27 July 2018
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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

24-27 July 2018

Opinions on paediatric investigation plans

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

- Mirikizumab, EMEA-002208-PIP01-17, from Eli Lilly and Company, for the treatment of Crohn's disease, treatment of psoriasis and treatment of ulcerative colitis;
- Interferon beta-1a, EMEA-002238-PIP01-17, from Faron Pharmaceuticals Ltd, for the treatment of Acute Respiratory Distress Syndrome (ARDS);
- Monovalent, recombinant, replication-incompetent human adenovirus serotype 26-vectored vaccine encoding the pre-fusion conformation-stabilised F protein derived from the RSV A2 strain, EMEA-002172-PIP02-17, from Janssen-Cilag International NV, for the prevention of lower respiratory tract disease caused by respiratory syncytial virus (RSV);
- Palovarotene, EMEA-001662-PIP03-17, from Clementia Pharmaceuticals Inc., for the treatment of multiple osteochondromas;
- Entrectinib, EMEA-002096-PIP01-16, from Roche Registration GmBH, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms);
- Sodium thiosulfate (STS), EMEA-002147-PIP02-17, from Fennec Pharmaceuticals, Inc., for the prevention of platinum-induced ototoxic hearing loss;
- Anti-mucosal addressin cell adhesion molecule antibody, EMEA-002218-PIP01-17, from Shire Pharmaceuticals Ireland Limited, for the treatment of Crohn's Disease and treatment of Ulcerative Colitis;
- Ivosidenib, EMEA-002247-PIP03-17, from Agios Pharmaceuticals, Inc., for the treatment of acute myeloid leukaemia;
- Onasemnogenum abeparvovecum, EMEA-002168-PIP01-17, from AveXis Netherlands B.V., for the treatment of spinal muscular atrophy;

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- Sarizotan (hydrochloride), EMEA-001808-PIP03-17, from Newron Pharmaceuticals SpA, for the treatment of Rett syndrome;
- Baricitinib, EMEA-001220-PIP03-16, from Eli Lilly and Company Limited, for the treatment of atopic dermatitis;
- Autologous cartilage derived cultured chondrocytes, EMEA-002217-PIP01-17, from TETEC AG, for the treatment of cartilage disorders;
- Recombinant human acid ceramidase, EMEA-002266-PIP01-17, from Enzyvant Farber Ireland Ltd, for the treatment of Farber disease;
- Afatinib, EMEA-001596-PIP02-17, from Boehringer Ingelheim International GmbH, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms) and treatment of malignant neoplasms of the central nervous system;
- Human donor haematopoietic stem and progenitor cells (HSPC) that have been treated ex vivo with the protein transduction domain of the HIV-1 transactivation protein fused to MYC transcription factor, EMEA-002185-PIP02-17, from Taiga Biotechnologies, Inc, for the treatment in haematopoietic stem cell transplantation in patients with severe combined immunodeficiency syndrome (SCID);
- Inclisiran sodium, EMEA-002214-PIP01-17, from The Medicines Company UK Ltd., for the treatment of elevated cholesterol;
- Ibalizumab, EMEA-002311-PIP01-17, from Theratechnologies International Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;

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:

- Retigabine, EMEA-000116-PIP01-07-M09, from Glaxo Group Limited, for the treatment of Lennox-Gastaut Syndrome and treatment of epilepsy with partial onset seizures;
- Emtricitabine / rilpivirine (hydrochloride) / tenofovir (disoproxil fumarate), EMEA-000774-PIP01-09-M03, from Gilead Sciences International Ltd., for the treatment of human immunodeficiency virus (HIV-1) infection;
- Acetylsalicylic acid / rosuvastatin (calcium) / perindopril (tert-butylamine) / indapamide (hemihydrate), EMEA-002366-PIP01-18, from SmartGenRx Pty Ltd, for the prevention of cardiovascular events;
- Levofloxacin / Dexamethasone, EMEA-002375-PIP01-18, from NTC srl, for the prevention and treatment of inflammation and prevention of infection associated with cataract surgery;

- Tepotinib, EMEA-002345-PIP01-18, from Merck KGaA, for the treatment of non-small cell lung carcinoma (NSCLC);
- Simeprevir, EMEA-000625-PIP01-09-M03, from Janssen-Cilag International NV, for the treatment of chronic viral hepatitis C;
- Nadofaragene firadenovec, EMEA-002376-PIP01-18, from Trizell Ltd., for the treatment of mesothelioma;
- Omega-3-acid ethyl esters 90 / rosuvastatin (calcium), EMEA-002384-PIP01-18, from Kuhnil Pharm. CO.,Ltd., for the treatment of hypercholesterolemia and hypertriglyceridaemia;
- Elotuzumab, EMEA-002377-PIP01-18, from Bristol-Myers Squibb Pharma EEIG, for the treatment of multiple myeloma;
- Arimoclomol citrate, EMEA-001748-PIP02-18, from Orphazyme A/S, for the treatment of sporadic inclusion body myositis;
- Anti-alpha synuclein monoclonal antibody, EMEA-002367-PIP01-18, from Biogen Idec Limited, for the treatment of Parkinson's disease

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

- Fasinumab, EMEA-002059-PIP01-16, from Regeneron Ireland U.C., for the treatment of chronic pain;
- Arimoclomol citrate, EMEA-001748-PIP02-18, from Orphazyme A/S, for the treatment of amyotrophic lateral sclerosis;

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:

