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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

23 – 26 January 2018

Opinions on paediatric investigation plans

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

- Vamorolone, EMEA-001794-PIP02-16, from ReveraGen BioPharma Ltd, for the treatment of Duchenne muscular dystrophy;
- (RS)-Bacoflen / Naltrexone HCl / D-Sorbitol, EMEA-002164-PIP01-17, from Pharnext SA, for the treatment of Charcot-Marie-Tooth disease Type 1A;
- Tanezumab, EMEA-001635-PIP03-17, from Pfizer Limited, for the treatment of chronic pain (excluding musculoskeletal pain) and treatment of chronic musculoskeletal pain;
- Anifrolumab, EMEA-001435-PIP02-16, from AstraZeneca AB, for the treatment of systemic lupus erythematosus;
- Upadacitinib, EMEA-001741-PIP03-16, from AbbVie Ltd, for the treatment of Crohn's Disease;
- Tralokinumab, EMEA-001900-PIP02-17, from LEO Pharma A/S, for the treatment of atopic dermatitis;
- Fluticasone furoate / Umeclidinium bromide / Vilanterol trifenatate, EMEA-002153-PIP01-17, from GlaxoSmithKline Trading Services Limited, for the treatment of asthma;
- Pevonedistat, EMEA-002117-PIP01-17, from Takeda Pharma A/S, for the treatment of acute myeloid leukaemia (AML) and treatment of myelodysplastic syndromes (MDS);
- Crizanlizumab, EMEA-002141-PIP01-17, from Novartis Europharm Limited, for the treatment of sickle cell disease;
- Adeno-Associated viral vector serotype rh.10 carrying the human N-sulfoglucosamine sulfohydrolase cDNA, EMEA-002122-PIP02-17, from LYSOGENE, for the treatment of mucopolysaccharidosis type IIIA;
- Brivaracetam, EMEA-000332-PIP02-17, from UCB Pharma S.A., for the treatment of paediatric

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epilepsy syndromes

- Ruxolitinib (phosphate), EMEA-000901-PIP04-17, from Novartis Europharm Limited, for the treatment of chronic Graft versus Host Disease (cGvHD)
- Durvalumab, EMEA-002028-PIP01-16, from AstraZeneca AB, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue) and treatment of malignant neoplasms of haematopoietic and lymphoid tissue
- Tremelimumab, EMEA-002029-PIP01-16, from AstraZeneca AB, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue) and treatment of malignant neoplasms of haematopoietic and lymphoid tissue
- Insulin human, EMEA-002116-PIP01-17, from Nutrinia, Ltd., for the treatment of intestinal malabsorption in preterm infants

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:

- Non-Pathogenic Bacterial Lysate of *Escherichia coli* and *Enterococcus faecalis*, EMEA-002155-PIP01-17, from SymbioPharm GmbH, for the treatment of irritable bowel syndrome (IBS);
- Rosuvastatin / Ezetimibe, EMEA-002257-PIP01-17, from ELPEN Pharmaceutical Co. Inc, for the treatment of hypercholesterolemia;
- Pemafibrate, EMEA-001573-PIP02-17, from Kowa Research Europe Ltd, for the prevention of cardiovascular events in patients with elevated triglycerides levels and treatment of hypertriglyceridaemia;
- Dapagliflozin / metformin (hydrochloride), EMEA-001151-PIP02-17, from AstraZeneca AB, for the treatment of type 2 diabetes mellitus;
- Dapagliflozin / saxagliptin / metformin (hydrochloride), EMEA-002249-PIP01-17, from AstraZeneca AB, for the treatment of type 2 diabetes mellitus;
- Candesartan (cilexetil) / amlodipine (besylate), EMEA-002248-PIP01-17, from Midas Pharma GmbH, for the treatment of hypertension;
- Niraparib, EMEA-002268-PIP01-17, from Janssen Research & Development, for the treatment of prostate malignant neoplasms;
- Entinostat Polymorph B, EMEA-002272-PIP01-17, from Syndax Pharmaceuticals, Inc., for the treatment of breast malignant neoplasm;
- Venglustat, EMEA-001716-PIP02-17, from Genzyme Europe B.V., for the treatment of Parkinson's disease;

- Veliparib, EMEA-000499-PIP04-17, from AbbVie Ltd, for the treatment of lung carcinoma (small cell and non-small cell lung carcinoma);
- Levothyroxine (sodium), EMEA-002259-PIP01-17, from IBSA Farmaceutici Italia Srl, for the treatment of hypothyroidism, treatment of benign thyroid nodules and treatment of goitre;
- Treprostinil, EMEA-002254-PIP01-17, from SciPharm Sàrl, for the treatment of chronic thromboembolic pulmonary hypertension (CTEPH);
- Trazodone (hydrochloride) / gabapentin, EMEA-002263-PIP01-17, from Aziende Chimiche Riunite Angelini Francesco - A.C.R.A.F. - S.p.A., for the treatment of painful diabetic neuropathy;
- T-cell bispecific antibody targeting carcinoembryonic antigen expressed on tumor cells and CD3 epsilon chain present on T-cells, EMEA-002252-PIP01-17, from Roche Registration Limited, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms);
- Ibuprofen, EMEA-002302-PIP01-17, from Farmalíder, S.A., for the treatment of pain and treatment of febrile disorders

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:

