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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

25-28 February 2020

Opinions on paediatric investigation plans

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

- Bintrafusp alfa, EMEA-002586-PIP01-19, 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);
- Pneumococcal polysaccharides individually biotinylated and complexed with a carrier protein (recombinant fusion construct of rhizavidin and *Streptococcus pneumoniae* derived proteins), 24-valent, EMEA-002641-PIP01-19, from Astellas Pharma Europe, B.V., for the prevention of disease caused by *Streptococcus pneumoniae*;
- Pracinostat, EMEA-002567-PIP01-19, from Helsinn Birex Pharmaceuticals limited, for the treatment of acute myeloid leukemia;
- N-(3-{6-Amino-5-[2-(N-methylprop-2-enamido)ethoxy]pyrimidin-4-yl}-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide (LOU064), EMEA-002582-PIP01-19, from Novartis Europharm Limited, for the treatment of chronic spontaneous urticaria;
- Polymyxin B, EMEA-002595-PIP01-19, from The GARDP Foundation, for the treatment of infections due to aerobic Gram-negative bacteria;
- Temozolomide, EMEA-002634-PIP01-19, from Accord Healthcare S.L.U., for the treatment of malignant glioma;
- Dihomo-γ-linolenic acid (DS107), EMEA-002364-PIP03-19, from DS Biopharma Ltd., for the treatment of atopic dermatitis;
- 2-[[2-ethyl-6-[4-[2-(3-hydroxyazetidin-1-yl)-2-oxoethyl]piperazin-1-yl]-8 -methylimidazo[1,2-a]pyridin-3-yl](methyl)amino]-4-(4-fluorophenyl)-1,3-thiazole-5-carbonitrile (GLPG1690), EMEA-002333-PIP02-19, from Galapagos NV, for the treatment of interstitial pulmonary diseases with fibrosis;

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
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- Leriglitazone, EMEA-002106-PIP01-16, from Minoryx Therapeutics S.L., for the treatment of adrenoleukodystrophy;
- Ladarixin, EMEA-002642-PIP01-19, from Dompé farmaceutici SpA, for the treatment of type 1 diabetes mellitus;
- Lenadogene nolparvovec (GS010), EMEA-001992-PIP02-16, from GenSight-Biologics, for the treatment of Leber hereditary optic neuropathy (LHON);
- Pegcetacoplan, EMEA-002600-PIP01-19, from Apellis Ireland Limited, for the paroxysmal nocturnal haemoglobinuria;
- Cenobamate, EMEA-002563-PIP02-19, from Arvelle Therapeutics Netherlands B.V., for the treatment of epilepsy;
- Alpha1-proteinase inhibitor (human) (A1-PI), EMEA-001312-PIP02-19, from CSL Behring GmbH, for the prevention of graft-versus-host disease;
- Lebrikizumab, EMEA-002536-PIP01-18, from Dermira Inc., for the treatment of atopic dermatitis;
- (S)-(2-(5-chloro-4-methyl-1H-benzo[d]imidazol-2-yl)-2-methylpyrrolidin-1-yl)(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone hydrochloride (daridorexant), EMEA-002121-PIP03-19, from Idorsia Pharmaceuticals Deutschland GmbH, for the treatment of insomnia;
- Pneumococcal Polyssacharide Serotype 6A conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 14 conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 3 conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 12F conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 23F conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 33F conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 5 conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 7F conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 6B conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 19A conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 19F conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 8 conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 11A conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 15B conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 1 conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 22F conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 4 conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 9V conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 10A conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate / Pneumococcal Polyssacharide Serotype 18C conjugated to CRM197 carrier protein and adsorbed on aluminium Phosphate, from Pfizer MA EEIG for the prevention of disease caused by *Streptococcus pneumoniae,* EMEA-002330-PIP01-18, from Pfizer MA EEIG, for the prevention of disease caused by *Streptococcus pneumoniae.*

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:

- 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, EMEA-002526-PIP02-19, from Deciphera Pharmaceuticals LLC, for the treatment of gastrointestinal stromal tumours;
- 3-(((1S,2S,3R)-2,3-difluoro-1-hydroxy-7-(methylsulfonyl)-2,3-dihydro-1H-inden-4-yl)oxy)-5-fluorobenzonitrile, EMEA-002619-PIP01-19, from Merck, Sharp & Dohme (Europe) Inc, for the treatment of renal neoplasms;
- Natalizumab, EMEA-001095-PIP03-19, from Biogen Limited Idec, for the treatment of multiple sclerosis;
- Lanadelumab, EMEA-001864-PIP02-19, from Shire Pharmaceuticals Ireland Limited, for the prevention of acquired angioedema attacks;
- Lazertinib (mesylate), EMEA-002725-PIP01-19, from Janssen-Cilag International N.V., for the treatment of lung carcinoma (small cell and non-small cell carcinoma);
- 4-[4-({4-[({2-[(3S)-2,6-dioxopiperidin-3-yl]-1-oxo-2,3-dihydro-1H-isoindol-4-yl}oxy)methyl]phenyl}methyl)piperazin-1-yl]-3-fluorobenzonitrile, EMEA-002714-PIP01-19, from Celgene Europe B.V., for the treatment of mature B-cell neoplasms;
- Glycerol / Urea, EMEA-002511-PIP02-19, from ACO Hud Nordic AB, for the treatment of dry skin.