- Exenatide, EMEA-000689-PIP01-09-M08, from AstraZeneca AB, for the treatment of type 2 diabetes mellitus;
- Emapalumab, EMEA-002031-PIP01-16-M02, from Novimmune B.V, for the treatment of haemophagocytic lymphohistiocytosis;
- Loxapine, EMEA-001115-PIP01-10-M06, from Ferrer Internacional, S.A., for the treatment of bipolar disorder and treatment of schizophrenia;
- Brexpiprazole, EMEA-001185-PIP01-11-M05, from Otsuka Europe Development and Commercialisation Limited, Zweigniederlassung, Frankfurt am Main, for the treatment of schizophrenia;
- Lanthanum carbonate hydrate, EMEA-000637-PIP02-10-M06, from Shire Pharmaceutical Contracts Ltd, for the treatment of hyperphosphataemia;

- Isavuconazonium (sulfate), EMEA-001301-PIP02-12-M02, from Basilea Pharmaceutica International Ltd., for the treatment of invasive aspergillosis and treatment of mucormycosis;
- Perampanel, EMEA-000467-PIP01-08-M10, from Eisai Europe Limited, for the treatment of treatment-resistant epilepsies;
- Autologous haematopoietic stem cells transduced with lentiviral vector Lenti-D encoding the human ATP-binding cassette, subfamily D, member 1 (ABCD1) cDNA, EMEA-001244-PIP01-11-M02, from bluebird bio France, for the treatment of adrenoleukodystrophy;
- Ponatinib, EMEA-001186-PIP01-11-M02, from Incyte Biosciences Distrubution B.V, for the treatment of acute lymphoblastic leukaemia and treatment of chronic myeloid leukaemia;
- Eftrenonacog alfa, EMEA-000914-PIP01-10-M04, from Biogen Idec Ltd, for the treatment of hereditary factor IX deficiency;
- Quizartinib, EMEA-001821-PIP01-15-M02, from Daiichi Sankyo Europe GmbH, for the treatment of acute myeloid leukaemia;
- Human fibrinogen concentrate, EMEA-001931-PIP01-16-M01, from Biotest AG, for the treatment of congenital fibrinogen deficiency;
- Recombinant human alpha-galactosidase A, EMEA-001828-PIP01-15-M01, from Protalix Ltd, for the treatment of Fabry disease;
- Dupilumab, EMEA-001501-PIP02-13-M03, from sanofi-aventis recherche & développement, for the treatment of asthma;
- Dapagliflozin, EMEA-000694-PIP01-09-M07, from AstraZeneca AB, for the treatment of type 2 diabetes mellitus;
- Darunavir / cobicistat / emtricitabine / tenofovir alafenamide, EMEA-001825-PIP01-15-M02, from Janssen-Cilag International NV, for the treatment of human immunodeficiency virus type-1 (HIV-1) infection;
- Omadacycline, EMEA-000560-PIP03-15-M01, from Paratek UK Limited, for the treatment of bacterial pneumonia;
- Ertugliflozin, EMEA-001533-PIP01-13-M01, from Merck Sharp & Dohme (Europe), Inc., for the treatment of type II diabetes mellitus;
- Macrogol 3350 / sodium ascorbate / sodium sulfate / ascorbic acid / sodium chloride / potassium chloride, EMEA-001705-PIP02-15-M01, from Norgine Limited, for the bowel cleansing prior to clinical procedures;
- Indacaterol (acetate) / mometasone (furoate) / EMEA-001217-PIP01-11-M05, from Novartis Europharm Limited, for the treatment of asthma;
- Tofacitinib, EMEA-000576-PIP03-12-M01, from Pfizer Limited, for the treatment of ulcerative colitis;
- Mepolizumab, EMEA-000069-PIP04-13-M02, from GSK Trading Services Limited, for the treatment of vasculitides;
- Belimumab, EMEA-000520-PIP02-13-M02, from Glaxo Group Limited, for the treatment of systemic lupus erythematosus;
- Cariprazine (hydrochloride), EMEA-001652-PIP01-14-M02, from Gedeon Richter Plc., for the

treatment of schizophrenia;

- Rilpivirine (hydrochloride), EMEA-000317-PIP01-08-M10, from Janssen-Cilag International NV, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Eliglustat, EMEA-000461-PIP02-11-M03, from Genzyme Europe B.V., for the treatment of Gaucher disease Type 1 and Type 3 and treatment of Gaucher disease Type 2;
- Caplacizumab, EMEA-001157-PIP01-11-M02, from Ablynx NV, for the treatment of thrombotic thrombocytopenic purpura;
- Vamorolone, EMEA-001794-PIP02-16-M01, from ReveraGen BioPharma Ltd, for the treatment of Duchenne muscular dystrophy;

In addition, the Paediatric Committee (PDCO) having revised its previous opinion adopted a positive opinion, agreeing change(s), for the following product:

- Landiolol (hydrochloride), EMEA-001150-PIP02-13-M02, from AOP Orphan Pharmaceuticals AG, for the treatment of supraventricular arrhythmias;

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

- Gadolinium, [α3,α6,α9-tris[3-[(2,3-dihydroxypropyl)amino]-3-oxopropyl]-3,6,9,15-tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene-3,6,9-triacetato(3-)-κN3,κN6,κN9,κN15,κO3,κO6,κO9], EMEA-001949-PIP01-16-M02, from GUERBET, for the detection and visualisation of areas with disruption of the blood brain barrier and/or abnormal vascularity for diagnostic purposes;

Opinion on compliance check

The PDCO adopted a positive opinion on full compliance check for:

- Lacosamide, EMEA-C-000402-PIP02-11-M05, from UCB Pharma S.A., for the treatment of epilepsy with partial onset seizures;

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 3 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 new alternate from Finland, Ms Pia Annunen.

The PDCO thanked Dr Immanuel Barth for his work as he has resigned from the Committee.

The next PDCO will be held via written procedure on 15-24 August 2018.

– 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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