4 September 2020
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Human Medicines Division

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

1-4 September 2020

Opinions on paediatric investigation plans

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

- Danicopan, EMEA-002310-PIP01-17, from Alexion Europe SAS, for the treatment of paroxysmal nocturnal haemoglobinuria;
- rAAVrh74.MHCK7.microdystrophin (SRP-9001), EMEA-002677-PIP01-19, from Sarepta Therapeutics Ireland, for the Duchenne muscular dystrophy;
- Doravirine / Islatravir, EMEA-002707-PIP01-19, from Merck Sharp & Dohme (Europe), Inc., for the treatment of human immunodeficiencyvirus-1 (HIV-1) infection;
- Plasma kallikrein inhibitor, EMEA-002723-PIP01-19, from KalVista Pharmaceuticals Ltd, for the treatment of hereditary angioedema;
- Glycopyrronium bromide, EMEA-002383-PIP01-18, from Dr. August Wolff GmbH & Co. KG - Arzneimittel, for the treatment of hyperhidrosis;
- The whole range of unmanipulated autologous mononuclear cells derived from human umbilical cord blood (Hau-UCB-mnc), EMEA-001799-PIP03-19, from BrainRepair UG (haftungsbeschränkt), for the treatment of periventricular leukomalacia;
- N-(3-cyano-4-fluorophenyl)-1-methyl-4-[[(2S)-1,1,1-trifluoro-2-propanyl]sulfamoyl]-1H-pyrrole-2-carboxamide, EMEA-002693-PIP01-19, from Janssen-Cilag International NV, for the treatment of chronic viral hepatitis B;
- (2S,4S)-2-(4-Carboxyphenyl)-4-ethoxy-1-[(5-methoxy-7-methyl-1H-indol-4-yl)methyl]piperidin-1-ium chloride—water (1/1), EMEA-002705-PIP02-19, from Novartis Europharm Limited, for the treatment of IgA Nephropathy;
- Mixture of 2 synthetic double-stranded N-acetyl-galactosamine conjugated siRNA oligonucleotides that are directed against the hepatitis B virus, EMEA-002694-PIP01-19, from Janssen-Cilag International NV, for the treatment of chronic viral hepatitis B;

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- (2S,4S)-2-(4-Carboxyphenyl)-4-ethoxy-1-[(5-methoxy-7-methyl-1H-indol-4-yl)methyl]piperidin-1-ium chloride—water (1/1), EMEA-002705-PIP01-19, from Novartis Europharm Limited, for the treatment of C3 Glomerulopathy;
- Recombinant human granulocyte colony-stimulating factor – human immunoglobulin Fc fusion protein (rhG-CSF-Fc), EMEA-002507-PIP02-19, from Generon (Shanghai) Corporation, for the prevention of chemotherapy-induced febrile neutropenia and treatment of chemotherapy-induced neutropenia;
- Dabrafenib, EMEA-001147-PIP02-20, from Novartis Europharm Limited, for the treatment of glioma;
- Trametinib, EMEA-001177-PIP02-20, from Novartis Europharm Limited for the treatment of glioma.

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

- Recombinant humanised monoclonal antibody (IgG1, Kappa) to IL-5, procedure number EMEA-002836-PIP01-20, from GlaxoSmithKline (Ireland) Limited, for the treatment of asthma.

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 does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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:

- Autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains (CT053), EMEA-002823-PIP01-20, from CARsgen Therapeutics Corporation, for the treatment of multiple myeloma;
- Dupilumab, EMEA-001501-PIP06-20, from sanofi-aventis recherche & développement, for the treatment of prurigo nodularis;
- Fenofibrate / ezetimibe / pravastatin (sodium), EMEA-002835-PIP01-20, from Laboratoires SMB S.A., for the treatment of mixed hyperlipidaemia;
- Brolucizumab, EMEA-002691-PIP02-20, from Novartis Europharm Limited, for the treatment of Diabetic retinopathy;
- Sacituzumab govitecan, EMEA-002645-PIP02-20, from Immunomedics GmbH, for the treatment of urothelial carcinoma;
- Tiragolumab, EMEA-002721-PIP03-20, from Roche Registration GmbH, for the treatment of oesophageal carcinoma;
- Alpha-R-lipoic acid choline ester tosilate, EMEA-002811-PIP01-20, from Novartis Europharm Limited,

for the treatment of Presbyopia;

- Tiragolumab, EMEA-002721-PIP02-20, from Roche Registration GmbH, for the treatment of cervical cancer;
- Colchicine, EMEA-002837-PIP01-20, from Disphar International B.V. for the prevention of cardiovascular events.