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:

- Blinatumomab, EMEA-000574-PIP02-12-M03, from Amgen Europe B.V., for the treatment of acute lymphoblastic leukaemia;
- Boceprevir, EMEA-000583-PIP01-09-M08, from Merck Sharp & Dohme (Europe), Inc, for the treatment of chronic hepatitis C;
- Regorafenib, EMEA-001178-PIP01-11-M05, from Bayer AG, for the treatment of all conditions contained in the category of malignant neoplasms (except haematopoietic and lymphoid tissue);
- Monovalent, live, recombinant, replication-incompetent adenoviral serotype 26 vectored vaccine expressing the full length glycoprotein of the Ebola virus Mayinga variant (Ad26.ZEBOV), EMEA-002307-PIP01-17-M01, from Janssen Cilag International NV, for the prevention of Ebola virus disease;
- Clostridium botulinum neurotoxin type A (150 kD), free from complexing proteins, EMEA-001039-PIP02-12-M04, from Merz Pharmaceuticals GmbH, for the treatment of sialorrhoea;
- Axicabtagene ciloleucel, EMEA-002010-PIP01-16-M02, from Kite Pharma EU B.V., for the treatment of mature B-cell neoplasms;

- Palovarotene, EMEA-001662-PIP01-14-M03, from Ipsen Pharma, for the treatment of fibrodysplasia ossificans progressiva;
- Semaglutide, EMEA-001441-PIP01-13-M03, from Novo Nordisk A/S, for the treatment of type 2 diabetes mellitus;
- Tralokinumab, EMEA-001900-PIP02-17-M03, from LEO Pharma A/S, for the treatment of atopic dermatitis;
- Linaclotide, EMEA-000927-PIP01-10-M05, from Allergan Pharmaceuticals International Limited, for the treatment of functional constipation;
- Galcanezumab, EMEA-001860-PIP03-16-M04, from Eli Lilly and Company Limited, for the prevention of migraine headaches;
- Tenofovir (disoproxil fumarate), EMEA-000533-PIP01-08-M08, from Gilead Sciences International Ltd, for the treatment of chronic viral hepatitis B and treatment of human immunodeficiency virus (HIV-1) infection;
- Autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti CD19 CD28/CD3-zeta chimeric antigen receptor and cultured (KTE-X19), EMEA-001862-PIP01-15-M02, from Kite Pharma EU B.V., for the treatment of acute lymphoblastic leukaemia;
- Copanlisib, EMEA-001757-PIP02-15-M01, 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;
- Multivalent, live, recombinant, non-replicating in human cells, Modified Vaccinia Ankara vectored vaccine, expressing the EBOV Mayinga glycoprotein, the Sudan virus Gulu GP, the Marburg virus Musoke GP, and the Taï Forest virus nucleoprotein (MVA-BN-Filo), EMEA-002308-PIP01-17-M01, from Janssen Cilag International NV, for the prevention of Ebola virus disease;
- Mirikizumab, EMEA-002208-PIP01-17-M01, from Eli Lilly and Company, for the treatment of Crohn's disease, treatment of psoriasis and treatment of ulcerative colitis;
- Etrolizumab, EMEA-001434-PIP01-13-M03, from Roche Registration GmbH, for the treatment of Crohn's disease and treatment of ulcerative colitis;
- Elafibranor, EMEA-001857-PIP01-15-M01, from Genfit SA, for the treatment of non-alcoholic fatty liver disease including non-alcoholic steatohepatitis.

Opinion on compliance check

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

- Sitagliptin, EMEA-C-000470-PIP01-08-M11, from Merck Sharp & Dohme (Europe), Inc., for the treatment of type 2 diabetes mellitus;
- Mepolizumab, EMEA-C-000069-PIP04-13-M02, from GSK Trading Services Limited, for the treatment of vasculitides;
- Lubiprostone, EMEA-C-000245-PIP01-08-M06, from Sucampo AG, for the treatment of constipation.

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 5 applications were withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure).

Other matters

The next meeting of the PDCO will be held on 24-27 March 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: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/pip_search.jsp&murl=menus/medicines/medicines.jsp&mid=WC0b01ac058001d129

3. More information about the PDCO and the Paediatric Regulation is available in the Regulatory section of the Agency's website: 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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