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Human Medicines Division

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

26-29 January 2021

Opinions on paediatric investigation plans

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

- COVID-19 vaccine (Ad26.COV2-S (recombinant)), EMEA-002880-PIP01-20, from Janssen-Cilag International NV, for the prevention of coronavirus disease 2019 (COVID-19);
- Baricitinib, EMEA-001220-PIP07-20, from Eli Lilly and Company Limited, for the treatment of coronavirus disease 2019 (COVID-2019);
- Secukinumab, EMEA-000380-PIP06-19, from Novartis Europharm Limited, for the treatment of systemic lupus erythematosus;
- Imetelstat, EMEA-001910-PIP03-20, from Geron Corporation, for the treatment of acute myeloid leukemia and treatment of myelodysplastic syndromes, including juvenile myelomonocytic leukemia;
- Seltorexant, EMEA-002746-PIP01-20, from Janssen-Cilag International NV, for the treatment of major depressive disorder;
- Tacrolimus, EMEA-001642-PIP02-20, from Proveca Pharma Limited, for the prevention of solid organ transplant rejection and treatment of solid organ transplant rejection;
- Rozibafusp alfa, EMEA-002815-PIP01-20, from Amgen Europe B.V., for the treatment of systemic lupus erythematosus;
- Rimegepant, EMEA-002812-PIP02-20, from Biohaven Pharmaceuticals, Inc., for the treatment of migraine headaches;
- Telitacicept, EMEA-002824-PIP01-20, from RemeGen, Ltd., for the treatment of systemic lupus erythematosus;
- Linear single strand of deoxyribonucleic acid (encoding human retinitis pigmentosa GTPase regulator [RPGR]) packaged in a recombinant adeno-associated virus protein capsid of serotype 5 (AAV5-hRKp.RPGR), EMEA-002827-PIP01-20, from MeiraGTx UK II Ltd, for the treatment of retinitis

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pigmentosa;

- Bimekizumab, EMEA-002189-PIP04-20, from UCB Biopharma SRL, for the treatment of hidradenitis suppurativa;
- Crovalimab, EMEA-002709-PIP01-19, from Roche Registration GmbH, for the treatment of atypical haemolytic uremic syndrome and treatment of paroxysmal nocturnal haemoglobinuria;
- Delgocitinib, EMEA-002329-PIP02-20, from LEO Pharma A/S, for the treatment of dermatitis and eczema;
- Respiratory Syncytial Virus (RSV) PreF3 recombinant Fusion protein, EMEA-002821-PIP01-20, from GlaxoSmithKline Biologicals SA, for the prevention of RSV-associated lower respiratory tract illness through maternal immunisation;
- Crinecerfont, EMEA-002700-PIP01-19, from Neurocrine Therapeutics Ltd, for the treatment of congenital adrenal hyperplasia;
- (S)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydrofuran 3 yl) pyrimidine-5-carboxamide (PF-06865571), EMEA-002773-PIP01-20, from Pfizer Europe MA EEIG, for the treatment of non-alcoholic steatohepatitis (NASH);

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

- Dupilumab, EMEA-001501-PIP08-20, from sanofi-aventis recherche et développement, for the treatment of chronic rhinosinusitis.

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 clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset.

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:

- Secukinumab, EMEA-000380-PIP07-20, from Novartis Europharm Limited, for the treatment of thyroid eye disease;
- Edaravone, EMEA-002897-PIP01-20, from Mitsubishi Tanabe Pharma GmbH, for the treatment of amyotrophic lateral sclerosis;
- Canakinumab, EMEA-000060-PIP09-20, from Novartis Europharm Limited, for the treatment of Schnitzler syndrome;
- Hydrochlorothiazide / Amlodipine / Ramipril, EMEA-002906-PIP01-20, from Sandoz GmbH, for the treatment of hypertension;

