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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

18-21 April 2017

Opinions on paediatric investigation plans

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

- Cannabidiol, EMEA-001964-PIP01-16, from GW Research Ltd, for the treatment of seizures associated with Dravet Syndrome (DS), treatment of seizures associated with Infantile Spasms (IS), treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) and treatment of seizures associated with Tuberous Sclerosis Complex (TSC);
- Expanded donor-derived allogenic T cells transduced with the retroviral vector expressing the transgenes for inducible caspase9 and the truncated CD19 selectable marker, EMEA-001869-PIP01-15, from Bellicum Pharma Ltd., for the adjunctive treatment in haematopoietic stem cell transplantation;
- Rimiducid, EMEA-001870-PIP01-15, from Bellicum Pharma Ltd., for the treatment of graft versus host disease;
- Pimodivir, EMEA-001975-PIP01-16, from Janssen-Cilag International NV, for the treatment of influenza.

The PDCO adopted an opinion(s) on the **refusal** of a PIP for:

- Polihexanide (PHMB), EMEA-002053-PIP01-16, from Società Industria Farmaceutica Italiana (S.I.F.I.) SpA, for the treatment of acanthamoeba keratitis.

For this medicine the PDCO granted a product-specific waiver on its own motion for all subsets of the paediatric population in the specified condition, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

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

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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:

- Nimodipine, EMEA-002097-PIP01-16, from Edge Therapeutics, Inc., for the treatment of aneurysmal subarchnoidal haemorrhage;
- Ezetimibe / Rosuvastatin (calcium), EMEA-002118-PIP01-17, from Neopharmed Gentili S.r.l, for the treatment of hypercholesterolaemia;
- Malic acid / Zinc sulphate / Sodium acetate / Potassium chloride / Magnesium sulphate / Sodium glycerophosphate / Calcium chloride / Glucose / Valine / Tyrosine / Tryptophan / Threonine / Serine / Proline / Phenylalanine / Methionine / Lysine acetate / Leucine / Isoleucin / Histidine / Glycine / Arginine / Alanine / Acetyl-cysteine / Fish oil / Olive oil / Medium-chain triglycerides / Soybean oil, EMEA-002067-PIP02-17, from Fresenius Kabi AB, for the parenteral nutrition;
- Buprenorphine hydrochloride, EMEA-002099-PIP01-16, from Titan Pharmaceuticals Inc., for the treatment of opioid dependence.

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:

- Enalapril (maleate), EMEA-001706-PIP01-14-M01, from Ethicare GmbH, for the treatment of heart failure;
- Cinacalcet hydrochloride, EMEA-000078-PIP01-07-M08, 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;
- Indacaterol (acetate) / mometasone (furoate), EMEA-001217-PIP01-11-M03, from NOVARTIS EUROPHARM LTD., for the treatment of asthma;
- Ivacaftor, EMEA-000335-PIP01-08-M11, from Vertex Pharmaceuticals (Europe) Limited, for the treatment of cystic fibrosis;
- Split influenza virus, inactivated containing antigens equivalent to the B-like strain (B/Victoria lineage) / Split influenza virus, inactivated containing antigens equivalent to the B-like strain (B/Yamagata lineage) / Split influenza virus, inactivated containing antigens equivalent to the

A/H3N2-like strain / Split influenza virus, inactivated containing antigens equivalent to the A/H1N1-like strain, EMEA-001254-PIP01-11-M02, from Sanofi Pasteur, for the prevention of influenza infection;

- Tapentadol (hydrochloride), EMEA-000325-PIP01-08-M07, from Grünenthal GmbH, for the treatment of chronic pain;
- Rubidium (Rb-82) Chloride, EMEA-000882-PIP03-11-M03, from Jubilant DraxImage Inc., for the visualization of myocardial perfusion for diagnostic purposes;
- Apremilast, EMEA-000715-PIP03-11-M04, from Celgene Europe Limited, for the treatment of psoriasis;
- Vedolizumab, EMEA-000645-PIP01-09-M05, from Takeda Pharma A/S, for the treatment of Crohn's disease and treatment of Ulcerative colitis;
- Rivaroxaban, EMEA-000430-PIP01-08-M10, from Bayer Pharma AG, for the prevention of thromboembolic events and treatment of thromboembolic events;
- Sirukumab, EMEA-001043-PIP01-10-M02, from Janssen-Cilag International N.V., for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Turoctocog alfa pegol, EMEA-001174-PIP02-12-M02, from Novo Nordisk A/S, for the treatment of Hereditary factor VIII deficiency;
- Isavuconazonium (sulfate), EMEA-001301-PIP02-12-M01, from Basilea Pharmaceutica International Ltd., for the treatment of invasive aspergillosis and treatment of mucormycosis;
- Human recombinant IgG1 monoclonal antibody targeting fibroblast growth factor 23 (KRN23), EMEA-001659-PIP01-15-M02, from Ultragenyx Pharmaceutical Inc., for the treatment of X-linked hypophosphataemia;
- Olaratumab, EMEA-001760-PIP01-15-M02, from Eli Lilly and Company Limited, for the treatment of soft tissue sarcoma and treatment of osteosarcoma;
- Telbivudine, EMEA-000065-PIP01-07-M05, from Novartis Europharm Limited, for the treatment of chronic hepatitis B, a product-specific waiver was granted for this medicine;

The PDCO adopted an opinion(s) on the **refusal** of a modification of an agreed PIP for:

- Laquinimod (sodium), EMEA-000972-PIP01-10-M05, from Teva GmbH, for the treatment of relapsing remitting multiple sclerosis.

For this medicine the PDCO granted a product-specific waiver on its own motion for all subsets of the paediatric population in the specified condition, on the grounds that the product is likely to be unsafe.

Opinion on compliance check

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

- Purified antigen fractions of inactivated split virion Influenza virus type A, H1N1 / Influenza virus type A, H3N2 / Influenza virus type B, Victoria lineage / Influenza virus type B, Yamagata lineage, EMEA-C-000817-PIP02-11-M01, from GlaxoSmithKline Biologicals S.A., for the prevention of influenza infection;

- Adenovirus associated viral vector serotype 2 containing the human RPE65 gene, EMEA-C-001684-PIP01-14, from Spark Therapeutics Inc., for the treatment of genetic congenital retinal disorders;
- Melatonin, EMEA-C-000440-PIP02-11-M05, from RAD Neurim Pharmaceuticals EEC Ltd, for the treatment of insomnia;
- Tetracaine (hydrochloride) / oxymetazoline (hydrochloride), EMEA-C-001764-PIP03-15, from St. Renatus, LLC, for local anaesthesia.

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/measures 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 1 application was 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 16-19 May 2017.

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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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