23 June 2014
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Paediatric Committee (PDCO)

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

18-10 June 2014

Opinions on paediatric investigation plans

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

- Recombinant parathyroid hormone, from NPS Pharma Holdings Limited, for the treatment of hypoparathyroidism;
- Tofacitinib, from Pfizer Limited, for the treatment of ulcerative colitis;
- Tobramycin, from Novartis Europharm Ltd., for the treatment of Pseudomonas aeruginosa pulmonary infection/colonisation in patients with cystic fibrosis;
- Ranibizumab, from Novartis Europharm Limited, for the treatment of retinopathy of prematurity;
- Captopril, from Proveca Limited, for the treatment of heart failure;
- Silicic acid, sodium zirconim (4+) salt (3:2:1) hydrate, from ZS Pharma, Inc., for the treatment of hyperkalaemia;
- N-[(1,3-dicyclohexyl-6-hydroxy-2,4-dioxo-1,2,3,4-tetrahydro-5-pyrimidinyl)carbonyl]glycine (GSK1278863), from GlaxoSmithKline Trading Services Limited, for the treatment of anaemia due to chronic disorders;
- Dupilumab, from Sanofi-Aventis Recherche & Développement, for the treatment of asthma;
- Vosaroxin, from Sunesis Europe Ltd, for the treatment of acute myeloid leukaemia;
- Daclatasvir (dihydrochloride) / asunaprevir / (1aR,12bS)-8-Cyclohexyl-N-(dimethylsulfamoyl)-11-methoxy-1a-(((1R,5S)-3-methyl-3,8-diazabicyclo[3.2.1]oct-8-yl)carbonyl)-1,1a,2,12b-tetrahydrocyclopropa[d]indolo[2,1-a][2]benzazepine-5-carboxamide hydrochloride (BMS-791325), from Bristol-Myers Squibb International Corporation, for the treatment of chronic hepatitis C;
- Valaciclovir Hydrochloride, from Pharmathen S.A., for the treatment of Herpes simplex virus infection and treatment of Varicella Zoster virus infection;

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- (S)-Pyrrolidine-2-carboxylic acid compound with (2S,3R,4R,5S,6R)-2-(3-((2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-4-ethylphenyl)-6-(hydroxymethyl)tetrahydro-2H-pyran-3,4,5-triol (2:1) (LIK066), from Novartis Europharm Ltd., for the treatment of type 2 diabetes mellitus.

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:

- Rosuvastatin / Acetylsalicylic acid, from EGIS Pharmaceuticals PLC, for the treatment of cardiovascular disease;
- Tirasemtiv, from Cytokinetics Inc., for the treatment of amyotrophic lateral sclerosis;
- Human recombinant follicle-stimulating hormone (FE 999049), from Ferring Pharmaceuticals A/S, for the treatment of female infertility and treatment of hypogonadotrophic hypogonadism;
- Ranibizumab, from Novartis Europharm Limited, for the treatment of choroidal neovascularisation and treatment of macular oedema;
- Pacritinib, from CTI Life Sciences, Ltd, for the treatment of post-polycythaemia vera myelofibrosis and treatment of post-essential thrombocythaemia myelofibrosis.

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:

- Sofosbuvir / ledipasvir, from Gilead Sciences International Ltd., for the treatment of chronic hepatitis C;
- Riociguat, from Bayer Pharma AG, for the treatment of pulmonary hypertension;
- Cangrelor (tetrasodium), from the Medicines Company UK Ltd, for the prevention of non-site specific embolism and thrombosis;
- Recombinant human lysosomal acid lipase, from Synageva BioPharma Ltd, for the treatment of Lysosomal Acid Lipase Deficiency;

- Rilpivirine (hydrochloride), from Janssen-Cilag International NV, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Sofosbuvir, from Gilead Sciences International Ltd., for the treatment of chronic hepatitis C;
- Sildenafil, from Pfizer Limited, for the treatment of pulmonary arterial hypertension;
- Recombinant single chain coagulation factor VIII, from CSL Behring GmbH, for the treatment of congenital factor VIII deficiency;
- Tobramycin, from Novartis Europharm Ltd., for the treatment of Pseudomonas aeruginosa pulmonary infection/colonisation in patients with cystic fibrosis;
- Asfotase alfa, from Alexion Europe SAS, for the treatment of hypophosphatasia;
- Human coagulation factor X, from Bio Products Laboratory, for the treatment of hereditary factor X deficiency;
- Deferasirox, from Novartis Europharm Limited, for the treatment of chronic iron overload requiring chelation therapy;
- Exenatide, from Bristol-Myers Squibb / AstraZeneca EEIG, for the treatment of type 2 diabetes mellitus;
- Mifepristone, from Corcept Therapeutics Incorporated, for the treatment of hypercortisolism (Cushing's syndrome) of endogenous origin;
- Vortioxetine, from H. Lundbeck A/S, for the treatment of major depressive disorder and treatment of generalised anxiety disorder;
- Autologous CD34+ Cells Transduced ex-vivo with Retroviral Vector (GIADAI) Containing Human Adenosine Deaminase Gene from cDNA, from GlaxoSmithKline Trading Services Limited, for the treatment of severe combined immunodeficiency due to adenosine deaminase deficiency;
- Daclatasvir, from Bristol-Myers Squibb International Corporation, for the treatment of chronic hepatitis C;
- Tralokinumab, from MedImmune Ltd, for the treatment of asthma.

Opinion on compliance check

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

- Vandetanib, from AstraZeneca AB, for the treatment of medullary thyroid carcinoma;
- Entecavir (monohydrate), from Bristol-Myers Squibb Pharma EEIG, for the treatment of chronic hepatitis B;
- Gadobutrol, from Bayer Pharma AG, for the diagnostic evaluation of tissue pathologies with contrast-enhanced magnetic resonance imaging (MRI);
- Adalimumab, from AbbVie Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis), treatment of Crohn's disease and treatment of psoriasis.

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).

New meeting dates adopted

PDCO meeting dates for 2016, 2017 and 2018 were adopted during the June meeting. These dates are important for applicants in planning the submission of applications for PIPs, requests for waivers, requests for modification of an agreed PIP, and requests for compliance checks. The dates are published on the Agency's website at:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000293.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac0580025b91&jsenabled=true

Other matters

The PDCO welcomed Peter Szitanyi in his new role as member and Marina Fertek in her new role as alternate, nominated to represent Czech Republic.

The PDCO thanked Jaroslav Sterba for his work following the end of his mandate.

The next meeting of the PDCO will be held on 16 - 18 July 2014.

– 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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