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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

11-14 December 2018

Opinions on paediatric investigation plans

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

- Filgotinib, EMEA-001619-PIP03-16, from Gilead Sciences International Ltd., for the treatment of Crohn's disease and treatment of ulcerative colitis;
- Rilpivirine, EMEA-000317-PIP02-18, from Janssen-Cilag International N.V., for the treatment of human immunodeficiency virus (HIV-1) infection;
- Ozanimod, EMEA-001710-PIP04-17, from Celgene Europe Limited, for the treatment of Crohn's disease;
- Etripamil, EMEA-002303-PIP01-17, from Milestone Pharmaceuticals Inc, for the treatment of supraventricular arrhythmia;
- Ianalumab, EMEA-002338-PIP01-18, from Novartis Europharm Limited, for the treatment of autoimmune hepatitis;
- Split influenza virus, inactivated containing antigens equivalent to the A/H1N1-like strain, A/H3N2-like strain, B-like strain (Victoria lineage) and B-like strain (Yamagata lineage), EMEA-002359-PIP01-18, from Sanofi Pasteur, for prevention of influenza infection

The PDCO adopted an opinion on the **refusal** of a PIP, including deferral for:

- Turoctocog alfa pegol, EMEA-001174-PIP03-18, from Novo Nordisk A/S, for the treatment of congenital haemophilia A

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 does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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

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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:

- Amantadine (hydrochloride), EMEA-002460-PIP01-18, from Adamas Pharmaceuticals LLC, for the treatment of Parkinson's disease and parkinsonism;
- Encorafenib, EMEA-001588-PIP03-18, from Pierre Fabre Medicament, for the treatment of colorectal carcinoma;
- Rifamycin, EMEA-002450-PIP01-18, from CRINOS S.P.A., for the treatment of acute infectious diarrhoea;
- Givosiran, EMEA-002048-PIP02-18, from Alnylam UK Limited, for the treatment of acute hepatic porphyria;
- Binimetinib, EMEA-001454-PIP05-18, from Pierre Fabre Medicament, for the treatment of colorectal carcinoma;
- Technetium (^{99m}Tc) trofolastat chloride, EMEA-002441-PIP01-18, from ROTOP Pharmaka GmbH, for the visualisation of prostate specific membrane antigen in prostate cancer;
- Ramipril / atorvastatin / amlodipine, EMEA-002416-PIP01-18, from Midas Pharma GmbH, for the treatment of hypercholesterolemia and treatment of hypertension;
- Telmisartan / indapamide, EMEA-002462-PIP01-18, from PRO.MED.CS Praha a.s., for the treatment of hypertension;
- Fibroblast activation protein alpha-targeted interleukin 2 variant immunocytokine, EMEA-002465-PIP01-18, from Roche Registration GmbH, for the treatment of non-small cell lung cancer;
- Human ciliary neurotrophic factor, EMEA-002477-PIP01-18, from Neurotech Pharmaceuticals, for the treatment of Macular Telangiectasia Type 2;
- Pexidartinib, EMEA-001939-PIP03-16, from Daiichi Sankyo Inc, for the treatment of benign soft tissue neoplasms

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:

- Venetoclax, EMEA-002018-PIP02-16-M01, from AbbVie Ltd, for the treatment of malignant neoplasms of the haematopoietic and lymphoid tissue and treatment of solid malignant tumours;
- Sodium sulphate / potassium sulphate / magnesium sulphate heptahydrate, EMEA-000816-PIP02-10-M02, from IPSEN Pharma, for the diagnosis of organic and/or functional bowel diseases;
- Fostemsavir (tromethamine), EMEA-001687-PIP01-14-M03, from ViiV Healthcare UK Ltd, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Semaglutide, EMEA-001441-PIP01-13-M02, from Novo Nordisk A/S, for the treatment of type 2 diabetes mellitus;
- Gadopiclenol, EMEA-001949-PIP01-16-M03, from GUERBET, for the detection and visualisation of areas with disruption of the blood brain barrier and/or abnormal vascularity for diagnostic purposes;
- Bivalent anti-human myostatin adnectin recombinant human IgG1-Fc fusion protein, EMEA-001793-PIP01-15-M03, from Roche Registration GmbH, for the treatment of Duchenne Muscular Dystrophy;
- 2-hydroxypropyl-ß-cyclodextrin (HP-ß-CD), EMEA-001866-PIP01-15-M03, from Mallinckrodt Pharmaceuticals Ireland Ltd, for the treatment of Niemann-Pick disease, type C;
- Rilpivirine / dolutegravir, EMEA-001750-PIP01-15-M02, from ViiV Healthcare UK Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Entrectinib, EMEA-002096-PIP01-16-M01, from Roche Registration GmbH, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms);
- Ocrelizumab, EMEA-000310-PIP03-10-M03, from Roche Registration GmBH, for the treatment of multiple sclerosis;
- Dienogest / ethinyl estradiol, EMEA-002229-PIP01-17-M01, from Exeltis France S.A., for the prevention of pregnancy;
- Azilsartan medoxomil, EMEA-000237-PIP01-08-M08, from Takeda Development Centre (Europe) Ltd., for the treatment of hypertension;
- Empagliflozin, EMEA-000828-PIP04-16-M02, from Boehringer Ingelheim International GmbH, for the treatment of type 1 diabetes mellitus;
- Naloxegol, EMEA-001146-PIP01-11-M04, from Kyowa Kirin Pharmaceutical Development Limited, for the treatment of opioid-induced constipation;
- Regadenoson, EMEA-000410-PIP01-08-M04, from Rapidscan Pharma EU Solutions (RPS) EU Limited, for the diagnosis of myocardial perfusion disturbances;
- Birch pollen extract, EMEA-000809-PIP01-09-M01, from Allergy Therapeutics (UK) Ltd, for the treatment of allergic rhinitis/rhino-conjunctivitis;
- Split influenza virus, inactivated containing antigen equivalent to A/California/7/2009(H1N1)-like strain (A/California/7/2009 (NYMC X-179A)), adjuvanted, EMEA-000669-PIP01-09-M02, from Sanofi Pasteur SA, for prevention of influenza

Opinion on compliance check

The PDCO adopted positive opinions on full compliance check for:

- Liraglutide, EMEA-C-000128-PIP01-07-M08, from Novo Nordisk, for the treatment of type 2 diabetes mellitus;

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 5 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 29 January 2019 – 1 February 2019.

– 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: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/pip_search.jsp&murl=menus/medicines/medicines.jsp&mid=WC0b01ac058001d129

3. More information about the PDCO and the Paediatric Regulation is available in the Regulatory section of the Agency's website: 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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