29 June 2018
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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

26-29 June 2018

Opinions on paediatric investigation plans

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

- Cefiderocol, EMEA-002133-PIP01-17, from Shionogi Limited, for the treatment of infections due to aerobic Gram-negative bacteria;
- Trimeric, recombinant HIV-1 envelope glycoprotein 140 of Clade C / trimeric, recombinant HIV-1 envelope glycoprotein 140 containing motifs of multiple HIV-1 variants, adjuvanted with aluminium phosphate [Clade C gp140/ Mosaic gp140], EMEA-002161-PIP01-17, from Janssen-Cilag International NV, for the prevention of human immunodeficiency virus (HIV-1) infection;
- Trimeric, recombinant HIV-1 envelope glycoprotein 140 of Clade C, adjuvanted with aluminium phosphate [Clade C gp140], EMEA-002221-PIP01-17, from Janssen-Cilag International NV, for the prevention of human immunodeficiency virus (HIV-1) infection;
- Risankizumab, EMEA-001776-PIP04-17, from AbbVie Ltd, for the treatment of ulcerative colitis;
- Serotype 26 adenovirus encoding mosaic 1 HIV-1 group-specific antigen and polymerase proteins (Ad26.Mos1.Gag-Pol) / serotype 26 adenovirus encoding mosaic 2 HIV-1 group-specific antigen and polymerase proteins (Ad26.Mos2.Gag-Pol) / serotype 26 adenovirus encoding mosaic 1 HIV-1 envelope protein (Ad26.Mos1.Env) / serotype 26 adenovirus encoding mosaic 2S HIV-1 envelope protein (Ad26.Mos2S.Env) [Ad26.Mos4.HIV], EMEA-002160-PIP01-17, from Janssen-Cilag International NV, for the prevention of human immunodeficiency virus (HIV-1) infection;
- Ferric Pyrophosphate Citrate, EMEA-002261-PIP01-17, from Rockwell Medical, Inc., for the treatment of anaemia of chronic kidney disease;
- Setrusumab, EMEA-002169-PIP01-17, from Mereo Biopharma 3 Ltd, for the treatment of osteogenesis imperfecta;
- Alicaforsen, EMEA-002060-PIP02-17, from Atlantic Pharmaceuticals (Holdings) Ltd, for the treatment of pouchitis;

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- Olaparib, EMEA-002269-PIP01-17, from AstraZeneca AB, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms);
- His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Lys(γ-Glu-palmitoyl)-Ser-Glu-Tyr-Leu-Asp-Ser-Glu-Arg-Ala-Arg-Asp-Phe-Val-Ala-Trp-Leu-Glu-Ala-Gly-Gly-OH, EMEA-002287-PIP01-17, from MedImmune Limited, for the treatment of Type 2 Diabetes Mellitus;
- Risankizumab, EMEA-001776-PIP03-17, from AbbVie Ltd, for the treatment of Crohn's Disease;

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

- Octenidine (dihydrochloride), EMEA-001384-PIP02-17, from Schülke & Mayr GmbH, for the prevention of oral soft tissue infections.

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.

Adoption of an opinion following re-examination

No items

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:

- Pixantrone (dimaleate), EMEA-000713-PIP02-10-M05, from CTI Life Sciences Limited, for the treatment of non-Hodgkin lymphoma;
- Navitoclax, EMEA-000478-PIP02-18, from AbbVie Ltd, for the treatment of myelofibrosis;
- Luspatercept, EMEA-001521-PIP02-18, from Celgene Europe Ltd, for the treatment of myelofibrosis;
- Veliparib, EMEA-000499-PIP05-18, from AbbVie Ltd, for the treatment of fallopian tube cancer, treatment of ovarian cancer and treatment of peritoneal cancer;
- Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3- zeta chimeric antigen receptor, EMEA-002335-PIP01-18, from Kite Pharma EU B.V., for the treatment of Mantle Cell Lymphoma;
- Glasdegib, EMEA-002199-PIP01-17, from Pfizer Limited, for the treatment of acute myeloid leukaemia;
- Irbesartan/amlodipine, EMEA-002352-PIP01-18, from Sanofi- Aventis Research & Development, for the treatment of hypertension;

The PDCO adopted an opinion on the **refusal** of a request for waiver for:

- Venglustat, EMEA-001716-PIP03-18, from Genzyme Europe B.V., for the treatment of polycystic kidney disease;

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:

