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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

12-15 November 2019

Opinions on paediatric investigation plans

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

- Abemaciclib, EMEA-002342-PIP02-18, from Eli Lilly and Company Limited, for the treatment of glioma and treatment of neuroblastoma.
- Aztreonam (ATM)/ avibactam (AVI) - EMEA-002283-PIP01-17, from Pfizer Europe MA EEIG, for the treatment of infections caused by aerobic gram-negative bacteria.

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:

- Iberdomide, EMEA-002636-PIP01-19, from Celgene Europe B.V., for the treatment of mature B-cell neoplasms;
- Masitinib (mesylate), EMEA-001266-PIP04-19, from AB Science, for the treatment of amyotrophic lateral sclerosis;
- Ethanol, EMEA-002672-PIP01-19, from Ablative Solutions Inc., for the treatment of uncontrolled primary hypertension;
- Autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced

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with retroviral vector expressing anti CD19 CD28/CD3-zeta chimeric antigen receptor and cultured (KTE-X19), EMEA-001862-PIP02-19, from Kite Pharma EU B.V., for the treatment of mantle cell lymphoma;

- Bispecific T-cell engager antibody with a single-chain fragment crystallizable moiety that binds to B cell maturation antigen surface receptor on tumour cells and the cluster of differentiation 3 receptor on T-cells, EMEA-002606-PIP02-19, from Amgen Europe BV, for the treatment of multiple myeloma;
- Sacituzumab govitecan, EMEA-002645-PIP01-19, from Immunomedics GmbH, for the treatment of breast cancer.

The PDCO adopted 2 opinions on the refusal of a request for waiver for:

- Chloroprocaine (hydrochloride), EMEA-000639-PIP05-19, from Sintetica GmbH, for the ocular surface anesthesia;
- Chloroprocaine (hydrochloride), EMEA-000639-PIP04-19, from Sintetica GmbH, for the epidural anaesthesia;

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:

- Daclizumab, EMEA-001349-PIP01-12-M03, from Biogen Idec Ltd, for the treatment of multiple sclerosis;
- Tezepelumab, EMEA-001613-PIP01-14-M04, from AstraZeneca AB, for the treatment of asthma;
- Lumasiran (ALN-GO1), EMEA-002079-PIP01-16-M01, from Alnylam UK Limited, for the treatment of hyperoxaluria;
- Avapritinib, EMEA-002358-PIP02-18-M01, from Blueprint Medicines (Netherlands) B.V., for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms);
- Belimumab, EMEA-000520-PIP02-13-M03, from Glaxo Group Limited, for the treatment of systemic lupus erythematosus;
- Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human betaA-T87Q-globin gene, EMEA-001665-PIP01-14-M03, from bluebird bio (Netherlands) B.V., for the treatment of β-thalassaemia;
- Edoxaban (tosylate), EMEA-000788-PIP02-11-M09, from Daiichi Sankyo Europe GmbH, for the prevention of arterial thromboembolism, prevention of venous thromboembolism and treatment of venous thromboembolism;
- Tolvaptan, EMEA-001231-PIP02-13-M07, from Otsuka Pharmaceutical Netherlands B.V., for the treatment of dilutional hyponatraemia and treatment of polycystic kidney disease;

- Brigatinib, EMEA-002296-PIP01-17-M01, from Takeda Pharm A/S, for the treatment of inflammatory myofibroblastic tumors, treatment of anaplastic large cell lymphoma and treatment of non-small cell lung cancer;
- Voxilaprevir / velpatasvir / sofosbuvir, EMEA-001822-PIP01-15-M01, from Gilead Sciences Ireland UC, for the treatment of chronic hepatitis C;
- Luspatercept, EMEA-001521-PIP01-13-M04, from Celgene Europe B.V., for the treatment of beta thalassaemia and treatment of myelodysplastic syndromes;
- Abrocitinib, EMEA-002312-PIP01-17-M01, from Pfizer Europe MA EEIG, for the treatment of atopic dermatitis;
- Human cell line recombinant human factor VIII (human-cl rhFVIII) / Human coagulation factor VIII (rDNA), EMEA-001024-PIP01-10-M02, from Octapharma Pharmazeutika Produktionsges.m.b.H, for the treatment of haemophilia A (congenital factor VIII deficiency);
- Ozanimod (hydrochloride), EMEA-001710-PIP03-17-M01, from Celgene Europe B.V., for the treatment of ulcerative colitis;
- Exenatide, EMEA-000689-PIP01-09-M09, from AstraZeneca AB, for the treatment of type 2 diabetes mellitus;
- Agomelatine, EMEA-001181-PIP01-11-M05, from Les Laboratoires Servier, for the treatment of major depressive episodes;
- Dupilumab, EMEA-001501-PIP02-13-M04, from sanofi-aventis recherche & développement, for the treatment of asthma;
- Lumacaftor / ivacaftor, EMEA-001582-PIP01-13-M09, from Vertex Pharmaceuticals (Europe) Limited, for the treatment of cystic fibrosis;

Opinion on compliance check

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

- Outer membrane vescicles (OMV) from *Neisseria meningitidis* serogroup B strain NZ98/254 measured as amount of total protein containing the PorA P1.4 / recombinant *Neisseria meningitidis* serogroup B NadA protein / recombinant *Neisseria meningitidis* serogroup B fHBP fusion protein / recombinant *Neisseria meningitidis* serogroup B NHBA fusion protein, EMEA-C-000139-PIP01-07-M03, from GSK Vaccines S.r.l., for the prevention of meningococcal meningitis;
- Ragweed pollen extract (Ambrosia artemisiifolia), EMEA-C-001881-PIP01-15, from ALK Abelló A/S, for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Nonacog beta pegol, EMEA-C-000731-PIP01-09-M03, from Novo Nordisk A/S, for the treatment of hereditary factor IX deficiency;
- Potassium hydrogen carbonate / Potassium citrate monohydrated, EMEA-C-001357-PIP01-12-M02, from ADVICENN, for the treatment of renal tubular acidosis;

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).

Other matters

The next meeting of the PDCO will be held on 09-11 December 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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