16 October 2020
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Human Medicines Division

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

13-16 October 2020

## Opinions on paediatric investigation plans

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

- Bimekizumab, EMEA-002189-PIP03-19, from UCB Biopharma SRL, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, spondyloarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Adrenaline (epinephrine), EMEA-002749-PIP01-19, from ARS Pharmaceuticals IRL, Limited, for the treatment of allergic reactions;
- Guselkumab, EMEA-001523-PIP04-19, from Janssen-Cilag International N.V., for the treatment of ulcerative colitis;
- Dapirolizumab pegol, EMEA-002702-PIP01-19, from UCB Biopharma SRL, for the treatment of systemic lupus erythematosus;
- Allogeneic bone marrow derived mesenchymal stromal cells, ex-vivo expanded (MC0518), EMEA-002706-PIP01-19, from medac Gesellschaft für klinische Spezialpräparate mbH, for the treatment of acute graft-versus-host disease;
- Alpha1-proteinase inhibitor (human), EMEA-001312-PIP03-19, from CSL Behring GmbH, for the treatment of acute graft-versus-host disease;
- Adeno-associated viral vector serotype 9 containing the human mini-dystrophin gene (PF-06939926), EMEA-002741-PIP01-20, from Pfizer Europe MA EEIG, for the treatment of Duchenne Muscular Dystrophy;
- Venglustat, EMEA-001716-PIP04-19, from Genzyme Europe B.V., for the treatment of GM1 gangliosidosis, treatment of GM2 gangliosidosis, treatment of galactosialidosis and treatment of sialidosis;
- Lanadelumab, EMEA-001864-PIP03-19, from Shire Pharmaceuticals Ireland Limited (a Takeda company), for the prevention of attacks of Idiopathic non-histaminergic angioedema (INHA);

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- Recombinant human acid alpha-glucosidase, EMEA-002447-PIP01-18, from Amicus Therapeutics Europe Limited, for the treatment of glycogen storage disease Type II (Pompe's disease);
- Taniborbactam / cefepime, EMEA-002576-PIP01-19, from Venatorx Pharmaceuticals, Inc., for the treatment of gram-negative bacterial infections;
- BI 425809, EMEA-002653-PIP01-19, from Boehringer Ingelheim International GmbH, for the treatment of schizophrenia;
- Cotadutide, EMEA-002712-PIP01-19, from AstraZeneca AB, for the treatment of non-alcoholic steatohepatitis (NASH);
- Garadacimab, EMEA-002726-PIP01-19, from CSL Behring GmbH, for the prevention of hereditary angioedema attacks (HAE);
- Vonoprazan fumarate, EMEA-002703-PIP01-19, from Phathom Pharmaceuticals, Inc , for the treatment of gastroesophageal reflux disease and treatment of *helicobacter pylori* infection;
- Bispecific antibody binding to clotting factor IX and X, EMEA-002762-PIP02-20, from Novo Nordisk A/S, for the treatment of haemophilia A.

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:

- Lurbinectedin, EMEA-002846-PIP01-20, from Pharma Mar, S.A., for the treatment of small cell lung cancer;
- Allogeneic BCMA-directed chimeric antigen receptor T Cell, EMEA-002834-PIP01-20, from CRISPR Therapeutics AG, for multiple myeloma;
- 2-(6-azaspiro[2.5]octan-6-yl)-N-[2-(4,4-difluoropiperidin-1-yl)-6-methylpyrimidin-4-yl]- 4-[(2-hydroxyethanesulfonyl)amino]benzamide hydrochloride, EMEA-002843-PIP02-20, from Amgen Europe BV, for the treatment of breast cancer;
- Fasudil hydrochloride, EMEA-002841-PIP01-20, from Aneuryst (Ireland) Limited, for the treatment of non-traumatic subarachnoid haemorrhage;
- Dapagliflozin, EMEA-000694-PIP05-20, from AstraZeneca AB, for the treatment of coronavirus disease 2019 (COVID-19);
- 2-(6-azaspiro[2.5]octan-6-yl)-N-[2-(4,4-difluoropiperidin-1-yl)-6-methylpyrimidin-4-yl]- 4-[(2-hydroxyethanesulfonyl)amino]benzamide hydrochloride, EMEA-002843-PIP01-20, from Amgen Europe BV, for the treatment of ovarian cancer;
- Chimeric fibril-reactive IgG1k monoclonal antibody 11-1F4, EMEA-002791-PIP01-20, from Real Regulatory Limited, for the treatment of systemic light chain amyloidosis;

- Perindopril arginine / Indapamide / Amlodipine besilate, EMEA-002849-PIP01-20, from Teva B.V., for the treatment of hypertension;
- (1R,2R,3S,4S,5R,6S)-cyclohexane-1,2,3,4,5,6-hexayl-hexakis (dihydrogen phosphate), EMEA-002854-PIP01-20, from Sanifit Therapeutics S.A., for the treatment of calciphylaxis;
- Ezetimibe / Atorvastatin, EMEA-002852-PIP01-20, from Sandoz B.V., for the prevention of cardiovascular events and treatment of hypercholesterolemia;
- Lixisenatide, EMEA-000916-PIP01-10-M07, from sanofi-aventis R&D, for the treatment of type 2 diabetes mellitus;
- Serplulimab, EMEA-002859-PIP01-20, from Shanghai Henlius Biotech, Inc., for the treatment of lung cancer (small cell and non-small cell lung cancer);

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:

