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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

26 February-01 March 2019

Opinions on paediatric investigation plans

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

- voclosporin, EMEA-002264-PIP01-17, from Aurinia Pharmaceuticals Ltd., for the treatment of systemic lupus erythematosus;
- nintedanib, EMEA-001006-PIP05-18, from Boehringer Ingelheim International GmbH, for the treatment of fibrosing interstitial lung diseases;
- autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains, EMEA-002369-PIP01-18, from Celgene Europe B.V., for the treatment of mature B-cell neoplasms;
- monovalent, live, recombinant, replication-incompetent adenoviral serotype 26 vectored vaccine expressing the full length glycoprotein of the Ebola virus Mayinga variant, EMEA-002307-PIP01-17, from Janssen Cilag International N.V., for the prevention of Ebola virus disease;
- multivalent, live, recombinant, non-replicating in human cells, Modified Vaccinia Ankara vectored vaccine, expressing the EBOV Mayinga glycoprotein, the Sudan virus Gulu GP, the Marburg virus Musoke GP, and the Taï Forest virus nucleoprotein, EMEA-002308-PIP01-17, from Janssen Cilag International N.V., for the prevention of Ebola virus disease (EVD);
- N-hydroxy-5-methylfuran-2-sulfonamide, EMEA-002378-PIP01-18, from Bristol-Myers Squibb International Corporation, for the treatment of acute heart failure;
- liposomal vinorelbine (tartrate), EMEA-002365-PIP01-18, from TLC Biopharmaceuticals B.V., for the treatment of rhabdomyosarcoma;
- oteseconazole, EMEA-002392-PIP01-18, from Mycovia Pharmaceuticals Inc, for the treatment of vulvovaginal candidiasis;
- aflibercept, EMEA-000236-PIP05-18, from Bayer AG, for the treatment of retinopathy of

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prematurity;

- ozanimod, EMEA-001710-PIP03-17, from Celgene Europe Limited, for the treatment of ulcerative colitis;
- anti-IL-21 humanized immunoglobulin G1-kappa monoclonal antibody, EMEA-002374-PIP01-18, from Boston Pharmaceuticals, Inc., for the treatment of systemic lupus erythematosus (SLE);
- ofatumumab, EMEA-002397-PIP01-18, from Novartis Europharm Limited, for the treatment of multiple sclerosis;
- abemaciclib, EMEA-002342-PIP01-18, from Eli Lilly and Company, for the treatment of Ewing's sarcoma;
- gadopiclenol, EMEA-001949-PIP02-18, from GUERBET, for detection and visualization of disorders or lesions with suspected abnormal vascularity in various body regions for diagnostic purposes

The PDCO adopted an opinion on the **refusal** of a PIP, including deferral for:

- secukinumab, EMEA-000380-PIP05-18, from Novartis Europharm Ltd, for the treatment of hidradenitis suppurativa

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 for paediatric patients.

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:

- rogaratinib, EMEA-002439-PIP01-18, from Bayer AG, for the treatment of urothelial carcinoma;
- tislelizumab, EMEA-002480-PIP01-18, from Celgene Europe B.V., for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue);
- L-asparaginase, EMEA-000341-PIP03-18, from ERYTECH Pharma S.A., for the treatment of pancreatic cancer;
- cenegermin, EMEA-001729-PIP02-18, from Dompé farmaceutici S.p.A., for the treatment of dry eye disease;
- rivoceranib (mesylate), EMEA-002489-PIP01-18, from LSK BioPharma Limited, for the treatment of gastric cancer and gastroesophageal junction adenocarcinoma;
- orvepitant, EMEA-002510-PIP01-18, from NeRRe Therapeutics Ltd, for the treatment of refractory chronic cough;

- serlopitant, EMEA-002496-PIP01-18, from Menlo Therapeutics Inc., for the treatment of prurigo nodularis;
- rosuvastatin (calcium) / fenofibrate, EMEA-002509-PIP01-18, from Mylan Healthcare GmbH, for the treatment of elevated cholesterol with elevated triglycerides;
- ^{177}Lu-PSMA-617, EMEA-002419-PIP02-18, from Endocyte, Inc., for the treatment of Prostate membrane antigen (PSMA)-expressing prostate cancer;
- N2'-Deacetyl-N2'-[4-methyl-4-(oxobutyldithio)-1-oxopentyl]-maytansine-hu769_4D4 Antibody, EMEA-002504-PIP01-18, from Sanofi-Aventis Recherche & Développement, for the treatment of all conditions included in the category of malignant neoplasms (excluding central nervous system, haematopoietic and lymphoid tissue neoplasms);
- delafloxacin, EMEA-001080-PIP03-18, from A. Menarini - Industrie Farmaceutiche Riunite - s.r.l., for the treatment of Community Acquired Pneumonia;

