13 November 2020
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Human Medicines Division

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

10-13 November 2020

Opinions on paediatric investigation plans

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

- Olinciguat, EMEA-002759-PIP01-19, from Cyclerion Therapeutics Inc., for the treatment of sickle cell disease;
- Tabelecleucel, EMEA-002025-PIP04-19, from Atara Biotherapeutics, Inc., for the treatment of Epstein-Barr virus associated post-transplant lymphoproliferative disorder;
- Venglustat, EMEA-001716-PIP05-20, from Genzyme Europe B.V., for the treatment of autosomal dominant polycystic kidney disease;
- Fully human IgG1 RB-1 YTE anti-RSV F monoclonal antibody (MK-1654), EMEA-002755-PIP01-19, from Merck Sharp & Dohme (Europe), Inc., for the prevention of lower respiratory tract infection caused by respiratory syncytial virus;
- Voxelotor, EMEA-002356-PIP02-20, from Synteract GmbH, for the treatment of sickle cell disease;
- Etrasimod L-arginine, EMEA-002713-PIP01-19, from Arena Pharmaceuticals, Inc., for the treatment of ulcerative colitis;
- (R)-2-(1-(6-Amino-5-chloropyrimidine-4- carboxamido)ethyl)-N-(5-chloro-4-(trifluoromethyl)pyridin- 2-yl)thiazole-5-carboxamide, EMEA-002763-PIP01-20, from DOT Therapeutics-1 Inc, for the treatment of paediatric low grade glioma;
- Etranacogene dezaparvovec, EMEA-002722-PIP01-19, uniQure biopharma B.V., for the treatment of Haemophilia B
- Sulbactam / durlobactam, EMEA-002807-PIP01-20, Entasis Therapeutics Inc., for the treatment of infections due to organisms of the Acinetobacter baumannii-calcoaceticus complex;

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

- Docosahexaenoic acid, EMEA-002808-PIP01-20, Natac Pharma S.L., for the treatment of retinitis

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pigmentosa;

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 specific medicinal product is likely to be ineffective.

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.

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:

- Efgartigimod alfa, EMEA-002597-PIP03-20, from argenx BV, for the treatment of pemphigus;
- Dapagliflozin, EMEA-000694-PIP06-20, from AstraZeneca AB, for the treatment of ischaemic heart disease;
- Ziltivekimab, EMEA-002840-PIP01-20, from Novo Nordisk A/S, for the prevention of cardiovascular events in patients with atherosclerosis;
- N-[(1R)-1-(1H-indol-3-ylmethyl)pentyl]-2-(4-methylpiperazin-1-yl)thiazole-5-carboxamide, EMEA-002866-PIP01-20, from UCB Pharma S.A., for the treatment of Parkinson's disease;
- Tipifarnib, EMEA-002871-PIP01-20, from Kura Oncology, Inc., for the treatment of head and neck epithelial malignant neoplasms;
- Tauroursodeoxycholic acid / Sodium phenylbutyrate, EMEA-002876-PIP01-20, from Drug Development and Regulation SL, for the treatment of amyotrophic lateral sclerosis;
- Bisoprolol (fumarate) / ramipril, EMEA-002860-PIP01-20, from Egis Pharmaceuticals PLC, for the treatment of hypertension;
- Delolimogene mupadenorepvec, EMEA-002864-PIP01-20, from Lokon Pharma AB, for the treatment of pancreatic cancer;
- Tipifarnib, EMEA-002871-PIP01-20, Kura Oncology, Inc., for the treatment of head and neck epithelial malignant neoplasms ;

The PDCO adopted 2 opinions on the **refusal** of a request for waiver for:

- Obinutuzumab, EMEA-001207-PIP03-20, from Roche Registration GmbH, for the treatment of glomerulonephritis and nephrotic syndrome;
- Fluciclovine (18F), EMEA-001644-PIP02-14-M02, from Blue Earth Diagnostics Ireland Ltd, for the diagnosis of amino acid metabolism in solid malignant tumours;

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:

- Avelumab, EMEA-001849-PIP02-15-M03, from Merck Healthcare GmbH, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoetic and lymphoid tissue neoplams), treatment of malignant neoplasms of lymphoid tissue and treatment of malignant neoplasms of the central nervous system;
- Calcifediol, EMEA-002093-PIP02-17-M01, from Vifor Fresenius Medical Care Renal Pharma France, for the treatment of secondary hyperparathyroidism (SHPT);
- Cholera vaccine, recombinant, live, oral (strain CVD 103-HgR), EMEA-001490-PIP01-13-M02, from Emergent Netherlands B.V., for the prevention of cholera;
- Ocrelizumab, EMEA-000310-PIP03-10-M04, from Roche Registration GmbH, for the treatment of Multiple Sclerosis;
- Naloxegol, EMEA-001146-PIP01-11-M06, from Kyowa Kirin Pharmaceutical Development Limited, for the treatment of opioid-induced constipation;
- Eltrombopag, EMEA-000170-PIP03-13-M04, from Novartis Europharm Limited, for the treatment of aplastic anaemia;
- Cobicistat / atazanavir sulphate, EMEA-001465-PIP01-13-M03, from Bristol-Myers Squibb Pharma EEIG, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Avatrombopag, EMEA-001136-PIP02-19-M01, from Dova Pharmaceuticals Ireland Limited, for the treatment of chemotherapy-induced thrombocytopenia;
- Testosterone, EMEA-001529-PIP02-14-M03, from Acerus Biopharma Inc., for the treatment of male hypogonadism;
- Eculizumab, EMEA-000876-PIP03-14-M05, from Alexion Europe SAS, for the treatment of neuromyelitis optica spectrum disorders;
- Ivacaftor / lumacaftor, EMEA-001582-PIP01-13-M10, from Vertex Pharmaceuticals (Europe) Ltd, for the treatment of cystic fibrosis;
- Cotadutide, EMEA-002287-PIP01-17-M01, from AstraZeneca AB, for the treatment of Type 2 Diabetes Mellitus;
- Burosumab, EMEA-001659-PIP01-15-M05, from Kyowa Kirin Holdings B.V., for the treatment of X-linked hypophosphatemia;
- Brigatinib, EMEA-002296-PIP01-17-M02, from Takeda Pharm A/S, for the treatment of anaplastic large cell lymphoma, treatment of inflammatory myofibroblastic tumours and treatment of non-small cell lung cancer;
- Aztreonam, EMEA-000827-PIP01-09-M05, from Gilead Sciences International Ltd., for the treatment of Pseudomonas aeruginosa infection/colonisation in patients with cystic fibrosis;

- Captopril, EMEA-001544-PIP01-13-M02, Proveca Pharma Limited, for treatment of heart failure;

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

- Fluciclovine (18F), EMEA-001644-PIP02-14-M02, from Blue Earth Diagnostics Ireland Ltd, for the diagnosis of amino acid metabolism in solid malignant tumours;

Opinion on compliance check

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

- Human normal immunoglobulin, EMEA-C-001853-PIP01-15-M02, from Grifols Therapeutics LLC, for the treatment of primary immunodeficiency;

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 PDCO thanked Petra Dominikova for her work as she has resigned from the Committee.

The next meeting of the PDCO will be held on 8-11 December 2020.

– END –

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

   http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000023.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800240cd

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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