17 September 2014
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Paediatric Committee (PDCO)

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

10 – 12 September 2014

Opinions on paediatric investigation plans

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

- Belimumab, from Glaxo Group Limited, for the treatment of systemic lupus erythematosus;
- Landiolol (hydrochloride), from AOP Orphan Pharmaceuticals AG, for the treatment of supraventricular arrhythmias and prevention of supraventricular arrhythmias;
- (3S,11aR)-N-[(2,4-Difluorophenyl)methyl]-6-hydroxy-3-methyl-5,7-dioxo-2,3,5,7,11,11a-hexahydro[1,3]oxazolo[3,2-a]pyrido [1,2-d]pyrazine-8-carboxamide (GSK1265744) , from ViiV Healthcare UK Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;
- 4-((2R,3S,4R,5S)-3-(3-chloro-2-fluorophenyl)-4-(4-chloro-2-fluorophenyl)-4-cyano-5-neopentylpyrrolidine-2-carboxamido)-3-methoxybenzoic acid (RO5503781), from Roche Registration Ltd, for the treatment of acute myeloid leukaemia, treatment of acute lymphoblastic leukaemia and treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue);
- Cholera vaccine, live attenuated, oral (strain CVD 103-HgR), from PaxVax Inc., for the prevention of cholera;
- Sotagliflozin, from Lexicon Celtic Limited, for the treatment of type 2 diabetes mellitus;
- (R)-7-Chloro-benzo[b]thiophene-2-carboxylic acid (1-aza-bicyclo[2.2.2]oct-3-yl)-amide hydrochloride hydrate (EVP-6124), from FORUM Pharmaceuticals, Inc., for the treatment of schizophrenia;
- Molidustat (sodium), from Bayer Pharma AG, for the treatment of anaemia due to chronic disorders;
- Allantoin, from Scioderm, Inc, for the treatment of epidermolysis bullosa.

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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 a positive opinion for a product-specific waiver, 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 medicine:

- Ibrutinib, from Janssen-Cilag International N.V., for the treatment of lymphoplasmacytic lymphoma.

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:

- Human coagulation Factor VIII / von Willebrand Factor, from CSL Behring GmbH, for the treatment of hereditary Factor VIII deficiency (Haemophilia A) and treatment of von Willebrand disease;
- Lacosamide, from UCB Pharma S.A., for the treatment of epilepsy with partial onset seizures and treatment of generalised epilepsy and epileptic syndromes;
- Ambrisentan, from Glaxo Group Limited, for the treatment of pulmonary arterial hypertension;
- Solifenacin (succinate), from Astellas Pharma Europe B.V., for the treatment of idiopathic overactive bladder;
- Solifenacin (succinate), from Astellas Pharma Europe B.V., for the treatment of neurogenic detrusor over activity;
- Fidaxomicin, from Astellas Pharma Europe B.V., for the treatment of enterocolitis caused by Clostridium difficile;
- Rufinamide, from Eisai Limited, for the treatment of Lennox-Gastaut Syndrome;
- Tabalumab, from Eli Lilly and Company Limited, for the treatment of systemic lupus erythematosus;
- Human normal immunoglobulin, from Baxter Innovations GmbH, for the treatment of primary immunodeficiency (PID);
- Bimatoprost, from Allergan Pharmaceuticals Ireland, for the treatment of glaucoma and treatment of non-scarring hair loss;

- Neisseria meningitidis serogroup B recombinant lipoprotein (rLP2086; subfamily A; Escherichia coli) / Neisseria meningitidis serogroup B recombinant lipoprotein (rLP2086; subfamily B; Escherichia coli), from Pfizer Ltd, for the prevention of invasive meningococcal disease caused by N. meningitidis serogroup B;
- Fibrinogen / thrombin / aprotinin / calcium chloride, from Kedrion S.p.A., for the treatment of haemorrhage resulting from a surgical procedure and prevention of haemorrhage resulting from a surgical procedure;
- MAGE-A3 recombinant protein, from GlaxoSmithKline Biologicals s.a, for the treatment of melanoma;
- Recombinant fusion protein linking human coagulation factor IX with human albumin, from CSL Behring GmbH, for the treatment of hereditary factor IX deficiency;
- Delamanid, from Otsuka Frankfurt Research Institute GmbH, for the treatment of multi drug resistant tuberculosis;
- Lenvatinib, from Eisai Europe Ltd, for the treatment of papillary thyroid cancer, treatment of follicular thyroid cancer and treatment of osteosarcoma;
- Turoctocog alfa pegol, from Novo Nordisk A/S, for the treatment of Hereditary factor VIII deficiency;
- Regorafenib, from Bayer Pharma AG, for the treatment of all conditions contained in the category of malignant neoplasms;
- Glycopyrronium (bromide), from Proveca Limited, for the treatment of sialorrhoea.

The PDCO adopted 1 opinion on the **refusal** of modifications to an agreed PIP for:

- Dihydroartemisinin / piperaquine phosphate anhydride, from Sigma-Tau SpA, for the treatment of uncomplicated malaria caused by Plasmodium falciparum.

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 modification to an agreed PIP adopted on 18 July 2014 for Tapentadol (hydrochloride), from Grünenthal GmbH, for the treatment of acute pain, the PDCO adopted a revised positive opinion;
- Following the re-examination of the positive opinion on a modification to an agreed PIP adopted on 20 June 2014 for Vortioxetine, from H. Lundbeck A/S, for the treatment of major depressive disorder and treatment of generalised anxiety disorder, the PDCO adopted a revised positive opinion.

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.

Opinion on compliance check

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

- Tobramycin, from Novartis Europharm Ltd., for the treatment of Pseudomonas aeruginosa pulmonary infection/colonisation in patients with cystic fibrosis;
- Sodium benzylpenilloate / benzylpenicilloyl octa- L-lysine, from Diater Laboratorio de Diagnóstico y Aplicaciones Terapéuticas, S.A., for the diagnosis of beta-lactam allergy.

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 4 applications were withdrawn during the late stages of the evaluation (30 days or less before adoption of opinion).

The PDCO also noted that the application leading to the opinion adopted during the August PDCO meeting for Sunitinib, from Pfizer Limited, for the condition treatment of gastro-intestinal stromal tumour, had been withdrawn before the decision was going to be adopted by the Agency.

Other matters

The next meeting of the PDCO will be held on 8 – 10 October 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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