EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 July 2020
EMEA/PDCO/419819/2020
Human Medicines Division

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

21-24 July 2020

Opinions on paediatric investigation plans

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

- Emixustat (hydrochloride), EMEA-002581-PIP01-19, from Kubota Pharmaceutical Holdings Co. Limited, for the treatment of Stargardt disease;
- Rebisufligene etisparvovec, EMEA-002206-PIP02-19, from Abeona Therapeutics Inc., for the treatment of mucopolysaccharidosis IIIA;
- Mitapivat, EMEA-002684-PIP01-19, from Agios Pharmaceuticals, Inc., for the treatment of pyruvate kinase deficiency;
- Bilayer, engineered, collagen hydrogel-based skin graft composed of autologous keratinocytes and fibroblasts, EMEA-002699-PIP01-19, from CUTISS AG, for the treatment of burns;
- Anti-neonatal Fc receptor human monoclonal antibody (m281), EMEA-002559-PIP03-19, from Momenta Pharmaceuticals, Inc., for the treatment of autoimmune haemolytic aneamia;
- Giroctocogene fitelparvovec, EMEA-002724-PIP01-19, from Pfizer Europe MA EEIG, for the treatment of haemophilia A;
- Diroximel fumarate (BIIB098), EMEA-002685-PIP02-19, from Biogen Netherlands B.V., for the treatment of multiple sclerosis;
- Artesunate, EMEA-002710-PIP01-19, from Amivas Ireland Ltd, for the treatment of malaria;
- (4S,7aR,9aR,10S,11E,14S,15R)-6'-chloro-10-methoxy-14,15-dimethyl-3',4',7a,8,9,9a,10,13,14,15-decahydro-2'H,7H-spiro[1,19-ethenocyclobuta[i][1,4]oxazepino[3,4-f][1,2,7]thiadiazacyclohexadecine-4,1'-naphthalen]-18(17H)-one 16,16-dioxide (AMG 176), EMEA-002631-PIP01-19, from Amgen Europe BV, for the treatment of acute myeloid leukaemia;
- Lerodalcibep, EMEA-002720-PIP01-19, from LIB Therapeutics, LLC, for the treatment of hypercholesterolaemia;

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

- Alpelisib, EMEA-002016-PIP03-19, from Novartis Europharm, for the pIK3CA related overgrowth spectrum;
- Relamorelin, EMEA-002323-PIP02-19, from Allergan Pharmaceuticals International Limited, for the treatment of gastroparesis;
- Nivolumab / relatlimab, EMEA-002727-PIP01-19, from Bristol-Myers Squibb International Corporation, for the treatment of melanoma;
- Odevixibat, EMEA-002054-PIP02-18, from Albireo AB, for the treatment of biliary atresia.

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

- Icosabutate, EMEA-002816-PIP01-20, from NorthSea Therapeutics BV, for the treatment of non-alcoholic fatty liver disease including non-alcoholic steatohepatitis

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 is likely to be ineffective or unsafe in part or all of the paediatric population.

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:

- Tezepelumab, EMEA-001613-PIP02-20, from AstraZeneca AB, for the treatment of nasal polyposis;
- Linerixibat, EMEA-002800-PIP01-20, from GlaxoSmithKline (Ireland) Ltd, for the treatment of primary biliary cholangitis;
- Dronabinol, EMEA-000643-PIP02-20, from Bionorica Ethics GmbH, for the treatment of spasticity;
- Retifanlimab, EMEA-002798-PIP01-20, from Incyte Biosciences Distribution B.V., for the treatment of squamous carcinoma of the anal canal;
- Bisoprolol (fumarate) / Ramipril, EMEA-002794-PIP01-20, from Adamed Pharma S.A., for the treatment of coronary artery disease, treatment of heart failure and treatment of hypertension;
- Fruquintinib, EMEA-002784-PIP01-20, from Hutchison MediPharma Ltd, for the treatment of colorectal carcinoma;
- Prolgolimab, EMEA-002792-PIP01-20, from JSC "BIOCAD", for the treatment of non-small cell lung cancer;
- VIB4920, EMEA-002825-PIP01-20, from Viela Bio Inc, for the treatment of Sjögren's syndrome;
- Ranibizumab, EMEA-002832-PIP01-20, from Roche Registration GmBH, for the treatment of diabetic retinopathy;

