29 May 2017
EMA/PDCO/308316/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

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

16-19 May 2017

Opinions on paediatric investigation plans

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

- Lacosamide, EMEA-000402-PIP03-17, from UCB Pharma S.A., for the treatment of generalised epilepsy and epileptic syndromes;
- Omadacycline, EMEA-000560-PIP02-15, from Paratek UK Limited, for the treatment of acute bacterial skin and skin structure infections (ABSSSI);
- Omadacycline, EMEA-000560-PIP03-15, Paratek UK Limited, for the treatment of bacterial pneumonia;
- Fluocinolone acetonide, EMEA-000801-PIP03-16, CAMPHARM Limited, for the treatment of chronic non-infectious uveitis;
- Empagliflozin, EMEA-000828-PIP04-16, Boehringer Ingelheim International GmbH, for the treatment of type 1 diabetes mellitus;
- Live, attenuated, chimeric dengue virus, serotype 1 / live, attenuated dengue virus, serotype 2 / live, attenuated, chimeric dengue virus, serotype 3 / live attenuated, chimeric dengue virus, serotype 4, EMEA-001888-PIP01-15, for the prevention of dengue fever;
- Larotrectinib, EMEA-001971-PIP02-16, Loxo Oncology, Inc., for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms);
- Mexiletine (hydrochloride), EMEA-002012-PIP01-16, from Lupin (Europe) Ltd., for the treatment of myotonic disorders.

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

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

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:

- Ezetimibe / Rosuvastatin (calcium), EMEA-002135-PIP01-17, from BENEDETTI & Co. S.r.l., for the treatment of elevated cholesterol;
- Ezetimibe / Rosuvastatin (calcium), EMEA-002131-PIP01-17, from Errekappa Euroterapici S.p.A., for the treatment of elevated cholesterol;
- Miridesap, EMEA-002111-PIP01-17, from GlaxoSmithKline Trading Services Limited, for the treatment of systemic light chain amyloidosis;
- Miridesap, EMEA-002111-PIP02-17, from GlaxoSmithKline Trading Services Limited, for the treatment of transthyretin amyloidosis (ATTR);
- Benzydamine (hydrochloride) / econazole (nitrate), EMEA-002143-PIP01-17, from Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A., for the treatment of vulvovaginal candidiasis;
- Radium Ra223 dichloride, EMEA-001986-PIP01-16, from Bayer AG, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms); and for the treatment of multiple myeloma
- Amlodipine / Rosuvastatin, EMEA-002130-PIP01-17, from CIPROS S.R.L., for the prevention of cardiovascular events, treatment of ischemic coronary artery disorders, treatment of hypertension and treatment of dyslipidaemia;
- Dezamizumab, EMEA-002110-PIP01-17, from GlaxoSmithKline Trading Services Limited, for the treatment of systemic light chain amyloidosis;
- Dezamizumab, EMEA-002110-PIP02-17, from GlaxoSmithKline Trading Services Limited, for the treatment of transthyretin amyloidosis (ATTR);
- Pseudoephedrine / ibuprofen, EMEA-002102-PIP01-16, from FARMALIDER, S.A, for the treatment of pain, treatment of febrile disorders and treatment of nasal congestion and inflammations;
- Amlodipine besilate / Hydrochlorothiazide / Olmesartan medoxomil, EMEA-002104-PIP01-16, from Accord Healthcare, S.L.U., for the treatment of hypertension;
- Efavirenz / lamivudine / abacavir, EMEA-002114-PIP01-16, from Lek Pharmaceuticals d.d., for the treatment of human immunodeficiency virus (HIV-1) infection;
- Amlodipine / Rosuvastatin, EMEA-002136-PIP01-17, from ERREKAPPA EUROTERAPICI S.p.A., for the prevention of cardiovascular events, treatment of ischemic coronary artery disorders, treatment dyslipidaemia and treatment of hypertension.