- Tazobactam / ceftolozane, EMEA-001142-PIP01-11-M04, from Merck Sharp & Dohme (Europe), Inc., for the treatment of intra-abdominal infections and treatment of urinary tract infections;
- Teduglutide, EMEA-000482-PIP01-08-M06, from Shire Pharmaceuticals Ireland Limited, for the treatment of short bowel syndrome;
- Inebilizumab, EMEA-001911-PIP01-15-M03, from Viela Bio, Inc, for the treatment of neuromyelitis optica spectrum disorders;
- Canagliflozin (1s)-1,5-anhydro-1-[3-[[5-(4-fluorophenyl)-2-thienyl]methyl]-4-methylphenyl]-D-glucitol hemihydrate, EMEA-001030-PIP01-10-M08, from Janssen-Cilag International NV, for the treatment of type 2 diabetes mellitus;
- Concentrate of proteolytic enzyme enriched in bromelain, EMEA-000142-PIP02-09-M10, from MediWound Germany GmbH, for the treatment of burns;
- Bilastine, EMEA-000347-PIP02-16-M02, from Faes Farma S.A., for the treatment of allergic conjunctivitis;
- Live attenuated, chimeric dengue virus, serotype 4 / Live, attenuated, chimeric dengue virus, serotype 1 / Live, attenuated, chimeric dengue virus, serotype 3 / Live, attenuated dengue virus, serotype 2, EMEA-001888-PIP01-15-M01, from Takeda Vaccines, Inc., for the prevention of dengue fever;
- Veliparib, EMEA-000499-PIP02-10-M01, from AbbVie Ltd, for the treatment of high-grade glioma;
- Fenfluramine hydrochloride, EMEA-001990-PIP01-16-M03, from Zogenix International Ltd, for the treatment of Dravet syndrome;

- Humanised anti-IL-6 receptor (IL-6R) monoclonal antibody (INN: satralizumab), EMEA-001625-PIP01-14-M06, from Roche Registration GmbH, for the treatment of neuromyelitis optica;
- Drospirenone / Estetrol, EMEA-001332-PIP01-12-M04, from Estetra SPRL, for the prevention of pregnancy;
- Ustekinumab, EMEA-000311-PIP03-11-M06, from Janssen-Cilag International NV, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis);
- Olipudase alfa, EMEA-001600-PIP01-13-M02, from Genzyme Europe B.V., for the treatment of Niemann-Pick disease;
- Tralokinumab, EMEA-001900-PIP02-17-M04, from LEO Pharma A/S, for the treatment of atopic dermatitis;
- Nivolumab, EMEA-001407-PIP01-12-M03, from Bristol-Myers Squibb Pharma EEIG, for the treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue);
- Potassium chloride / Sodium chloride / Ascorbic acid / sodium sulfate / Sodium ascorbate / Polyethylene Glycol 3350, EMEA-001705-PIP02-15-M03, from Norgine Limited, for the bowel cleansing prior to clinical procedures;
- Recombinant parathyroid hormone: rhPTH (1-84), EMEA-001526-PIP01-13-M04, from Shire Pharmaceuticals Ireland Limited, for the hypoparathyroidism;
- Vonicog alfa, EMEA-001164-PIP01-11-M04, from Baxalta Innovations GmbH, for the treatment of von Willebrand Disease;
- Tedizolid, EMEA-001379-PIP01-12-M05, from Merck Sharp & Dohme (Europe), Inc., for the treatment of acute bacterial skin and skin structure infections;
- Nivolumab, EMEA-001407-PIP02-15-M04, from Bristol-Myers Squibb Pharma EEIG, for the treatment of malignant neoplasms of lymphoid tissue and treatment of malignant neoplasms of the central nervous system;
- Palovarotene, EMEA-001662-PIP01-14-M04, from Ipsen Pharma, for the treatment of fibrodysplasia ossificans progressiva;
- Tenofovir (disoproxil fumarate), EMEA-000533-PIP01-08-M09, from Gilead Sciences International Limited, for the treatment of chronic viral hepatitis B and treatment of human immunodeficiency virus (HIV-1) infection;
- Birch pollen extract (Betula verrucosa), EMEA-001879-PIP01-15-M02, from ALK-Abelló A/S, for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Tenofovir Alafenamide / Emtricitabine / Elvitegravir / Cobicistat, EMEA-001460-PIP01-13-M05, from Gilead Sciences International Ltd., for the treatment of human immunodeficiency virus (HIV-1) infection;
- Apremilast, EMEA-000715-PIP03-11-M06, from Amgen Europe B.V., for the treatment of psoriasis;

# Opinion on compliance check

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

- Sofosbuvir / Voxilaprevir / Velpatasvir, EMEA-C-001822-PIP01-15-M01, from Gilead Sciences Ireland UC, for the treatment of chronic hepatitis C;

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).

## Cooperation with Health Canada

At the October meeting, the PDCO welcomed representative(s) of Health Canada (HC), who attended the PDCO plenary meeting as observers.

## Other matters

The PDCO welcomed the new members Fernando Cabanas, Francesca Rocchi and alternates Johannes Taminiau, Doina Anca Plesca and Catherine Cornu representing the healthcare professionals and members Jaroslav Sterba, Dimitrios Athanasiou and alternates Tomasz Grybek, Nora Kriauzaite representing patients' organisations, Marleen Renard as new member from Belgium and Eva Agurell as member for Sweden.

The PDCO thanked Ninna Gulberg, Roel Bolt and Melinda Sobor for their work as they resigned from the Committee.

The next meeting of the PDCO will be held on 10-13 November 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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