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Human Medicines Division

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

7-10 September 2021

Opinions on paediatric investigation plans

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

- AZD8233 sodium, PCSK9-targeted, antisense oligonucleotide (ASO), EMEA-002962-PIP01-21, from AstraZeneca AB, for the treatment of elevated cholesterol and treatment of mixed dyslipideamia;
- 2-[(4-{6-[(4-cyano-2-fluorobenzyl)oxy]pyridin-2-yl}piperidin-1-yl)methyl]-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid tris(hydroxymethyl)aminomethane salt (1:1), EMEA-002944-PIP01-20, from Pfizer Europe MA EEIG, for the treatment of type 2 diabetes mellitus;
- Propan-2-yl (2S)-2-{[(S)-({(2R,3R,4R,5R)-5-[2-amino-6-(methylamino)-9H-purin-9-yl]-4-fluoro-3-hydroxy-4-methyloxolan-2-yl}methoxy)(phenoxy)phosphoryl]amino}propanoate; sulfuric acid (2:1) (AT-527 / RO7496998), EMEA-002963-PIP01-21, from Roche Registration GmbH for Treatment of coronavirus disease 2019 (COVID-19);
- Semaglutide, EMEA-001441-PIP05-20, from Novo Nordisk A/S, for the treatment of non-alcoholic steatohepatitis;
- Glepaglutide, EMEA-002926-PIP01-20, from Zealand Pharma A/S, for the treatment of short bowel syndrome;
- Adalimumab conjugated with (4S)-4-[2-(2-bromoacetamido)acetamido]-5-{3-[(4-{(4aR,4bS,5S,6aS,6bS,8R,9aR,10aS,10bS)-5-hydroxy-4a,6a-dimethyl-2-oxo-6b-[(phosphonooxy)acetyl]-4a,4b,5,6,6a,6b,9a,10,10a,10b,11,12-dodecahydro-2H,8H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-8-yl}phenyl)methyl] anilino}-5-oxopentanoic acid; (ABBV-154), EMEA-002927-PIP01-20, from AbbVie Ltd, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis);
- Pritelivir (mesylate monohydrate), EMEA-002180-PIP02-19, from AiCuris Anti-infective Cures AG, for the treatment of herpes simplex virus disease;

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- Islatravir, EMEA-002938-PIP01-20, from Merck Sharp & Dohme (Europe), Inc., for the prevention of human immunodeficiency virus (HIV-1) infection;
- Terbinafine hydrochloride, EMEA-002984-PIP01-21, from Moberg Pharma AB, for the treatment of onychomycosis;
- Loncastuximab tesirine, EMEA-002665-PIP02-20, from ADC Therapeutics SA, for the treatment of mature B-cell neoplasms;
- Crisantaspase, EMEA-002934-PIP01-20, from Jazz Pharmaceuticals Ireland Ltd., for the treatment of acute lymphoblastic leukaemia / lymphoma;
- Thienopyrimidine derivative, EMEA-002901-PIP01-20, from Boehringer Ingelheim International GmbH, for the treatment of fibrosing interstitial lung disease;
- Brensocatib, EMEA-002905-PIP01-20, from Insmed Netherlands B.V., for the treatment of non-cystic fibrosis bronchiectasis;
- Ravulizumab, EMEA-001943-PIP02-20, from Alexion Europe SAS, for the treatment in haematopoietic stem cell transplantation;
- Live-attenuated La Reunion strain of chikungunya virus (VLA1553), EMEA-002873-PIP01-20, from Valneva Austria GmbH, for the prevention of chikungunya disease
- Respiratory Syncytial Virus (RSV) PreF3 recombinant Fusion protein/AS01, EMEA-002904-PIP01-20, GlaxoSmithKline Biologicals SA, for the prevention of lower respiratory tract disease caused by respiratory syncytial virus;

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 0 opinions.

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:

- Ezetimibe / rosuvastatin, EMEA-001447-PIP02-21, from Egis Pharmaceuticals PLC, for the prevention of cardiovascular events;

