26 March 2021
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Human Medicines Division

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

23-26 March 2021

Opinions on paediatric investigation plans

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

- RAAV8 viral vector encoding the human UGT1A1 transgene (rAAV8-hUGT1A1), EMEA-002021-PIP01-16, from GENETHON, for the treatment of Crigler-Najjar syndrome;
- Vedolizumab, EMEA-000645-PIP04-20, from Takeda Pharma A/S, for the treatment of pouchitis;
- Pegfilgrastim, EMEA-002671-PIP02-20, from Accord Healthcare S.L.U., for the prevention of chemotherapy-induced febrile neutropenia and treatment of chemotherapy-induced neutropenia;
- Respiratory syncytial virus stabilised prefusion f subunit vaccine (RSVpreF), EMEA-002795-PIP01-20, from Pfizer Europe MA EEIG, for the prevention of lower respiratory tract disease caused by respiratory syncytial virus via maternal immunisation;

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

- No item.

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

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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:

- (S)-N-(1-amino-4-(dimethylamino)-1-oxobutan-2-yl)-5-(2,4-difluorophenoxy)-1-isobutyl-1H-indazole-6-carboxamide, EMEA-002948-PIP01-20, from Pfizer Europe MA EEIG, for the treatment of dilated cardiomyopathy due to lamin A/C gene mutations;
- Human anti-interleukin-15 (IL-15) monoclonal antibody, EMEA-002775-PIP01-20, from Provention Bio, Inc., for the treatment of coeliac disease;
- Anti-CD40L humanized monoclonal antibody (SAR441344), EMEA-002945-PIP01-20, from Sanofi-aventis recherche & développement, for the treatment of Sjogren's Syndrome;
- Edaravone, EMEA-002785-PIP01-20, from Treeway B.V., for the treatment of amyotrophic lateral sclerosis;
- Obinutuzumab, EMEA-001207-PIP01-11-M01, from Roche Registration GmbH, for the treatment of acute lymphoblastic leukaemia and treatment of mature B-cell lymphoma;
- (S)-5-amino-3-(4-((5-fluoro-2-methoxybenzamido)methyl)phenyl)-1-(1,1,1-trifluoropropane-2-yl)-1H-pyrazole-4-carboxamide, EMEA-002943-PIP01-20, from Eli Lilly and Company, for the treatment of mature B-cell malignancies;
- Pembrolizumab / quavonlimab, EMEA-002949-PIP01-20, from Merck, Sharp & Dohme (Europe) Inc, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue and melanoma);

The PDCO adopted 1 opinion on the **refusal** of a request for waiver for:

- Reparixin, EMEA-001693-PIP02-20, from Dompé farmaceutici S.p.A., for the treatment of coronavirus disease 2019 (COVID-2019);

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:

- Remimazolam (as besylate), EMEA-001880-PIP02-19-M02, from PAION Deutschland GmbH, for the general Anaesthesia and sedation;

