plasma derived c1-inhibitor, EMEA-002818-PIP01-20, from Octapharma Pharmazeutika Produktionsges.m.b.H, for the treatment of hereditary angioedema;
- Iscalimab, EMEA-002842-PIP01-20, from Novartis Europharm Limited, for the prophylaxis of solid organ transplant rejection;
- Ravulizumab, EMEA-001943-PIP03-20, from Alexion Europe SAS, for the treatment of myasthenia gravis;
- Erdafitinib, EMEA-002042-PIP02-20, from Janssen-Cilag International N.V., for the treatment of all conditions included in the category of malignant neoplasms (except urothelial carcinoma, haematopoietic and lymphoid tissue neoplasms);
- Talazoparib, EMEA-002066-PIP01-20, from Pfizer Europe MA EEIG, for the treatment of Ewing sarcoma;
- Atropine sulfate, EMEA-002744-PIP01-19, from Nevakar Inc., for the treatment of myopia;
- Bamlanivimab, EMEA-002952-PIP01-21, from Eli Lilly and Company Limited, for the treatment of Coronavirus disease 2019 (COVID-19);
- Etesevimab, EMEA-002966-PIP01-21, from Eli Lilly and Company Limited, for the treatment of Coronavirus disease 2019 (COVID-19);

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
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- Zorecimeran, EMEA-002986-PIP01-21, from CureVac AG; for the prevention of Coronavirus disease 2019 (COVID-19);

The PDCO adopted an opinion(s) on the **refusal** of a PIP, for:

- No item

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:

- Naproxen sodium / sumatriptan, EMEA-002959-PIP01-21, from Orion Corporation, for the treatment of migraine headaches;
- Savolitinib, EMEA-002627-PIP02-21, from AstraZeneca AB, for the treatment of renal neoplasms;
- Synthetic hypericin, EMEA-002956-PIP01-21, from Soligenix NL B.V, for the treatment of cutaneous T-cell lymphoma;
- Immunoglobulin G4 [449-cysteine], anti-(human vascular endothelial growth factor A) (human-Mus musculus monoclonal OG1950 gamma-4-chain), disulfide with human-Mus musculus monoclonal OG1950 kappa-chain, (232 - 232'),(235 - 235')-bis(disulfide) with immunoglobulin G4 anti-(human vascular endothelial growth factor A) (human-Mus musculus monoclonal OG1950 gamma-4-chain) disulfide with human-Mus musculus monoclonal OG1950 kappa-chain, 449-thioether with 1,1'-[2-[11,11-bis[15-bromo-11,11-bis[(2-bromo-2-methyl-1-oxopropoxy)methyl]-15-methyl-3,7,14-trioxo-9,13-dioxa-2,6-diazahexadec-1-yl]-44-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-4,8,26,42-tetraoxo-2,13,16,19,22,29,32,35,38-nonaoxa-5,9,25,41-tetraazatetratetracont-1-yl]-2-[(2-bromo-2-methyl-1-oxopropoxy)methyl]-1,3-propanediyl] bis(2-bromo-2-methylpropanoate) core 9-arm star compd. with 4-hydroxy-N,N,N,10-tetramethyl-9-oxo-3,5,8-trioxa-4-phosphaundec-10-en-1-aminium inner salt 4-oxide homopolymer, EMEA-002895-PIP02-21, from Kodiak Sciences Inc., for the treatment of choroidal neovascularisation, treatment of diabetic retinopathy and treatment of retinal vein occlusion;

The PDCO adopted no opinions on the **refusal** of a request for waiver for:

- No item

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:

- Liquid ethanolic extract 30 per cent (w/w) of Allium cepa L. (fresh bulb) and Citrus limon (L.) Burm. f. (fresh fruit), Paullinia cupana Kunth, Theobroma cacao L., EMEA-001835-PIP01-15-M05, from Legacy Healthcare, for the treatment of alopecia;
- Denosumab, EMEA-000145-PIP02-12-M04, from Amgen Europe B.V., for the treatment of osteoporosis;
- Sotagliflozin, EMEA-001517-PIP02-14-M03, from Guidehouse Germany GmbH, for the treatment of type 1 diabetes mellitus;
- Linaclotide, EMEA-000927-PIP01-10-M06, from Allergan Pharmaceuticals International Limited, for the treatment of functional constipation;
- Betibeglogene autotemcel, EMEA-001665-PIP01-14-M05, from bluebird bio (Netherlands) B.V., for the treatment of β-thalassaemia;
- Setmelanotide, EMEA-002209-PIP01-17-M02, from Rhythm Pharmaceuticals, Inc, for the treatment of appetite and general nutrition disorders;
- Venetoclax, EMEA-002018-PIP02-16-M04, from AbbVie Ltd, for the treatment of haematopoietic and lymphoid malignant neoplasms and treatment of solid tumour malignant neoplasms;

The following product(s) was/were granted a product-specific waiver in replacement of an agreed PIP:

- No item

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

- No item

Opinion on compliance check

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

- Velmanase alfa, EMEA-C-001056-PIP02-12-M01, from Chiesi Farmaceutici S.p.A, for the treatment of alpha-Mannosidosis;
- Afatinib, EMEA-C-001596-PIP02-17-M02, from Boehringer Ingelheim International GmbH, for the treatment of malignant neoplasms of the central nervous system and treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic

and lymphoid tissue neoplasms);

- Secukinumab, EMEA-C-000380-PIP01-08-M04, from Novartis Europharm Ltd, for the treatment of psoriasis;

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 4 applications were withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure).

Other matters

The next meeting of the PDCO will be held on 18-21 May 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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