- Indacaterol (acetate) / Mometasone (furoate), EMEA-001217-PIP01-11-M04, from Novartis Europharm Limited, for the treatment of asthma;
- Octocog alfa, EMEA-001064-PIP01-10-M03, from Bayer AG, for the treatment of hereditary factor VIII deficiency;
- Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human betaA-T87Q-globin gene, EMEA-001665-PIP01-14-M02, from bluebird bio France, for the treatment of β-thalassaemia;
- Ivacaftor, EMEA-000335-PIP01-08-M12, from Vertex Pharmaceuticals (Europe) Limited, for the treatment of Cystic Fibrosis;
- [7-(4,7-diazaspiro[2.5]octan-7-yl)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)pyrido[1,2-a]pyrimidin-4-one, EMEA-002070-PIP01-16-M01, from Roche Registration Limited, for the treatment of spinal muscular atrophy;
- Denosumab, EMEA-000145-PIP01-07-M09, from Amgen Europe B.V., for the prevention of skeletal related events in patients with bone metastases, treatment of bone loss associated with sex hormone ablative therapy, treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis), treatment of giant cell tumour of bone and treatment of hypercalcaemia of malignancy;

- Alirocumab, EMEA-001169-PIP01-11-M04, from Sanofi-aventis Recherche & Developpement, for the treatment of elevated cholesterol;
- Lonoctocog alfa, EMEA-001215-PIP01-11-M06, from CSL Behring GmbH, for the treatment of congenital factor VIII deficiency;
- Lacosamide, EMEA-000402-PIP03-17-M02, from UCB Pharma S.A., for the treatment of generalised epilepsy and epileptic syndromes;
- Ivacaftor, EMEA-001640-PIP01-14-M04, from Vertex Pharmaceuticals (Europe) Ltd., for the treatment of Cystic Fibrosis;
- Dermatophagoides pteronyssinus / Dermatophagoides farinae allergen extract, EMEA-001258-PIP01-11-M03, from ALK-Abelló A/S, for the treatment of allergic rhinitis and treatment of asthma;
- Fidaxomicin, EMEA-000636-PIP01-09-M07, from Astellas Pharma Europe B.V., for the treatment of enterocolitis caused by *Clostridium difficile*;
- Brivaracetam, EMEA-000332-PIP01-08-M13, from UCB Pharma S.A., for the treatment of epilepsy with partial onset seizures and treatment of neonatal seizures;
- Influenza virus surface antigens (haemagglutinin and neuraminidase) of the following strains: A/(H1N1), A/(H3N2), B/Yamagata lineage, B/Victoria lineage, EMEA-001782-PIP01-15-M02, from Abbott Biologicals B.V., for the prevention of Influenza infection;
- Sodium zirconium cyclosilicate, EMEA-001539-PIP01-13-M03, from AstraZeneca AB, for the treatment of Hyperkalemia;
- Golimumab, EMEA-000265-PIP02-11-M02, from Janssen Biologics B.V., for the treatment of Ulcerative Colitis;
- Rolapitant, EMEA-001768-PIP02-15-M01, from Tesaro UK Ltd, for the prevention of nausea and vomiting
- Erenumab, EMEA-001664-PIP02-15-M02, from Novartis Europharm Limited, for the prevention of migraine headaches;
- Osilodrostat, EMEA-000315-PIP02-15-M01, from Novartis Europharm Limited, for the treatment of adrenal cortical hyperfunction;
- Dasatinib, EMEA-000567-PIP01-09-M05, from Bristol-Myers Squibb Pharma EEIG, for the treatment of Philadelphia chromosome (BCR-ABL translocation)-positive chronic myeloid leukaemia and treatment of Philadelphia chromosome (BCR-ABL translocation)-positive acute lymphoblastic leukaemia
- Nivolumab, EMEA-001407-PIP01-12-M01, from Bristol-Myers Squibb Pharma EEIG, for the treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue)
- Nivolumab, EMEA-001407-PIP02-15-M02, from Bristol-Myers Squibb Pharma EEIG, for the treatment of malignant neoplasms of lymphoid tissue and treatment of malignant neoplasms of the central nervous system
- Binimetinib, EMEA-001454-PIP03-15-M01, from Pierre Fabre Médicament, for the treatment of melanoma

- Pembrolizumab, EMEA-001474-PIP01-13-M01, from Merck Sharp & Dohme (Europe), Inc., for the treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue)
- Selumetinib, EMEA-001585-PIP01-13-M02, from AstraZeneca AB, for the treatment of neurofibromatosis type 1, treatment of thyroid cancer and treatment of melanoma
- Encorafenib, EMEA-001588-PIP01-13-M01, from Pierre Fabre Médicament, for the treatment of melanoma

Opinion on compliance check

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

- Plerixafor, EMEA-C-000174-PIP01-07-M03, from Genzyme Europe B.V., for the myelosuppression caused by chemotherapy to treat malignant disorders, which requires an autologous haematopoietic stem cell transplant;
- Human coagulation factor X, EMEA-C-000971-PIP01-10-M03, from Bio Products Laboratory Ltd, for the treatment of hereditary factor X deficiency;
- Artenimol / piperaquine phosphate anhydride, EMEA-C-000153-PIP01-07-M05, from Alfasigma S.p.A., for the treatment of uncomplicated malaria caused by *Plasmodium faciparum*;

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 3 applications were withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure).

Other matters

The PDCO welcomed the new alternate from Norway, Mrs Anette Solli Karlsen.

The next meeting of the PDCO will be held on 20 – 23 February 2018.

– 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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