21 May 2021
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Human Medicines Division

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

18-21 May 2021

Opinions on paediatric investigation plans

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

- Macitentan, EMEA-001032-PIP03-19, from Janssen-Cilag International N.V., for the treatment of functional single ventricle heart disease with total cavo-pulmonary connection;
- Finerenone, EMEA-001623-PIP03-20, from Bayer AG, for the treatment of heart failure;
- Ralinepag, EMEA-002432-PIP02-20, from United Therapeutics Corporation, for the treatment of pulmonary arterial hypertension;
- Allogeneic skin-derived ABCB5-positive mesenchymal stem cells, EMEA-002875-PIP01-20, from RHEACELL GmbH & Co. KG, for the treatment of epidermolysis bullosa;
- Adeno-associated viral vector serotype 8 containing the human glucose-6-phosphatase gene (DTX401), EMEA-002734-PIP01-19, from Ultragenyx Germany GmbH, for the treatment of glycogen storage disease type Ia;
- Maralixibat Chloride, EMEA-001475-PIP04-20, from Mirum Pharmaceuticals Inc., for the treatment of biliary atresia;
- Odevixibat, EMEA-002054-PIP03-20, from Albireo AB, for the treatment of Alagille syndrome;
- Recombinant monoclonal antibody to sialic acid-binding Ig-like lectin 8, EMEA-002856-PIP01-20, from Allakos Inc, for the treatment of eosinophilic gastrointestinal inflammatory disorders;
- Cilgavimab (AZD1061), EMEA-002925-PIP01-20, from AstraZeneca AB, for the prevention or treatment of COVID-19;
- Tixagevimab (AZD8895), EMEA-002900-PIP01-20, from AstraZeneca AB for the prevention or treatment of COVID-19;
- Pralsetinib, EMEA-002575-PIP02-20, from Roche Registration GmbH, for the treatment of thyroid neoplasms;

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
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- Autologous selected renal cells, EMEA-002844-PIP01-20, from ProKidney, for the treatment of chronic kidney disease;

The PDCO adopted an opinion(s) on the **refusal** of a PIP, including a *full waiver* for:

- No item

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 condition for which the specific medicinal product is intended does not occur in the specified paediatric subsets.

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

The PDCO adopted opinions for the following products:

- No item

A re-examination of the opinion can be requested by the applicant within 30 days following receipt of the opinion of the PDCO. The grounds for the re-examination should be based only on the original information and scientific data provided in the application that were previously available to the PDCO and on which the initial opinion was based. This may include new analysis of the same data or minor protocol amendments to a previously proposed study. Significant changes to the previous plan cannot be part of the re-examination process.

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:

- Selatogrel, EMEA-002967-PIP01-21, from Idorsia Pharmaceuticals Deutschland GmbH, for the treatment of acute myocardial infarction (AMI);
- Vupanorsen, EMEA-002973-PIP01-21, from Pfizer Europe MA EEIG, for the prevention of cardiovascular events and treatment of hypertriglyceridaemia;
- Mannitol, EMEA-002968-PIP01-21, from NTC Srl, for bowel cleansing prior to clinical procedure;
- Anti-C1s Humanized IgG4 Monoclonal Antibody, EMEA-002903-PIP02-21, from Genzyme Europe B.V., for the treatment of Cold Agglutinin Disease;
- Human Papilloma Virus Type 16 E6 001-032/Human Papilloma Virus Type 16 E6 019-050/Human Papilloma Virus Type 16 E6 041-065/Human Papilloma Virus Type 16 E6 055-080/Human Papilloma Virus Type 16 E6 085-109/Human Papilloma Virus Type 16 E6 091-122/Human Papilloma Virus Type 16 E6 127-158 / Human Papilloma Virus Type 16 E6 071-095/Human Papilloma Virus Type 16 E6 109-140/Human Papilloma Virus Type 16 E7 001-035/Human Papilloma Virus Type 16 E7 022-056/Human Papilloma Virus Type 16 E7 064-098, EMEA-001055-PIP02-21, from ISA Therapeutics B.V., for the treatment of HPV16 positive malignancies;

