30 May 2016
EMA/PDCO/376295/2016
Procedure Management and Committees Support Division

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

25-27 May 2016

Opinions on paediatric investigation plans

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

- Metreleptin, EMEA-001701-PIP01-14, from Aegerion Pharmaceuticals Ltd, for the treatment of lipodystrophy;
- Eleclazine, EMEA-001697-PIP01-14, from Gilead Sciences International Ltd, for the treatment of congenital long QT syndromes;
- Eleclazine, EMEA-001697-PIP02-14, from Gilead Sciences International Ltd, for the treatment of hypertrophic cardiomyopathy;
- Cadazolid, EMEA-001108-PIP02-15, from Actelion Registration Ltd., for treatment of Clostridium difficile infection;
- Indacaterol acetate / Glycopyrronium bromide / Mometasone furoate (QVM149), EMEA-001812-PIP01-15, from Novartis Europharm Ltd., for the treatment of asthma;
- Humanized monoclonal modified immunoglobulin G4 (IgG4) antibody with bispecific structure targeting factors IX, IXa, X and Xa (Emicizumab), EMEA-001839-PIP01-15, from Roche Registration Limited, for the treatment of hereditary factor VIII deficiency.

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 modifications to an agreed PIP

The PDCO also adopts, every month, opinions on modifications to an agreed PIP, which can be

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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:

- belimumab, EMEA-000520-PIP01-08-M05, from Glaxo Group Limited, for the treatment of systemic lupus erythematosus;
- Regorafenib, EMEA-001178-PIP01-11-M02, from Bayer Pharma, for the treatment of all conditions contained in the category of malignant neoplasms (except haematopoietic and lymphoid tissue);
- Deferasirox, EMEA-001103-PIP01-10-M03, from Novartis Europharm Limited, for the treatment of chronic iron overload requiring chelation therapy;
- Liraglutide, EMEA-000128-PIP01-07-M07, from Novo Nordisk A/S, for the treatment of type 2 diabetes mellitus;
- Landiolol hydrochloride, EMEA-001150-PIP02-13-M01, from AOP Orphan Pharmaceuticals AG, for the treatment of supraventricular arrhythmias;
- recombinant dimer of 6 kD early secretory antigenic target / recombinant 10 kD culture filtrate protein, EMEA-001156-PIP01-11-M07, from Statens Serum Institut, for the diagnosis of tuberculosis;
- Eculizumab, EMEA-000876-PIP05-15-M01, from Alexion Europe SAS, for the treatment of myasthenia gravis;
- caplacizumab, EMEA-001157-PIP01-11-M01, from Ablynx NV, for the treatment of thrombotic thrombocytopenic purpura;
- 1-(2,2-difluoro-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluoro-2-(1-hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl}cyclopropanecarboxamide / Ivacaftor, EMEA-001640-PIP01-14-M01, from Vertex Pharamceuticals (Europe) Ltd, for the treatment of cystic fibrosis;
- corifollitropin alfa, EMEA-000306-PIP01-08-M03, from Merck Sharp & Dohme Limited, for the treatment of hypogonadotrophic hypogonadism;
- baricitinib, EMEA-001220-PIP01-11-M01, from Eli Lilly & Company Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Agomelatine, EMEA-001181-PIP01-11-M03, from Les Laboratoires Servier, for the treatment of major depressive episodes;
- Eltrombopag, EMEA-000170-PIP03-13-M01, from Novartis Europharm Limited, for the treatment of aplastic anaemia;
- Sofosbuvir / ledipasvir, EMEA-001411-PIP01-12-M03, from Gilead Sciences International Ltd, for the treatment of chronic hepatitis C;
- Brivaracetam, EMEA-000332-PIP01-08-M10, from UCB Pharma SA, for the treatment of paediatric epilepsy syndromes, treatment of neonatal seizures and treatment of epilepsy with partial onset seizures;
- Dulaglutide, EMEA-000783-PIP01-09-M04, from Eli Lilly & Company, for the treatment of type 2 diabetes mellitus.

The PDCO adopted an opinion on the **refusal** of a modification to an agreed PIP for the following

application:

- Decitabine, EMEA-000555-PIP01-09-M05, from Janssen-Cilag International NV, for the treatment of acute myeloid leukaemia.

Opinion on compliance check

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

- Cinacalcet hydrochloride, EMEA-C-000078-PIP01-07-M07, from Amgen Europe B.V., for the treatment of parathyroid carcinoma, treatment of primary hyperparathyroidism and treatment of secondary hyperparathyroidism in patients with end-stage renal disease;
- Tiotropium bromide (monohydrate), EMEA-C-000035-PIP02-09-M02, from Boehringer Ingelheim International GmbH, for the treatment of asthma;
- Diphtheria toxoid / Tetanus toxoid / Bordetella pertussis antigen: Pertussis toxoid / Bordetella pertussis antigen: Filamentous Haemagglutinin / Bordetella pertussis antigen: Pertactin / Inactivated poliovirus: type 1 (Mahoney strain) / Inactivated poliovirus: type 2 (MEF-1 strain) / Inactivated poliovirus: type 3 (Saukett strain), EMEA-C-000500-PIP01-08-M03, from GlaxoSmithKline Biologicals S.A., for the prevention of infectious diseases caused by Corynebacterium diphtheriae / Clostridium tetani / Bordetella pertussis / Poliovirus types 1, 2 and 3.

The PDCO adopted a negative opinion on compliance with a PIP for recombinant human tripeptidyl peptidase 1 (rhTPP1), EMEA-C-001362-PIP01-12-M02, from BioMarin International Limited, for the treatment of Neuronal Ceroid Lipofuscinosis type 2.

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/measured 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).

The PDCO also noted that the application leading to the opinion adopted during the PDCO April 2016 meeting for Pimavanserin, EMEA-001688-PIP02-15, from ACADIA Pharmaceuticals Inc., for the treatment of schizophrenia and other psychotic disorders, was withdrawn before the decision was adopted by the Agency.

Other matters

The next meeting of the PDCO will be held on 22-24 June 2016.

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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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