EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Human Medicines Division

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

26-29 May 2020

Opinions on paediatric investigation plans

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

- Ondansetron (hydrochloride), EMEA-002623-PIP01-19, from Adial Pharmaceuticals, for the treatment of alcohol use disorder;
- Tominersen, EMEA-002546-PIP01-19, from Roche Registration GmbH, for the treatment of Huntington's disease;
- Pegzilarginase, EMEA-001925-PIP02-19, from Aeglea BioTherapeutics, Inc., for the treatment of hyperargininaemia;
- Tecovirimat (monohydrate), EMEA-001205-PIP02-19, from SIGA Technologies, Inc., for the treatment of orthopoxvirus disease (smallpox, monkeypox, cowpox, and vaccinia);
- Rozanolixizumab, EMEA-002681-PIP01-19, from UCB Pharma S.A., for the treatment of myasthenia gravis;
- Recombinant human IgG1λ monoclonal Fab antibody, EMEA-002766-PIP01-20, from PhaseBio Pharmaceuticals Inc., for the reversal of antiplatelet effects of ticagrelor in patients with uncontrolled major or life-threatening bleeding or requiring urgent surgery or invasive procedure;
- Bisoprolol (fumarate) / Trimetazidine (dihydrochloride), EMEA-002768-PIP01-20, from Les Laboratoires Servier, for the treatment of ischaemic coronary artery disorders;
- Humanised antibody targeting the inducible T cell co-stimulatory receptor, EMEA-002781-PIP01-20, from GlaxoSmithKline (Ireland) Limited, for the treatment of head and neck epithelial malignant neoplasms;
- Remdesivir, EMEA-002826-PIP01-20, from Gilead Sciences International Ltd, for the treatment of coronavirus disease 19 (COVID19).

The PDCO adopted two opinion(s) on the **refusal** of a PIP, including a waiver and a deferral. 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

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therapeutic benefit over existing treatments for paediatric patients for:

- Des-ThrB30-[GluA14, HisB16, HisB25,[Ne-(S)-(22,42-dicarboxy-10,19,24-trioxo-3,6,12,15-tetraoxa9,18,23-triazadotetracontan-1-oyl)]LysB29]-insulin (human), (Insulin 287)- EMEA-002761-PIP01-20, from Novo Nordisk A/S, for the treatment of type 1 diabetes mellitus and the treatment of type 2 diabetes mellitus;
- Human fibrinogen, EMEA-002769-PIP01-20, from Instituto Grifols, S.A., for the treatment of congenital fibrinogen deficiency;

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:

- Icosasodium{26-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]-14,14-bis{[(3-{6-[(2-acetamido-2-deoxy-β-D-galactopyranosyl)oxy]hexyl}amino)-3-oxopropoxy)]methyl}-8,12,19-trioxo-16-oxa-7,13,20-triazahexacosyl}2′-O-(2-methoxyethyl)-(3′→5′)-[2′-O-(2-methoxyethyl)guanylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methylcytidylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methyluridylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methylcytidylyl-(3′→5′)-2′-deoxy-5-methyl-P-sulfidocytidylyl-(3′→5′)-2′-deoxy-P-sulfidoguanylyl-(3′→5′)-P-sulfidothymidylyl-(3′→5′)-P-sulfidothymidylyl-(3′→5′)-2′-deoxy-P-sulfidoguanylyl-(3′→5′)-2′-deoxy-P-sulfidoguanylyl-(3′→5′)-P-sulfidothymidylyl-(3′→5′)-2′-deoxy-P-sulfidoguanylyl-(3′→5′)-2′-deoxy-5-methyl-P-sulfidocytidylyl-(3′→5′)-P-sulfidothymidylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methyluridylyl-(3′→5′)-2′-O-(2-methoxyethyl)guanylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methyl-P-sulfidouridylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methyl-P-sulfidouridylyl-(3′→5′)-2′-O-(2-methoxyethyl)-5-methylcytidine]-5-methyl-P-sulfidouridylyl-5′-yl phosphate, EMEA-002786-PIP01-20, from Novartis Europharm Ltd., for the prevention of cardiovascular events due to atherosclerotic cardiovascular disease in patients with elevated lipoprotein(a);
- Rosuvastatin / ezetimibe, EMEA-002202-PIP02-20, from Krka, d.d., Novo mesto, for the prevention of cardiovascular events;
- Ravagalimab, EMEA-002617-PIP02-19, from AbbVie Ltd, for the treatment of Sjögren's syndrome;
- Ravagalimab, EMEA-002617-PIP01-19, from AbbVie Ltd, for the treatment of ulcerative colitis;
- Neratinib, EMEA-002783-PIP01-20, from Pierre Fabre Médicament, for the treatment of breast cancer;
- Niraparib (tosylate monohydrate) / abiraterone (acetate) /, EMEA-002789-PIP01-20, from Janssen Research & Development, for the treatment of prostate malignant neoplasms;
- Sutimlimab, EMEA-002542-PIP02-19, from Genzyme Europe B.V., for the treatment of immune thrombocytopenia purpura;

