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Procedure Management and Committees Support Division

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

9-11 September 2015

Opinions on paediatric investigation plans

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

- Ibrutinib, from Janssen-Cilag International N.V., for the treatment of mature B-cell neoplasm;
- Simtuzumab, from Gilead Sciences International Ltd, for the treatment of interstitial pulmonary diseases with fibrosis;
- Fluciclovine (18F), from Blue Earth Diagnostics Ltd, for the diagnosis of amino acid metabolism in solid malignant tumours;
- Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human βA-T87Q-globin gene, from bluebird bio France, for the treatment of β-thalassaemia;
- (3-((4-Benzoyl-1-piperazinyl)(oxo)acetyl)-4-methoxy-7-(3-methyl-1H-1,2,4-triazol-1-yl)-1H-pyrrolo[2,3-c]pyridin-1-yl)methyl dihydrogen phosphate, 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (BMS-663068), from Bristol-Myers Squibb International Corporation, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Patiromer calcium, from Relypsa, Inc, for the treatment of hyperkalaemia;
- Meropenem trihydrate (in combination with vaborbactam), from Rempex Pharmaceuticals, a wholly-owned subsidiary of The Medicines Company, for the treatment of Gram-negative bacterial infections;
- Vaborbactam (in combination with meropenem trihydrate), from Rempex Pharmaceuticals, a wholly-owned subsidiary of The Medicines Company, for the treatment of Gram-negative bacterial infections;
- Begelomab, from Adienne S.r.l. S.U., for the treatment of acute graft-versus-host disease (aGvHD).

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The PDCO adopted an opinion on the **refusal** of a PIP, including a deferral, for Dasabuvir / ombitasvir / paritaprevir / ritonavir, from AbbVie Ltd., for the treatment of chronic hepatitis C.

The PDCO subsequently granted on its own motion a product-specific waiver for this medicine for all subsets of the paediatric population in the specified condition, 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).

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:

- Nintedanib, from Boehringer Ingelheim International GmbH, for the treatment of systemic sclerosis;
- Ciclosporin, from Allergan Pharmaceuticals Ireland, for the treatment of dry eye disease;
- Gevokizumab, from Les Laboratoires Servier, for the treatment of Schnitzler Syndrome;
- L-Cysteine, L-leucyl-L-α-glutamyl-L-α-glutamyl-L-lysyl-L-lysylglycyl-L-asparaginyl-L-tyrosyl-L-valyl-L-valyl-L-threonyl-L-α -aspartyl-L-histidyl-S-[1-[(4-carboxycyclohexyl)methyl]-2,5-dioxo-3-pyrrolidinyl]-, complex with keyhole limpet haemocyanin, from Celldex Therapeutics, Inc., for the treatment of high-grade glioma;
- Mogamulizumab, from ProStrakan Ltd, for the treatment of adult T-cell leukaemia / lymphoma;
- Mogamulizumab, from ProStrakan Ltd, for the treatment of cutaneous T-cell lymphoma;
- 18F-fluoroestradiol, from Laboratoires Cyclopharma, for the detection of pathological expression of estrogen receptors in organs and tissues.

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:

- Everolimus, from Novartis Europharm Limited, for the treatment of Tuberous Sclerosis Complex;
- Maraviroc, from ViiV Healthcare UK Ltd, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Canakinumab, from Novartis Europharm Ltd, for the treatment of familial Mediterranean fever and treatment of hyperimmunoglobulin D syndrome;
- Canakinumab, from Novartis Europharm Limited, for the treatment of tumour necrosis factor receptor associated periodic syndrome;
- Sacubitril / valsartan (LCZ696), from Novartis Europharm Ltd., for the treatment of heart failure;
- Darbepoetin alfa, from Amgen Europe B.V., for the treatment of anaemia due to chronic disorders;
- Brivaracetam, from UCB Pharma SA, for the treatment of paediatric epilepsy syndromes, treatment of neonatal seizures and treatment of epilepsy with partial onset seizures;
- Icatibant acetate, from Shire Orphan Therapies GmbH, for the treatment of hereditary angioedema (HAE);
- Melatonin, from RAD Neurim Pharmaceuticals EEC Ltd, for the treatment of insomnia;
- Teduglutide, from NPS Pharma Holdings Limited, for the treatment of short bowel syndrome;
- Chloroprocaine (hydrochloride), from Sintetica Italia Srl, for intrathecal anaesthesia;
- Volasertib, from Boehringer Ingelheim International GmbH, for the treatment of acute myeloid leukaemia;
- Dapagliflozin, from AstraZeneca AB, for the treatment of type 2 diabetes mellitus;
- Emtricitabine / rilpivirine (hydrochloride) / tenofovir (disoproxil fumarate), from Gilead Sciences International Ltd, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Ex-vivo expanded human autologous epithelium containing stem cells, from Chiesi Farmaceutici S.p.A., for the treatment of limbal stem cell deficiency due to ocular burns;
- Lonoctocog alfa, from CSL Behring GmbH, for the treatment of congenital factor VIII deficiency;
- Split influenza virus, inactivated containing antigens equivalent to the B-like strain (B/Yamagata lineage) / Split influenza virus, inactivated containing antigens equivalent to the B-like strain (B/Victoria lineage) / Split influenza virus, inactivated containing antigens equivalent to the A/H1N1-like strain / Split influenza virus, inactivated containing antigens equivalent to the A/H3N2-like strain, from Sanofi Pasteur, Sanofi Pasteur MSD, for the prevention of influenza infection;
- Gabapentin, from PHARM SRL, for the treatment of chronic pain;

- 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;
- Recombinant parathyroid hormone, from NPS Pharma Holdings Limited, for the treatment of hypoparathyroidism.

The following product(s) was granted a product-specific waiver:

- Chloroprocaine (hydrochloride), from Sintetica Italia Srl, for intrathecal anaesthesia on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible in the paediatric population from 12 to less than 18 years of age.

Opinion on compliance check

The PDCO adopted a positive opinion on (full) compliance check for Insulin degludec / insulin aspart, from Novo Nordisk A/S, for the treatment of type I diabetes mellitus and treatment of type II diabetes mellitus.

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 3 applications were withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure), plus one request for re-examination of a modification to an agreed PIP.

The next meeting of the PDCO will be held on 7-9 October 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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