- Ticagrelor, EMEA-000480-PIP01-08-M14, from AstraZeneca AB, for the prevention of thromboembolic events;
- Spesolimab, EMEA-002475-PIP02-19-M01, from Boehringer Ingelheim International GmbH, for the prevention of Generalized Pustular Psoriasis and treatment of Generalized Pustular Psoriasis;
- Pegunigalsidase alfa, EMEA-001828-PIP01-15-M02, from Chiesi Farmaceutici S.p.A., for the treatment of Fabry disease;
- Cipaglucosidase alfa, EMEA-002447-PIP01-18-M01, from Amicus Therapeutics Europe Limited, for the treatment of glycogen storage disease Type II (Pompe's disease);
- Avacopan, EMEA-002023-PIP01-16-M05, from ChemoCentryx Ireland Ltd., for the treatment of ANCA-associated vasculitis;
- Doravirine, EMEA-001676-PIP01-14-M04, from Merck Sharp & Dohme (Europe), Inc., for the treatment of human immunodeficiency virus type 1 (HIV-1) infection;
- Tenofovir disoproxil fumarate / lamivudine / doravirine, EMEA-001695-PIP01-14-M04, from Merck Sharp & Dohme (Europe), Inc., for the treatment of human immunodeficiency virus type 1 (HIV-1) infection;
- Rilpivirine / Dolutegravir, EMEA-001750-PIP01-15-M04, from ViiV Healthcare UK Limited, for the treatment of human immunodeficiency
  virus (HIV-1) infection;
- Tenofovir alafenamide / emtricitabine / cobicistat / darunavir, EMEA-001825-PIP01-15-M03, from Janssen-Cilag International NV, for the treatment of human immunodeficiency virus type-1 (HIV-1) infection;
- Ataluren, EMEA-000115-PIP01-07-M11, from PTC Therapeutics International, Limited, for the treatment of dystrophinopathy;
- Brivaracetam, EMEA-000332-PIP01-08-M16, from UCB Pharma S.A., for the treatment of epilepsy with partial onset seizures;
- Brivaracetam, EMEA-000332-PIP02-17-M02, from UCB Pharma S.A., for the treatment of neonatal seizures and treatment of paediatric epilepsy syndromes;
- Bumetanide, EMEA-001303-PIP01-12-M03, from Les Laboratoires Servier, for the autism Spectrum Disorder;
- Ganaxolone, EMEA-002341-PIP01-18-M01, from Marinus Pharmaceuticals Inc., for the treatment of cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder;
- Ruxolitinib (phosphate), EMEA-000901-PIP03-16-M02, from Novartis Europharm Limited, for the treatment of acute Graft versus Host Disease (aGvHD);
- Lenvatinib, EMEA-001119-PIP03-19-M01, from Eisai GmbH, for the treatment of all conditions included in the category of malignant neoplasms except haematopoietic and lymphoid tissue neoplasms, papillary thryoid cancer, follicular thyroid cancer and osteosarcoma;
- Isatuximab, EMEA-002205-PIP01-17-M02, from Sanofi-Aventis Recherche & Développement, for the treatment of malignant neoplasms of the haematopoietic and lymphoid tissue;
- Niraparib (as tosylate monohydrate), EMEA-002268-PIP02-18-M01, from GlaxoSmithKline (Ireland) Limited, for the treatment of all conditions included in the category of malignant neoplasms (except

haematopoietic and lymphoid malignancies).;

- Dostarlimab, EMEA-002463-PIP01-18-M01, from GlaxoSmithKline (Ireland) Limited, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid malignancies).;
- Concentrate of proteolytic enzyme enriched in bromelain, EMEA-000142-PIP02-09-M11, from MediWound Germany GmbH, for the treatment of burns;
- Meloxicam / Bupivacaine, EMEA-002246-PIP01-17-M02, from Heron Therapeutics B.V., for the treatment of acute postoperative pain;
- Birch pollen extract (Betula verrucosa), EMEA-001879-PIP01-15-M03, from ALK-Abelló A/S, for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Brexpiprazole, EMEA-001185-PIP01-11-M07, from Otsuka Pharmaceutical Development & Commercialisation Europe GmbH, for the treatment of schizophrenia;
- Pegcetacoplan, EMEA-002600-PIP01-19-M01, from Apellis Ireland Limited, for the treatment of paroxysmal nocturnal haemoglobinuria;

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

- No item.

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

- No item.

Opinion on compliance check

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

- Teduglutide, EMEA-C-000482-PIP01-08-M06, from Takeda Pharmaceuticals International AG, for the treatment of short bowel syndrome;
- Simoctocog alfa, EMEA-C-001024-PIP01-10-M02, from Octapharma Pharmazeutika Produktionsges.m.b.H., for the treatment of haemophilia A (congenital Factor VIII 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 2 applications were withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure).

Other matters

The PDCO welcomed the new member from Finland, Dr Pauliina Lehtolainen Dalkilic and the new alternate from Finland Ms Anne Paavola.

The next meeting of the PDCO will be held on 20-23 April 2021.

– 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
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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