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:

- Aciclovir, EMEA-001066-PIP02-11-M02, from ONXEO, for the treatment of herpes simplex labialis;
- Apremilast, EMEA-000715-PIP05-13-M01, from Celgene Europe Limited, for the treatment of Behcet's disease;
- Fluticasone (furoate) / vilanterol, EMEA-000431-PIP01-08-M10, from Glaxo Group Limited, for the treatment of asthma;
- Methoxyflurane, EMEA-000334-PIP01-08-M06, from Medical Developments UK Ltd, for the treatment of acute pain;
- Ticagrelor, EMEA-000480-PIP01-08-M10, from AstraZeneca AB, for the prevention of thromboembolic events;
- Ozanimod, EMEA-001710-PIP02-14-M01, from Celgene Europe Limited, for the treatment of multiple sclerosis;
- Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with lentiviral vector that encodes for the human ARSA cDNA sequence, EMEA-001765-PIP02-15-M01, from GlaxoSmithKline Trading Services Limited, for the treatment of metachromatic leukodystrophy (MLD);
- Pazopanib, EMEA-000601-PIP01-09-M04, from Novartis Europharm Limited, for the Ewing sarcoma family of tumours, non-rhabdomyosarcoma soft tissue sarcoma and rhabdomyosarcoma;
- Lonoctocog alfa, EMEA-001215-PIP01-11-M05, from CSL Behring GmbH, for the treatment of congenital factor VIII deficiency;
- Cobicistat / atazanavir sulphate, EMEA-001465-PIP01-13-M01, from Bristol-Myers Squibb Pharma EEIG, for the treatment of HIV-1 infection;
- Velpatasvir / sofosbuvir, EMEA-001646-PIP01-14-M01, from Gilead Sciences International Ltd., for the treatment of chronic hepatitis C;
- Dimethyl fumarate, EMEA-000832-PIP01-10-M04, from Biogen Idec Ltd, for the treatment of multiple sclerosis;
- Teriflunomide, EMEA-001094-PIP01-10-M04, from Genzyme Europe B.V. / Sanofi-Aventis groupe, for the treatment of multiple sclerosis;
- Dobutamine, EMEA-001262-PIP01-12-M03, from Proveca Limited, for the treatment of neonatal circulatory failure;
- Colistimethate sodium, EMEA-000176-PIP01-07-M05, from TEVA B.V., for treatment of Pseudomonas aeruginosa pulmonary infection / colonisation in patients with cystic fibrosis;
- Ferric maltol, EMEA-001195-PIP01-11-M03, from Shield TX (UK) Limited, for the treatment of iron deficiency anaemia (IDA);
- Ivacaftor / 1-(2,2-difluoro-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluoro-2-(1-

hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl}cyclopropanecarboxamide, EMEA-001640-PIP01-14-M02, from Vertex Pharamceuticals (Europe) lTd, for the treatment of cystic fibrosis;

- Lacosamide, EMEA-000402-PIP02-11-M04, from UCB Pharma S.A., for the treatment of epilepsy with partial onset seizures;
- Cysteamine (hydrochloride), EMEA-000322-PIP01-08-M05, from ORPHAN EUROPE SARL, for the treatment of corneal cystine crystal deposits in cystinosis.

The PDCO adopted an opinion on the refusal of modifications to an agreed PIP for Certolizumab pegol, EMEA-001071-PIP02-12-M02, from UCB Pharma S.A., for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis).

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 over existing treatments.

Opinion on compliance check

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

- cinacalcet, EMEA-C-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.

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).

Paediatric Addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections

An updated proposal of the paediatric addendum to the guideline on antibacterial agents was presented to the committee.

The committee discussed that the collection of safety data post-authorisation should be encouraged and concrete proposals discussed when granting the paediatric marketing authorisation. It was also stressed that paediatric antibiotic studies are global studies; therefore requirements for paediatric development should be discussed with FDA.

Other matters

The PDCO welcomed the new alternate from Belgium, Karen Van Malderen.

The PDCO thanked Jacqueline Carleer for her work as alternate for Belgium, leaving the committee, at the end of her mandate

The next meeting of the PDCO will be held on 20-23 June 2017.

– 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

Enquiries to: AskEMA
(http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/landing/ask_ema_landing_page.jsp&mid=)