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:

- Trametinib, EMEA-001177-PIP01-11-M06, from Novartis Europharm Limited, for the treatment of all conditions included in the category of malignant neoplasms (except melanoma, haematopoietic and lymphoid tissue, and glioma) and treatment of melanoma;
- Velmanase alfa, EMEA-001056-PIP02-12-M01, from Chiesi Farmaceutici S.p.A., for the treatment of alpha-mannosidosis;
- Daratumumab, EMEA-002152-PIP01-17-M02, from Janssen-Cilag International NV, for the treatment of lymphoid malignancies (except mature B-cell neoplasms);
- Edoxaban (tosylate), EMEA-000788-PIP02-11-M10, from Daiichi Sankyo Europe GmbH, for the prevention of arterial thromboembolism, prevention of venous thromboembolism and treatment of venous thromboembolism;
- Birch bark extract, EMEA-001299-PIP03-17-M01, from Amryt Research Limited, for the treatment of epidermolysis bullosa;
- Lenvatinib, EMEA-001119-PIP02-12-M07, from Eisai GmbH, for the treatment of follicular thyroid cancer, treatment of osteosarcoma and treatment of papillary thyroid cancer;
- Dabrafenib, EMEA-001147-PIP01-11-M07, from Novartis Europharm Limited, for the treatment of melanoma and treatment of solid malignant tumours (excluding melanoma and glioma);
- Dupilumab, EMEA-001501-PIP02-13-M06, from sanofi-aventis recherche & développement, for the treatment of asthma;
- Peanut Allergen Extract, EMEA-001481-PIP01-13-M04, from DBV Technologies S.A., for the treatment of peanut allergy;
- Ivacaftor / tezacaftor / elexacaftor, EMEA-002324-PIP01-17-M01, from Vertex Pharmaceuticals (Ireland) Limited, for the treatment of cystic fibrosis;
- Pegylated-fibroblast growth factor 21 (BMS-986036), EMEA-002448-PIP01-18-M01, from Bristol-Myers Squibb International Corporation, for the treatment of non-alcoholic steatohepatitis (NASH);
- Mepolizumab, EMEA-000069-PIP01-07-M07, from GSK Trading Services Limited, for the treatment of

hypereosinophilic syndrome;

- Ravulizumab, EMEA-002077-PIP01-16-M03, from Alexion Europe SAS, for the treatment of paroxysmal nocturnal haemoglobinuria (PNH);
- Ravulizumab, EMEA-001943-PIP01-16-M05, from Alexion Europe SAS, for the treatment of atypical haemolytic uremic syndrome (aHUS);
- Zanamivir, EMEA-001318-PIP01-12-M04, from GlaxoSmithKline Trading Services Limited, for the prevention of influenza and treatment of influenza;
- Ozanimod (hydrochloride), EMEA-001710-PIP03-17-M02, from Celgene Europe B.V., for the treatment of ulcerative colitis;
- Copanlisib, EMEA-001757-PIP02-15-M02, from Bayer AG, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue) and treatment of mature B-cell neoplasms;
- Vadadustat, EMEA-001944-PIP01-16-M02, from Akebia Therapeutics, Inc., for the treatment of anaemia due to chronic disorders;
- Eculizumab, EMEA-000876-PIP05-15-M04, from Alexion Europe SAS, for the treatment of myasthenia gravis;
- Filgotinib, EMEA-001619-PIP03-16-M01, from Gilead Sciences International Ltd, for treatment of ulcerative colitis and treatment of Crohn's disease.

Opinion on compliance check

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

- Elivaldogene autotemcel, EMEA-C-001244-PIP01-11-M02, from bluebird bio (Netherlands) B.V., for the treatment of adrenoleukodystrophy;
- Influenza virus surface antigens (haemagglutinin and neuraminidase) of the following strains: A/(H1N1), A/(H3N2), B/Yamagata lineage, B/Victoria lineage, EMEA-C-001782-PIP01-15-M03, from Abbott Biologicals B.V., for the prevention of influenza infection;
- Lonapegsomatropin, EMEA-C-002692-PIP01-19, from Ascendis Pharma Endocrinology Division A/S, for the treatment of growth hormone deficiency;
- Eptacog beta (activated), EMEA-C-001203-PIP02-14-M02, from LFB SA, for the treatment of congenital coagulation disorders.

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 thanked Günter Karl-Heinz Auerswald, Michal Odermarsky, Jorrit Gerritsen, Milena Stevanovic, Paola Baiardi and Viviana Giannuzzi for their work as their mandate has expired.

The next meeting of the PDCO will be held on 13-16 October 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

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