- Eptinezumab, EMEA-002243-PIP02-20, from H. Lundbeck A/S, for the prevention of cluster headache;
- Anti-C1s Humanized IgG4 Monoclonal Antibody, EMEA-002903-PIP01-20, from Genzyme Europe B.V., for the treatment of immune thrombocytopenia;
- Autologous CD4+ and CD8+ T cells genetically modified with a lentiviral vector encoding a B cell maturation antigen-specific chimeric antigen receptor (JCARH125), EMEA-002909-PIP01-20, from Celgene Europe B.V., for the treatment of mature B cell neoplasms;
- Isopropyl alcohol / Povidone EMEA-002902-PIP01-20, from BD Switzerland Sàrl, for the prevention of infection prior to invasive procedures;
- Alpelisib, EMEA-002016-PIP04-20, from Novartis Europharm Limited, for the treatment of fallopian tube carcinoma (excluding rhabdomyosarcoma and germ cell tumours), treatment of ovarian carcinoma (excluding rhabdomyosarcoma and germ cell tumours) and treatment of peritoneal carcinoma (excluding blastomas and sarcomas);
- Olpasiran, EMEA-002910-PIP01-20, from Amgen Europe B.V., for the prevention of cardiovascular events;

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

- None

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:

- 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-M02, from Dicerna Ireland Limited, for the treatment of primary hyperoxaluria;
- Ibrutinib, EMEA-001397-PIP03-14-M05, from Janssen-Cilag International N.V., for the treatment of mature B-cell neoplasm;
- Roxadustat, EMEA-001557-PIP01-13-M05, from Astellas Pharma Europe B.V., for the treatment of anaemia due to chronic disorders;
- Glycopyrronium bromide / Formoterol fumarate dihydrate / Beclometasone dipropionate, EMEA-001875-PIP02-18-M03, from Chiesi Farmaceutici S.p.A., for the treatment of asthma;
- Exenatide, EMEA-000689-PIP01-09-M11, from AstraZeneca AB, for the treatment of type 2 diabetes mellitus;
- Linagliptin, EMEA-000498-PIP01-08-M09, from Boehringer Ingelheim International GmbH, for the treatment of type 2 diabetes mellitus;

- Ozanimod (hydrochloride), EMEA-001710-PIP04-17-M02, from Celgene Europe B.V., for the treatment of Crohn's disease;
- Sarilumab, EMEA-001045-PIP01-10-M02, from sanofi-aventis recherche & développement, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Ustekinumab, EMEA-000311-PIP04-13-M04, from Janssen-Cilag International NV, for the treatment of Crohn's Disease;
- Islatravir / doravirine, EMEA-002707-PIP01-19-M01, from Merck Sharp & Dohme (Europe), Inc., for the treatment of human immunodeficiency virus-1 (HIV-1) infection;
- Efgartigimod alfa, EMEA-002597-PIP01-19-M01, from argenx BV, for the treatment of myasthenia gravis;
- Ponesimod, EMEA-000798-PIP01-09-M03, from Janssen-Cilag International NV, for the treatment of multiple sclerosis;
- Larotrectinib, EMEA-001971-PIP02-16-M03, from Bayer AG, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms);
- Empagliflozin, EMEA-000828-PIP01-09-M08, from Boehringer Ingelheim International GmbH, for the treatment of type 2 diabetes mellitus;
- Deucravacitinib, EMEA-002350-PIP01-18-M01, from Bristol-Myers Squibb International Corporation, for the treatment of psoriasis;
- Midostaurin, EMEA-000780-PIP01-09-M06, from Novartis Europharm Limited, for the treatment of acute myeloid leukaemia, treatment of malignant mastocytosis and treatment of mast cell leukaemia;
- Eladocagene exuparvovec, EMEA-002435-PIP01-18-M02, from PTC Therapeutic International Limited, for the treatment of aromatic L-amino acid decarboxylase deficiency;
- Bupivacaine, EMEA-000877-PIP03-17-M02, from Pacira Ltd, for the postsurgical analgesia;
- Vamorolone, EMEA-001794-PIP02-16-M03, from ReveraGen BioPharma Ltd, for the treatment of Duchenne muscular dystrophy;
- Ustekinumab, EMEA-000311-PIP05-17-M02, from Janssen-Cilag International NV, for the treatment of ulcerative colitis;
- AGOMELATINE, EMEA-001181-PIP01-11-M06, from Les Laboratoires Servier, for the treatment of major depressive episodes;
- Evinacumab, EMEA-002298-PIP01-17-M02, from Regeneron Ireland DAC, for the treatment of elevated cholesterol;
- Larotrectinib, EMEA-001971-PIP03-18-M01, from Bayer AG, for the treatment of malignant neoplasms of the central nervous system;
- Palbociclib, EMEA-002146-PIP01-17-M02, from Pfizer Europe MA EEIG, for the treatment of Ewing sarcoma;
- Tremelimumab, EMEA-002029-PIP01-16-M02, from AstraZeneca AB, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system,