- Olipudase alfa, EMEA-001600-PIP01-13-M01, from Genzyme Europe B.V., for the treatment of Niemann-Pick disease;
- Febuxostat, EMEA-001417-PIP01-12-M04, from Menarini International Operations Luxembourg S.A., for the prevention and treatment of hyperuricemia;
- Avelumab, EMEA-001849-PIP02-15-M02, from Merck KGaA, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoetic and lymphoid tissue neoplams), treatment of malignant neoplasms of lymphoid tissue and treatment of malignant neoplasms of the central nervous system;
- Balovaptan, EMEA-001918-PIP01-15-M01, from Roche Registration Ltd, for the treatment of autism spectrum disorder;
- Paclitaxel, EMEA-001308-PIP01-12-M02, from Celgene Europe Limited, for the treatment of solid malignant tumours;
- Romosozumab, EMEA-001075-PIP04-15-M01, from UCB Pharma S.A., for the treatment of osteoporosis;
- Osilodrostat, EMEA-000315-PIP02-15-M02, from Novartis Europharm Limited, for the treatment of adrenal cortical hyperfunction;
- Vortioxetine, EMEA-000455-PIP02-10-M04, from H. Lundbeck A/S, for the treatment of major depressive disorder;
- Influenza virus surface antigens - A/turkey/Turkey/1/05 (H5N1), EMEA-000599-PIP01-09-M06, from Seqirus S.r.l., for the prevention of influenza;
- Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted), EMEA-001830-PIP01-15-M01, from Seqirus S.r.l., for the prevention of influenza infection;
- Tralokinumab, EMEA-001900-PIP02-17-M01, from LEO Pharma A/S, for the treatment of atopic dermatitis;
- Benralizumab, EMEA-001214-PIP01-11-M08, from AstraZeneca AB, for the treatment of asthma;
- Eribulin, EMEA-001261-PIP01-11-M05, from Eisai Europe Ltd, for the treatment of soft tissue sarcoma;

- (Z)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-4-(2-(sulfamoylamino)ethylamino)-1,2,5-oxadiazole-3-carboximidamide, EMEA-002072-PIP01-16-M01, from Incyte Corporation, for the treatment of all conditions included in the category of malignant neoplasms including Hodgkin lymphoma (except nervous system, haematopoietic and lymphoid tissue other than Hodgkin lymphoma);
- Ciprofloxacin (hydrochloride), EMEA-001563-PIP02-15-M01, from Aradigm Limited, for the treatment of chronic pulmonary infections caused by *Pseudomonas aeruginosa*;
- Andexanet alfa, EMEA-001902-PIP01-15-M03, from Portola Pharma UK Limited, for the prevention of factor Xa inhibitor associated haemorrhage and treatment of factor Xa inhibitor associated haemorrhage;
- Oseltamivir (phosphate), EMEA-000365-PIP01-08-M10, from Roche Registration Limited, for the treatment and prevention of influenza;
- Fc- and CDR-modified humanized monoclonal antibody against C5, EMEA-001943-PIP01-16-M01, from Alexion Europe SAS, for the treatment of atypical haemolytic uremic syndrome;

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

- Landiolol (hydrochloride), EMEA-001150-PIP02-13-M02, from AOP Orphan Pharmaceuticals AG, for the treatment of supraventricular arrythmias;
- Roxadustat, EMEA-001557-PIP01-13-M02, from Astellas Pharma Europe B.V., for the treatment of anaemia due to chronic disorders;

Opinion on compliance check

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

- Nonacog gamma, EMEA-C-001139-PIP01-11-M02, from Baxalta Innovations GmbH, for the treatment of haemophilia B (congenital factor IX deficiency);
- Nusinersen, EMEA-C-001448-PIP01-13-M03, from Biogen Idec Ltd, for the treatment of spinal muscular atrophy;
- Trifarotene, EMEA-C-001492-PIP01-13-M01, from Galderma R&D, for the treatment of acne;
- Sunitinib, EMEA-C-000342-PIP01-08-M07, from Pfizer Limited, for the treatment of gastro-intestinal stromal tumours;

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

The PDCO also noted that the application leading to the opinion adopted during the May PDCO meeting for EMEA-000410-PIP01-08-M03, from GE Healthcare AS, for the diagnosis of Myocardial perfusion disturbances, has been withdrawn before the decision was adopted by the Agency.

Other matters

The PDCO thanked Melinda Sobor for her work as she has resigned from the Committee.

The next meeting of the PDCO will be held on 24-27 July 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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