- Ezetimibe / Rosuvastatin, EMEA-003018-PIP01-21, from Qualipharmacon Kft., for the prevention of cardiovascular events and treatment of hypercholesterolemia;
- Zofenopril (calcium) / amlodipine, EMEA-003036-PIP01-21, from Menarini Ricerche S.p.A., for the treatment of hypertension;
- Ezetimibe / Rosuvastatin, EMEA-003039-PIP01-21, from Sandoz s.r.o., for the prevention of cardiovascular events and treatment of hypercholesterolemia;
- Drospirenone, EMEA-001495-PIP02-21, from Chemo Research, S.L., for the treatment of endometriosis;
- Pyridoxine (hydrochloride) / doxylamine (succinate), EMEA-001608-PIP02-21, from EXELTIS HEALTHCARE S.L., for the treatment of nausea and vomiting of pregnancy;
- Rusfertide, EMEA-003045-PIP01-21, from Protagonist Therapeutics, Inc., for the treatment of polycythaemia vera;
- Anti-C1s Humanized IgG4 Monoclonal Antibody, EMEA-002903-PIP03-21, from Genzyme Europe B.V., for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy;
- Ravulizumab, EMEA-001943-PIP05-21, from Alexion Europe SAS, for the treatment of amyotrophic lateral sclerosis;
- Anti-neonatal Fc receptor human monoclonal antibody, EMEA-002559-PIP04-21, from Janssen-Cilag International NV, for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy;
- Efgartigimod alfa, EMEA-002597-PIP06-21, from argenx BV, for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy;
- Izaflortaucipir (18F), EMEA-003040-PIP01-21, from Life Molecular Imaging GmbH, for the diagnosis of corticobasal degeneration and diagnosis of progressive supranuclear palsy;
- Pralsetinib, EMEA-002575-PIP03-21, from Roche Registration GmbH, for the treatment of all conditions included in the category of malignant neoplasms [except lung cancer (small cell and non-small cell cancer), thyroid neoplasms, central nervous system tumours, haematopoietic and lymphoid tissue neoplasms], treatment of malignant neoplasms of haematopoietic and lymphoid tissue and treatment of malignant neoplasms of the central nervous system;
- 5'-capped mRNA encoding HPV16 oncoprotein E6 and E7, EMEA-003023-PIP01-21, from BioNTech SE, for the treatment of head and neck squamous cell carcinoma;
- Senaparib, EMEA-003034-PIP01-21, from IMPACT Therapeutics US, Inc., for the treatment of metastatic castrate-resistant prostate cancer;
- Batiraxcept, EMEA-003042-PIP01-21, from Aravive, Inc, for the treatment of fallopian tube cancer, treatment of ovarian cancer and treatment of primary peritoneal cancer;
- Anti-CD123 IgG1 humanised monoclonal antibody conjugated to N1-(2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)ethyl)-N6-((S)-1-(((S)-1-((3-((((S)-8-methoxy-6-oxo-11,12,12a,13-tetrahydro-6H-benzo[5,6][1,4]diazepino[1,2-a]indol-9-yl)oxy)methyl)-5-((((S)-8-methoxy-6-oxo-12a,13-dihydro-6Hbenzo[5,6][1,4]diazepino[1,2-a]indol-9-yl)oxy)methyl)phenyl)amino)-1-oxopropan-2-yl)amino)-1-oxopropan-2-yl)adipamide, EMEA-003044-PIP01-21, from Immunogen BioPharma (Ireland) Limited, for the treatment of blastic plasmacytoid dendritic cell neoplasm;
- Alnuctamab, EMEA-003046-PIP01-21, from Bristol-Myers Squibb International Corporation, for the treatment of mature B cell malignancies;

- B cell maturation antigen antibody-drug conjugate comprised of an immunoglobulin G1 humanized antibody conjugated covalently to the dibenzocyclooctyne noncleavable linker maytansinoid warhead (BMS-986352), EMEA-003047-PIP01-21, from Bristol-Myers Squibb International Corporation, for the treatment of mature B cell neoplasms;
- Humanized monoclonal antibody of IgG1 sub-type targeting the human SEMA3A polypeptide, EMEA-002957-PIP02-21, from Boehringer Ingelheim International GmbH, for the treatment of diabetic retinopathy;
- Ofloxacin / Dexamethasone (sodium phosphate), EMEA-003031-PIP01-21, from Laboratório Edol - Produtos Farmacêuticos S.A., for the prevention and treatment of ocular infections, inflammations and associated manifestations;
- Pyridine-3-carboxamide derivative (K-161), EMEA-003048-PIP01-21, from Kowa Pharmaceuticals Europe AG, for the treatment of dry eye disease;
- Lutetium (177Lu) chloride, EMEA-003038-PIP01-21, from Eckert & Ziegler Radiopharma GmbH, for the radiolabelling agent;
- Depemokimab, EMEA-003051-PIP01-21, from GlaxoSmithKline Trading Services Limited, for the treatment of nasal polyposis;

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

- Perflubutane, EMEA-003037-PIP01-21, from GE Healthcare AS, for the diagnostic evaluation of focal hepatic lesions;
- Tocilizumab, EMEA-000309-PIP06-21, from Roche Registration GmbH, for the treatment of systemic sclerosis;

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-M03, from PAION Deutschland GmbH, for general anesthesia and sedation;
- Edoxaban (tosylate), EMEA-000788-PIP02-11-M11, from Daiichi Sankyo Europe GmbH, for the prevention of arterial thromboembolism, prevention of venous thromboembolism and treatment of venous thromboembolism;
- Linagliptin, EMEA-000498-PIP01-08-M10, from Boehringer Ingelheim International GmbH, for the treatment of type 2 diabetes mellitus;
- Recombinant human glutamic acid dexarboxylase (rhGAD65), EMEA-000609-PIP01-09-M03, from Diamyd Medical AB, for the treatment of type 1 diabetes;
- Dulaglutide, EMEA-000783-PIP01-09-M06, from Eli Lilly and Company, for the treatment of type 2

diabetes mellitus;