haematopoietic and lymphoid tissue) and treatment of malignant neoplasms of lymphoid tissue;

- Cobimetinib, EMEA-001425-PIP01-13-M05, from Roche Registration GmbH, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue) with Ras, Raf or MEK pathway activation;
- Interferon beta-1a, EMEA-002238-PIP01-17-M01, from Faron Pharmaceuticals Ltd., for the treatment of acute respiratory distress syndrome (ARDS);
- Vilanterol / fluticasone furoate, EMEA-000431-PIP01-08-M12, from Glaxo Group Limited, for the treatment of asthma;
- Cabotegravir, EMEA-001418-PIP02-15-M01, from ViiV Healthcare UK Limited, for the prevention of human immunodeficiency virus (HIV-1) infection;
- Remdesivir, EMEA-002826-PIP01-20-M01, from Gilead Sciences International Ltd., for the treatment of coronavirus disease 2019 (COVID-19);
- Gilteritinib (as fumarate), EMEA-002064-PIP01-16-M03, from Astellas Pharma Europe B.V., for the treatment of acute myeloid leukaemia;
- Lamivudine (3TC) / Abacavir (ABC) / Dolutegravir (DTG), EMEA-001219-PIP01-11-M05, from ViiV Healthcare UK Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Enalapril maleate, EMEA-001706-PIP01-14-M03, from Proveca Pharma Limited, for the treatment of heart failure;
- Bintrafusp alfa, EMEA-002586-PIP01-19-M01, from Merck Europe B.V., for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system neoplasms, haematopoietic and lymphoid tissue neoplasms);
- Tildrakizumab, EMEA-001451-PIP01-13-M01, from Almirall, S.A, for the treatment of psoriasis;
- Durvalumab, EMEA-002028-PIP01-16-M02, from AstraZeneca AB, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue) and treatment of malignant neoplasms of lymphoid tissue;
- Nivolumab / relatlimab, EMEA-002727-PIP01-19-M01, from Bristol-Myers Squibb International Corporation, for the treatment of melanoma;
- Idecabtagene vicleucel, EMEA-002369-PIP01-18-M02, from Celgene Europe B.V.; for the treatment of mature B-cell neoplasms;

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

- None

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

- Cariprazine (hydrochloride), EMEA-001652-PIP01-14-M03, from Gedeon Richter Plc., for the treatment of schizophrenia;

Opinion on compliance check

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

- Corifollitropin alfa, EMEA-C-000306-PIP01-08-M04, from Merck Sharp & Dohme B.V., for the treatment of hypogonadotrophic hypogonadism;

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 7 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 Cyprus, Mrs Elena Kaisis, the new member and alternate from Lithuania, Mrs Dovile Zacharkiene and Mr. Silvijus Abramavicius and new member from The Netherlands, Mr Roderick Houwen.

The PDCO thanked Eirini Perikleous and Ann Marie Totterman for their work as they have resigned from the Committee.

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

   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

3. 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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