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Paediatric Committee (PDCO)

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

11-13 February 2015

Opinions on paediatric investigation plans

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

- Canakinumab, from Novartis Europharm Ltd, for the treatment of familial Mediterranean fever and treatment of hyperimmunoglobulin D syndrome;
- Canakinumab, from Novartis Europharm Ltd, for the treatment of tumour necrosis factor receptor associated periodic syndrome;
- Dapagliflozin, from AstraZeneca AB, for the treatment of type 1 diabetes mellitus;
- Tetrabenazine (ADV6979), from Advicenne Pharma, for the treatment of dystonia;
- (1,1-Dioxo-1,6-thiomorpholin-4-yl)-{6-[3-(4-fluoro-phenyl)-5-methyl-isoxazol-4-ylmethoxy]-pyridin-3-yl}-methanone (RG1662), from Roche Registration Ltd, for the treatment of Down syndrome;
- Ceftriaxone / Sulbactam, from Venus Pharma GmbH, for the treatment of bacterial infections;
- Olipudase alfa, from Genzyme Europe B.V., for the treatment of Niemann-Pick disease;
- Anti-programmed death-ligand 1 (PD-L1) monoclonal antibody (MPDL3280A), from Roche Registration Ltd, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms).

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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

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:

- Autologous bone marrow-derived cardiopoietic stem cells, from Cardio3 BioSciences SA, for the treatment of ischemic heart disease;
- Ibuprofen/Codeine, from Laboratórios Vitória, S.A., for the treatment of pain.

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:

- Tapentadol (hydrochloride), from Grünenthal GmbH, for the treatment of acute pain;
- Ferumoxytol, from AMAG Pharmaceuticals, Inc., for the treatment of iron deficiency anaemia;
- Dolutegravir, from ViiV Healthcare UK Ltd., for the treatment of human immunodeficiency virus (HIV-1) infection;
- Sitagliptin, from Merck Sharp and Dohme (Europe), Inc., for the treatment of type 2 diabetes mellitus;
- Belimumab, from Glaxo Group Limited, for the treatment of systemic lupus erythematosus;
- Agomelatine, from Les Laboratoires Servier, for the treatment of major depressive episodes and treatment of generalised anxiety disorder;
- Dolutegravir / abacavir / lamivudine, from ViiV Healthcare UK Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Damoctocog alfa pegol, from Bayer Pharma AG, for the treatment of hereditary factor VIII deficiency;
- Evolocumab, from Amgen Europe B.V, for the treatment of elevated cholesterol and treatment of mixed dyslipidaemia;
- Obeticholic acid (6 alpha-ethylchenodeoxycholic acid), from Intercept Italia s.r.l., for the treatment of primary biliary cirrhosis and treatment of biliary atresia;
- Ceftazidime / avibactam, from AstraZeneca AB, for the treatment of intra-abdominal infections, treatment of urinary tract infections, treatment of pneumonia and treatment of Gram-negative bacterial infections;
- Glibenclamide, from AMMTeK, for the treatment of neonatal diabetes mellitus;

- Retosiban, from GlaxoSmithKline Trading Services Limited, for the treatment of labour onset and length abnormalities;
- Dulaglutide, from Eli Lilly & Company, for the treatment of type 2 diabetes mellitus;
- Bedaquiline (fumarate), from Janssen Infectious Diseases BVBA, for the treatment of multi-drug resistant tuberculosis;
- Clostridium Botulinum neurotoxin type A (150 kD), free of complexing proteins, from Merz Pharmaceuticals GmbH, for the treatment of muscle spasticity, treatment of dystonia and treatment of muscle-induced wrinkles.

The PDCO adopted 2 opinions on the **refusal** of modifications to an agreed PIP for:

- Treprostinil, from United Therapeutics Europe Limited, for the treatment of pulmonary arterial hypertension;
- Canagliflozin, from Janssen-Cilag International N.V., for the treatment of type 2 diabetes mellitus.

The PDCO adopted an opinion on the refusal of a modification to an agreed PIP for, for Sunitinib, from Pfizer Limited, for the treatment of gastro-intestinal stromal tumour.

The PDCO subsequently granted on its own motion a product-specific waiver for this medicine on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

Opinion on compliance check

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

- Formoterol fumarate dihydrate / Fluticasone Propinate, from Mundipharma Research Limited, for the treatment of asthma;
- Atazanavir (sulphate), from Bristol-Myers Squibb Pharma EEIG, for the treatment of human immunodeficiency virus (HIV-1) infection.

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 2 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 18-20 March 2015.

– 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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