- Faricimab, EMEA-002817-PIP04-20, from Roche Registration GmbH, for the treatment of retinal vein occlusion;
- Faricimab, EMEA-002817-PIP03-20, from Roche Registration GmbH, for the treatment of diabetic retinopathy;
- Acetylsalicylic acid / rosuvastatin (calcium), EMEA-002831-PIP01-20, from IBSA Farmaceutici Italia s.r.l, for the prevention of cardiovascular events;
- Live attenuated poliovirus type 1 / Live attenuated poliovirus type 3, EMEA-002799-PIP01-20, from Bilthoven Biologicals, for the prevention of poliomyelitis viral infection.

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:

- Tadalafil, EMEA-000452-PIP02-10-M06, from Eli Lilly and Company Ltd, for the treatment of benign prostatic hyperplasia and pulmonary arterial hypertension;
- Treosulfan, EMEA-000883-PIP01-10-M05, from medac Gesellschaft für klinische Spezialpräparate mbH, for the conditioning treatment prior to haematopoietic progenitor cell transplantation;
- Venetoclax, EMEA-002018-PIP02-16-M03, from AbbVie Ltd, for the treatment of malignant neoplasms of the haematopoietic and lymphoid tissue / Treatment of solid malignant tumours;
- Iodine (131-I) murine IgG1 monoclonal antibody against B7-H3 (^{131}I-omburtamab), EMEA-002101-PIP02-18-M01, from Y-mAbs Therapeutics A/S, for the treatment of neuroblastoma;
- Oseltamivir (phosphate), EMEA-000365-PIP01-08-M11, from Roche Registration GmbH, for the treatment and prevention of influenza;
- Potassium chloride / sodium chloride / citric acid (as citric acid anhydrous) / sodium citrate / simeticone / sodium sulfate (as sodium sulfate anhydrous) / macrogol 4000, EMEA-001356-PIP02-12-M03, from Alfasigma S.p.A., for bowel cleansing prior to clinical procedures;
- Tofacitinib, EMEA-000576-PIP03-12-M04, from Pfizer Europe MA EEIG, for the treatment of ulcerative colitis;
- Vilanterol / fluticasone (furoate), EMEA-000431-PIP01-08-M11, from Glaxo Group Limited, for the treatment of asthma;
- Ixazomib, EMEA-001410-PIP02-17-M03, from Takeda Pharm A/S, for the treatment of lymphoid malignancies (excluding multiple myeloma) and treatment of multiple myeloma;
- Cannabidiol, EMEA-001964-PIP01-16-M02, from GW Pharma (International) B.V., for the treatment of seizures associated with Lennox-Gastaut Syndrome, treatment of seizures associated with Dravet Syndrome, treatment of seizures associated with Infantile Spasms and treatment of seizures associated with Tuberous Sclerosis Complex;
- Bedaquiline (fumarate), EMEA-000912-PIP01-10-M05, from Janssen-Cilag International NV, for the treatment of multi-drug resistant tuberculosis;