- Rucaparib (camsylate), EMEA-002760-PIP01-19, from Clovis Oncology Ireland Ltd., for the treatment of fallopian tube cancer, the treatment of ovarian cancer, the treatment of prostate malignant neoplasms and the treatment of primary peritoneal cancer;
- Sitagliptin (hydrochloride monohydrate) / metformin (hydrochloride), EMEA-002732-PIP02-20, from Adamed Pharma S.A., for the treatment of type 2 diabetes mellitus;

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

- Recombinant human IgG1λ monoclonal Fab antibody, EMEA-002766-PIP01-20, from PhaseBio Pharmaceuticals Inc., for the reversal of antiplatelet effects of ticagrelor in patients with uncontrolled major or life-threatening bleeding or requiring urgent surgery or invasive procedure;

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:

- Recombinant human monoclonal antibody to GM-CSF (otilimab)EMEA-001882-PIP02-16-M02, from GlaxoSmithKline Trading Services Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis);
- Bempegaldesleukin, EMEA-002492-PIP01-18-M01, from Nektar Therapeutics, for the treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoetic, and lymphoid tissue neoplasms);
- Meropenem (trihydrate) / vaborbactam, EMEA-001731-PIP01-14-M02, from Menarini International Operations Luxembourg S.A., for the treatment of Gram-negative bacterial infections;
- Anifrolumab, EMEA-001435-PIP02-16-M01, from AstraZeneca AB, for the treatment of systemic lupus erythematosus;
- Factor VIII Fc – von Willebrand factor – XTEN fusion protein (rFVIIIFc-VWF-XTEN), EMEA-002501-PIP01-18-M01, from Bioverativ Therapeutics, Inc., a Sanofi Company, for the treatment of congenital haemophilia A;
- Doravirine / lamivudine / tenofovir disoproxil (fumarate), EMEA-001695-PIP01-14-M03, from Merck Sharp & Dohme (Europe), Inc., for the treatment of human immunodeficiency virus-1 (HIV-1) infection;
- Estetrol /drospirenone, EMEA-001332-PIP01-12-M03, from Estetra SPRL, for the prevention of pregnancy;
- Brivaracetam, EMEA-000332-PIP02-17-M01, from UCB Pharma S.A., for the treatment of paediatric epilepsy syndromes;
- Tapentadol, EMEA-000325-PIP01-08-M10, from Grünenthal GmbH, for the treatment of chronic pain;

- Doravirine, EMEA-001676-PIP01-14-M03, from Merck Sharp & Dohme (Europe), Inc., for the treatment of human immunodeficiency virus type 1 (HIV-1) infection;
- Brentuximab vedotin, EMEA-000980-PIP01-10-M06, from Takeda Pharma A/S, for the treatment of Hodgkin lymphoma and the treatment of anaplastic large cell lymphoma
- Alogliptin benzoate (as alogliptin), EMEA-000496-PIP01-08-M08, from Takeda Development Centre Europe Ltd, for the treatment of type 2 diabetes mellitus;
- Olaparib, EMEA-002269-PIP01-17-M01, from AstraZeneca AB, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms);
- Fostemsavir (tromethamine), EMEA-001687-PIP01-14-M04, from ViiV Healthcare UK Ltd, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Eravacycline, EMEA-001555-PIP01-13-M04, from Tetraphase Pharmaceuticals, Inc., for the treatment of complicated intra-abdominal infection;
- Vortioxetine, EMEA-000455-PIP02-10-M06, from H. Lundbeck A/S, for the treatment of major depressive disorder;
- Bosutinib, EMEA-000727-PIP01-09-M04, from Pfizer Europe MA EEIG, for the treatment of chronic myeloid leukaemia

The following product(s) was granted a product-specific waiver in replacement of an agreed PIP:

- Alemtuzumab, EMEA-001072-PIP01-10-M04, Genzyme Europe B.V., for the treatment of multiple sclerosis;

Opinion on compliance check

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

- Live, attenuated, chimeric dengue virus, serotype 1 / Live, attenuated, chimeric dengue virus, serotype 2 / Live, attenuated, chimeric dengue virus, serotype 3 / Live, attenuated, chimeric dengue virus, serotype 4, EMEA-C-001545-PIP01-13-M02, from Sanofi Pasteur, for the prevention of dengue.

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).

Interaction with external experts

The PDCO has regular interactions with academic experts, with a view to bringing state-of-the-art knowledge to the PDCO scientific discussions. There were 2 experts that were invited to the May meeting with a clinical expertise in paediatric asthma. The PDCO discussed the severe paediatric asthma collaborative in Europe (SPACE). The collaborative was initiated in cooperation with the European network of paediatric research at the EMA (Enpr-EMA) in 2016 to bring together paediatricians across the EU who are active in the respiratory field in a Clinical Research Collaboration (CRC). In 2019, SPACE also became a member of the Enpr-EMA network. The aim of the initiative is to support collaborative participation of sponsors developing paediatric asthma treatment and to enhance the involvement of children with severe asthma in clinical trials.

Other matters

The next meeting of the PDCO will be held on 23-26 June.

– 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: https://www.ema.europa.eu/en/medicines/ema_group_types/ema_pip

3. More information about the PDCO and the Paediatric Regulation is available in the Regulatory section of the Agency's website:

   https://www.ema.europa.eu/en/committees/paediatric-committee-pdco

   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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