29 March 2019
EMA/PDCO/213525/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

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

PDCO 26-29 March 2019

Opinions on paediatric investigation plans

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

- Ustekinumab, EMEA-000311-PIP06-18, from Janssen-Cilag International NV, for the treatment of systemic lupus erythematosus;
- Efpeglenatide, EMEA-001903-PIP01-15, from Sanofi-aventis recherche et développement, for the treatment of type 2 diabetes mellitus;
- Dusquetide, EMEA-002306-PIP02-18, from Soligenix UK Limited, for the prevention of oral mucositis;
- Fitusiran, EMEA-001855-PIP01-15, from Genzyme Europe B.V., for the treatment of congenital Haemophilia A and treatment of congenital Haemophilia B;
- N-(trans-3-(5-((R)-1-hydroxyethyl)-1,3,4-oxadiazol-2-yl) cyclobutyl)-3-phenylisoxazole-5-carboxamide, EMEA-002398-PIP01-18, from SFL Regulatory Services GmbH, for the treatment of cystic fibrosis;
- Beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium bromide, EMEA-001875-PIP02-18, from Chiesi Farmaceutici S.p.A., for the treatment of asthma;
- Mometasone (furoate monohydrate) / olopatadine (hydrochloride), EMEA-002514-PIP01-18, from Glenmark Pharmaceuticals Europe Ltd., for the treatment of allergic rhinitis / rhino-conjunctivitis

The PDCO adopted an opinion on the **refusal** of a PIP and a deferral for the following medicines:

- Salbutamol sulfate / budesonide, EMEA-002533-PIP01-18, from AstraZeneca AB, for the treatment of asthma

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

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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:

Following the re-examination of the positive opinion on a PIP with Deferral adopted on 1 February 2019 for the following product:

- Chemically modified recombinant human sulfamidase, EMEA-002380-PIP01-18, from Swedish Orphan Biovitrum AB (publ), for the treatment of mucopolysaccharidosis type IIIA, the PDCO adopted a revised positive Opinion and agreed the paediatric investigation plan in accordance with Article 17(1) of Regulation (EC) No 1901/2006 as amended, and granted a deferral in accordance with Article 21 of said Regulation.

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:

- Inactivated patient's own (autologous) microorganism (Escherichia coli, Candida spp., Enterococcus spp., Streptococcus spp., Staphylococcus spp., Prevotella intermedia, Fusobacterium nucleatum and others), EMEA-002442-PIP01-18, from SymbioVaccin GmbH, for the treatment and prevention of bacterial upper respiratory tract infections, treatment and prevention of dermatitis and eczema and treatment and prevention of genitourinary tract infections and inflammations;
- Seladelpar, EMEA-002527-PIP01-18, from CymaBay Ireland Limited, for the treatment of primary biliary cholangitis;
- Clarithromycin (in combination with pantoprazole + amoxicillin), EMEA-002549-PIP01-19, from Micro Labs GmbH, for the treatment of *Helicobacter spp*. infections;
- Humanized antibody targeting B cell maturation antigen conjugated with maleimidocaproyl monomethyl auristatin F, EMEA-002468-PIP02-18, from GlaxoSmithKline Trading Services, for the treatment of multiple myeloma;
- Niraparib, EMEA-002268-PIP03-18, from Janssen Research & Development, for the treatment of malignant prostate neoplasms;
- Pantoprazole (in combination with amoxicillin + clarithromycin), EMEA-002512-PIP01-18, from Micro Labs GmbH, for the treatment of *Helicobacter spp*. infections;

- Colecalciferol, EMEA-002553-PIP01-19, from Pharma Patent Kft., for the treatment of osteoporosis;
- Candesartan / atorvastatin / amlodipine, EMEA-002520-PIP01-18, from Midas Pharma GmbH, for the treatment of hypertension and treatment of hypercholesterolemia;
- Recombinant human lecithin cholesterol acyltransferase, EMEA-002497-PIP01-18, from AstraZeneca AB, for the treatment of acute ST- elevation myocardial infarction;
- Carfilzomib, EMEA-001806-PIP03-18, from Amgen Europe BV, for the treatment of multiple myeloma;
- Ibandronic acid (in the form of ibandronate sodium monohydrate), EMEA-002331-PIP01-18, from Pharma Patent Kft., for the treatment of osteoporosis;
- Amoxicillin (in combination with pantoprazole + clarithromycin), EMEA-002548-PIP01-19, from Micro Labs GmbH, for the treatment of *Helicobacter spp*. infections

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:

- Asfotase alfa, EMEA-000987-PIP01-10-M04, from Alexion Europe SAS, for the treatment of hypophosphatasia;
- Angiotensin II, EMEA-001912-PIP02-16-M02, from La Jolla Pharmaceutical II B.V., for the treatment of hypotension associated with distributive or vasodilatory shock;
- Deferiprone, EMEA-001126-PIP01-10-M03, from Consorzio per Valutazioni Biologiche e Farmacologiche, for the treatment of chronic iron overload;
- Fc- and CDR-modified humanised monoclonal antibody against C5, EMEA-002077-PIP01-16-M02, from Alexion Europe SAS, for the treatment of paroxysmal nocturnal haemoglobinuria;
- Finerenone, EMEA-001623-PIP01-14-M02, from Bayer AG, for the treatment of chronic kidney disease;
- Baricitinib, EMEA-001220-PIP01-11-M05, from Eli Lilly and Company Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Adalimumab, EMEA-000366-PIP02-09-M06, from AbbVie Limited, for the treatment of ulcerative colitis;
- Imipenem (monohydrate) / cilastatin (sodium) / relebactam, EMEA-001809-PIP01-15-M01, from Merck Sharp & Dohme (Europe), Inc., for the treatment of Gram-negative bacterial infections;
- Onasemnogene abeparvovec, EMEA-002168-PIP01-17-M01, from AveXis Netherlands B.V., for the treatment of spinal muscular atrophy;
- Clostridium botulinum neurotoxin type A, free from complexing proteins, EMEA-001039-PIP02-12-M03, from Merz Pharmaceuticals GmbH, for the treatment of sialorrhea;

- Omecamtiv mecarbil, EMEA-001696-PIP01-14-M01, from Amgen Europe B.V., for the treatment of heart failure;
- Quizartinib, EMEA-001821-PIP01-15-M03, from Daiichi Sankyo Europe GmbH, for the treatment of acute myeloid leukaemia;
- Ruxolitinib (phosphate), EMEA-000901-PIP03-16-M01, from Novartis Europharm Limited, for the treatment of acute Graft versus Host Disease;
- Gilteritinib (as fumarate), EMEA-002064-PIP01-16-M01, from Astellas Pharma Europe B.V., for the treatment of acute myeloid leukemia

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

- Agomelatine, EMEA-001181-PIP01-11-M04, from Les Laboratoires Servier, for the treatment of major depressive episodes

Opinion on full compliance check

No items

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 23-26 April 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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