- Upadacitinib, EMEA-001741-PIP01-14-M03, from AbbVie Ltd, for the treatment of chronic idiopathic arthritis;
- Brivaracetam, EMEA-000332-PIP01-08-M15, from UCB Pharma S.A., for the treatment of neonatal seizures and treatment of epilepsy with partial onset seizures;
- Vedolizumab, EMEA-000645-PIP01-09-M07, from Takeda Pharma A/S, for the treatment of Crohn's Disease and treatment of ulcerative colitis;
- Cenicriviroc, EMEA-001999-PIP02-17-M01, from Allergan Pharmaceuticals International Limited, for the treatment of non-alcoholic steatohepatitis;
- Lenadogene nolparvovec (GS010), EMEA-001992-PIP02-16-M01, from GenSight-Biologics, for the treatment of Leber hereditary optic neuropathy;
- Cefiderocol, EMEA-002133-PIP01-17-M01, from Shionogi B.V., for the treatment of infections due to aerobic Gram-negative bacteria;
- Onasemnogene abeparvovec, EMEA-002168-PIP01-17-M03, from AveXis EU Limited, for the treatment of spinal muscular atrophy;
- Hydrocortisone, EMEA-002305-PIP01-17-M01, from LABORATOIRE AGUETTANT, for the prevention of bronchopulmonary dysplasia;
- Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1), EMEA-001715-PIP01-14-M04, from Seqirus Netherlands B.V., for the prevention of influenza infection;
- Cabotegravir, EMEA-001418-PIP01-13-M02, from ViiV Healthcare UK Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Quizartinib, EMEA-001821-PIP01-15-M04, from Daiichi Sankyo Europe GmbH, for the treatment of acute myeloid leukaemia;
- Exenatide, EMEA-000689-PIP01-09-M10, from AstraZeneca AB, for the treatment of type 2 diabetes mellitus;
- Lacosamide, EMEA-000402-PIP03-17-M04, from UCB Pharma S.A., for the treatment of generalised epilepsy and epileptic syndromes;
- Andexanet alfa, EMEA-001902-PIP01-15-M04, from Portola Netherlands B.V., for the prevention of factor Xa inhibitor associated haemorrhage and treatment of factor Xa inhibitor associated haemorrhage;
- Tenofovir alafenamide / emtricitabine / bictegravir, EMEA-001766-PIP01-15-M02, from Gilead Sciences International Ltd., for the treatment of human immunodeficiency virus (HIV-1) infection;
- Ozanimod (hydrochloride), EMEA-001710-PIP02-14-M05, from Celgene Europe B.V., for the treatment of multiple sclerosis;
- Maribavir, EMEA-000353-PIP02-16-M01, from Shire Pharmaceuticals Ireland Limited, for the treatment of cytomegalovirus infection;
- Odevixibat, EMEA-002054-PIP01-16-M02, from Albireo AB, for the treatment of progressive familial intrahepatic cholestasis;

- Synthetic double-stranded siRNA oligonucleotide directed against lactate dehydrogenase A mRNA and containing four modified nucleosides which form a ligand cluster of four N-acetylgalactosamine residues (DCR-PHXC), EMEA-002493-PIP01-18-M01, from Dicerna Ireland Limited, for the treatment of primary hyperoxaluria;
- Pretomanid, EMEA-002115-PIP01-17-M02, from Global Alliance for TB Drug Development, for the treatment of multi-drug-resistant tuberculosis;
- Lamivudine / dolutegravir, EMEA-001940-PIP01-16-M03, from Viiv Healthcare UK Limited, for the treatment of human immunodeficiency virus type 1 (HIV-1).
- Rilpivirine / dolutegravir, EMEA-001750-PIP01-15-M03, from Viiv Healthcare UK Limited, for the treatment of human deficiency virus (HIV-1) infection.

Opinion on compliance check

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

- Eftrenonacog alfa, EMEA-C-000914-PIP01-10-M05, from Swedish Orphan Biovitrum AB (publ), for the treatment of hereditary factor IX deficiency;
- Clostridium Botulinum neurotoxin type A (150 kD), free of complexing proteins, EMEA-C-001039-PIP02-12-M04, from Merz Pharmaceuticals GmbH, for the treatment of sialorrhea;
- Idarucizumab, EMEA-C-001438-PIP01-13-M01, from Boehringer Ingelheim International GmbH, for the prevention of dabigatran associated haemorrhage and treatment of dabigatran associated haemorrhage;
- Delamanid, EMEA-C-001113-PIP01-10-M06, from Otsuka Pharmaceutical Development & Commercialisation Europe GmbH, for the treatment of multi-drug-resistant-tuberculosis;
- Spheroids of human autologous matrix-associated chondrocytes, EMEA-C-001264-PIP01-12-M02, from CO.DON AG, for the treatment of cartilage defects;
- Glucarpidase, EMEA-C-001391-PIP01-12, from Protherics Medicines Development BV, for the treatment of methotrexate toxicity;
- Pazopanib, EMEA-C-000601-PIP01-09-M06, from Novartis Europharm Limited, forvtreatment of rhabdomyosarcoma, treatment of non-rhabdomyosarcoma soft tissue sarcoma and treatment of family of 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 10 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 Denmark, Nanna Borup Johansen.

The PDCO thanked Kirstine Moll-Harboe for her work as she has resigned from the Committee.

The next meeting of the PDCO will be held on 1-4 September 2020.

– 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

Enquiries to: AskEMA

(https://www.ema.europa.eu/en/about-us/contact/send-question-european-medicines-agency)