- Empagliflozin, EMEA-000828-PIP01-09-M09, from Boehringer Ingelheim International GmbH, for the treatment of type 2 diabetes mellitus;
- Semaglutide, EMEA-001441-PIP03-17-M02, from Novo Nordisk A/S, for the treatment of obesity;
- Oxalobacter formigenes Strain HC-1, EMEA-000370-PIP02-18-M01, from OxThera AB, for the treatment of hyperoxaluria;
- Recombinant human A disintegrin and metalloprotease with thrombospondin type-1 motifs 13, EMEA-001160-PIP01-11-M02, from Baxalta Innovations GmbH own by Takeda Pharmaceutical International AG, for the treatment of thrombotic thrombocytopenic purpura;
- Fostemsavir (tromethamine), EMEA-001687-PIP01-14-M05, from ViiV Healthcare UK Ltd, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Oteseconazole, EMEA-002392-PIP01-18-M02, from Gedeon Richter Plc., for the treatment of vulvovaginal candidiasis;
- Ozanimod hydrochloride, EMEA-001710-PIP02-14-M06, from Celgene Europe B.V., for the treatment of multiple sclerosis;
- Galcanezumab, EMEA-001860-PIP03-16-M06, from Eli Lilly and Company Limited, for the prevention of migraine headaches;
- Leriglitazone, EMEA-002106-PIP01-16-M01, from Minoryx Therapeutics S.L., for the treatment of adrenoleukodystrophy;
- Ganaxolone, EMEA-002341-PIP01-18-M02, from Marinus Pharmaceuticals Inc., for the treatment of cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder;
- Acalabrutinib, EMEA-001796-PIP03-16-M02, from Acerta Pharma, BV, for the treatment of mature B cell neoplasms;
- Selpercatinib, EMEA-002544-PIP01-18-M01, from Eli Lilly and Company, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms).;
- Palbociclib, EMEA-002146-PIP01-17-M03, from Pfizer Europe MA EEIG, for the treatment of Ewing sarcoma;
- Brigatinib, EMEA-002296-PIP01-17-M03, from Takeda Pharm A/S, for the treatment of anaplastic large cell lymphoma, treatment of inflammatory myofibroblastic tumours and treatment of non-small cell lung cancer ;
- Abemaciclib, EMEA-002342-PIP01-18-M02, from Eli Lilly and Company Limited, for the treatment of Ewing's sarcoma;
- Abemaciclib, EMEA-002342-PIP02-18-M01, from Eli Lilly and Company Limited, for the treatment of glioma and treatment of neuroblastoma;
- Temozolomide, EMEA-002634-PIP01-19-M01, from Accord Healthcare S.L.U., for the treatment of malignant glioma;
- Imatinib (as imatinib mesylate), EMEA-002643-PIP01-19-M01, from Accord Healthcare S.L.U., for the treatment of Ph+ acute lymphoblastic leukaemia and treatment of Ph+ chronic myeloid leukemia;

- Fluocinolone acetonide, EMEA-000801-PIP03-16-M01, from Alimera Sciences Limited, for the treatment of chronic non-infectious uveitis and secondary prevention of non-infectious uveitis ;
- Ivacaftor / tezacaftor, EMEA-001640-PIP01-14-M07, from Vertex Pharmaceuticals (Ireland) Limited, for the treatment of cystic fibrosis;
- Elexacaftor / Tezacaftor / Ivacaftor , EMEA-002324-PIP01-17-M02, from Vertex Pharmaceuticals (Ireland) Limited, for the treatment of cystic fibrosis;
- Nintedanib, EMEA-001006-PIP05-18-M01, from Boehringer Ingelheim International GmbH, for the treatment of fibrosing interstitial lung diseases;
- Mirabegron, EMEA-000597-PIP03-15-M04, from Astellas Pharma Europe B.V., for the treatment of neurogenic detrusor overactivity;
- CX-024414 (single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free in vitro transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2), EMEA-002893-PIP01-20-M01, from MODERNA BIOTECH SPAIN, S.L., for the prevention of COVID-19;
- Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live) EMEA-001786-PIP01-15-M02, from Merck Sharp & Dohme (Europe) inc., for the prevention of Ebola disease;

Opinion on compliance check

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

- Lonoctocog alfa, EMEA-C-001215-PIP01-11-M07, from CSL Behring GmbH, for the treatment of congenital factor VIII deficiency;
- Nivolumab / relatlimab, EMEA-C-002727-PIP01-19-M01, from Bristol-Myers Squibb International Corporation, for the treatment of melanoma;

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).

The next meeting of the PDCO will be held on 12-15 October 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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