- [18F]CTT1057, EMEA-002975-PIP01-21, from Advanced Accelerator Applications SA, for the visualisation of prostate-specific membrane antigen in adenocarcinoma of the prostate;
- Datopotamab deruxtecan, EMEA-002976-PIP01-21, from Daiichi Sankyo Europe GmbH, for the treatment of lung cancer;
- Patritumab deruxtecan, EMEA-002977-PIP01-21, from Daiichi Sankyo Europe GmbH, for the treatment of lung cancer;
- Trastuzumab deruxtecan, EMEA-002978-PIP01-21, from Daiichi Sankyo Europe GmbH, for the treatment of lung cancer;
- Dapagliflozin (propanediol monohydrate) / Zibotentan, EMEA-002969-PIP01-21, from AstraZeneca AB, for the treatment of chronic kidney disease;
- Bentracimab, EMEA-002766-PIP02-21, from PhaseBio Pharmaceuticals Inc., for the treatment of ticagrelor associated haemorrhage / Prevention of ticagrelor associated haemorrhage.

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

- No item

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:

- Nemolizumab, EMEA-001624-PIP01-14-M03, from Galderma International S.A., for the treatment of atopic dermatitis;
- Canagliflozin (1s)-1,5-anhydro-1-[3-[[5-(4-fluorophenyl)-2-thienyl]methyl]-4-methylphenyl]-D-glucitol hemihydrate, EMEA-001030-PIP01-10-M09, from Janssen-Cilag International NV, for the treatment of type 2 diabetes mellitus;
- Romosozumab, EMEA-001075-PIP04-15-M03, from UCB Pharma S.A., for the treatment of osteoporosis;
- Bis-choline tetrathiomolybdate, EMEA-002232-PIP02-19-M01, from Alexion Europe S.A.S., for the treatment of Wilson Disease;
- Cotadutide, EMEA-002287-PIP01-17-M02, from AstraZeneca AB, for the treatment of Type 2 Diabetes Mellitus;
- Ozanimod hydrochloride, EMEA-001710-PIP03-17-M03, from Celgene Europe B.V., for the treatment of ulcerative colitis;
- Garadacimab, EMEA-002726-PIP01-19-M01, from CSL Behring GmbH, for the prevention of hereditary angioedema attacks;
- Guselkumab, EMEA-001523-PIP03-18-M01, from Janssen-Cilag International NV, for the treatment

of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis);

- Rilzabrutinib, EMEA-002438-PIP02-19-M01, from Principia Biopharma, Inc., for the treatement of immune thrombocytopenia;
- Cotadutide, EMEA-002712-PIP01-19-M01, from AstraZeneca AB, for the treatment of non-alcoholic steatohepatitis (NASH);
- Oseltamivir (phosphate), EMEA-000365-PIP01-08-M12, from Roche Registration GmbH, for the treatment and prevention of influenza;
- Dolutegravir, EMEA-000409-PIP01-08-M06, from ViiV Healthcare UK Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Cobicistat / darunavir, EMEA-001280-PIP01-12-M04, from Janssen-Cilag International NV, for the treatment of HIV-1 Infection;
- Tenofovir alafenamide, EMEA-001584-PIP01-13-M06, from Gilead Sciences International Ltd., for the treatment of chronic viral hepatitis B;
- Vaborbactam / meropenem, EMEA-001731-PIP01-14-M03, from Menarini International Operations Luxembourg S.A., for the treatment of Gram-negative bacterial infections;
- Peramivir, EMEA-001856-PIP02-16-M02, from BioCryst Ireland Limited, for the treatment of influenza;
- Ibalizumab , EMEA-002311-PIP01-17-M02, from Theratechnologies Europe Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Nivolumab, EMEA-001407-PIP02-15-M05, 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;
- Lanadelumab, EMEA-001864-PIP01-15-M05, from Shire Pharmaceuticals Ireland Limited, for the treatment of hereditary angioedema;
- Ravulizumab, EMEA-001943-PIP01-16-M06, from Alexion Europe SAS, for the treatment of atypical haemolytic uremic syndrome;
- Ravulizumab, EMEA-002077-PIP01-16-M04, from Alexion Europe SAS, for the treatment of paroxysmal nocturnal haemoglobinuria;
- COVID-19 Vaccine (ChAdOx1-S [recombinant]), EMEA-002862-PIP01-20-M01, from AstraZeneca AB, for the prevention of COVID-19;

Opinion on compliance check

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

- Exenatide, EMEA-C-000689-PIP01-09-M11, from AstraZeneca AB, for the treatment of type 2 diabetes mellitus;

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 thanked Lucie Kravackova for her work as she has resigned from the Committee.

The next meeting of the PDCO will be held on 22-25 June 2021.

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
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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