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:

- etravirine, EMEA-000222-PIP01-08-M09, from Janssen-Cilag International NV, for the treatment of human immunodeficiency virus type-1 (HIV-1) infection;
- oritavancin (diphosphate), EMEA-001270-PIP01-12-M02, from Menarini International Operations Luxembourg S.A., for the treatment of acute bacterial skin and skin structure infections;
- idarucizumab, EMEA-001438-PIP01-13-M01, from Boehringer Ingelheim international GmbH, for the prevention of dabigatran associated haemorrhage and treatment of dabigatran associated haemorrhage;
- recombinant parathyroid hormone, EMEA-001526-PIP01-13-M03, from Shire Pharmaceuticals Ireland Limited, for the treatment of hypoparathyroidism;
- glecaprevir / pibrentasvir, EMEA-001832-PIP01-15-M02, from AbbVie Ltd, for the treatment of chronic hepatitis C;
- ertugliflozin, EMEA-001533-PIP01-13-M02, from Merck Sharp & Dohme (Europe), Inc., for the treatment of type 2 diabetes mellitus;
- ceftolozane / tazobactam, EMEA-001142-PIP01-11-M03, from Merck Sharp & Dohme (Europe), Inc., for the treatment of intra-abdominal infections and treatment of urinary tract infections;
- nonacog beta pegol, EMEA-000731-PIP01-09-M03, from Novo Nordisk A/S, for the treatment of hereditary factor IX deficiency;
- *neisseria meningitidis* serogroup A polysaccharide conjugated to tetanus toxoid / *N. meningitidis* serogroup C polysaccharide conjugated to tetanus toxoid / *N. meningitidis* serogroup Y

polysaccharide conjugated to tetanus toxoid / *N. meningitidis* serogroup W polysaccharide conjugated to tetanus toxoid, EMEA-001930-PIP01-16-M01, from Sanofi Pasteur, for the prevention of meningococcal disease;

- roxadustat, EMEA-001557-PIP01-13-M03, from Astellas Pharma Europe B.V., for the treatment of anaemia due to chronic disorders;
- rivaroxaban, EMEA-000430-PIP01-08-M11, from Bayer AG, for the prevention of thromboembolic events and treatment of thromboembolic events;
- corifollitropin alfa, EMEA-000306-PIP01-08-M04, from Merck Sharp & Dohme B.V., for the treatment of hypogonadotrophic hypogonadism;
- inebilizumab, EMEA-001911-PIP01-15-M02, from Viela Bio, for the treatment of neuromyelitis optica spectrum disorders;
- selexipag, EMEA-000997-PIP01-10-M02, from Janssen Cilag International NV, for the treatment of pulmonary arterial hypertension;
- regorafenib, EMEA-001178-PIP01-11-M04, from Bayer Pharma AG, for the treatment of all conditions contained in the category of malignant neoplasms (except haematopoietic and lymphoid tissue);
- luspatercept, EMEA-001521-PIP01-13-M03, from Celgene Europe B.V., for the treatment of beta-thalassaemia and treatment of myelodysplastic syndromes;
- migalstat (hydrochloride), EMEA-001194-PIP01-11-M04, from Amicus Therapeutics UK Limited, for the treatment of Fabry disease;
- tofacitinib, EMEA-000576-PIP01-09-M10, from Pfizer Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis);
- peanut flour, EMEA-001734-PIP01-14-M04, from Aimmune Therapeutics Inc, for the treatment of peanut allergy;
- tenofovir alafenamide (as fumarate), EMEA-001584-PIP01-13-M04, from Gilead Sciences International Ltd., for the treatment of chronic viral hepatitis B;

The PDCO adopted opinions on the **refusal** of modifications to an agreed PIP for the following applications:

- fevipiprant, EMEA-001315-PIP02-16-M01, from Novartis EuroPharm Limited, for the treatment of asthma;

Opinion on compliance check

The PDCO adopted positive opinions on full compliance check for:

- conestat alfa, EMEA-C-000367-PIP01-08-M08, from Pharming Group N.V., for the treatment of hereditary angioedema (HAE);
- denosumab, EMEA-C-000145-PIP01-07-M09, from Amgen Europe B.V., for the treatment of bone loss associated with sex hormone ablative therapy, prevention of skeletal related events in patients with bone metastases, treatment of giant cell tumour of bone, treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile

idiopathic arthritis), treatment of hypercalcemia of malignancy;

- sebelipase alfa, EMEA-C-001331-PIP01-12-M02, from Alexion Europe SAS, for the treatment of lysosomal acid lipase deficiency;

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 5 applications were 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 26-29 March 2019.

– 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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