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Human Medicines Division

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

9-12 November 2021

Opinions on paediatric investigation plans

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

- Autologous CD34+ hematopoietic stem cells with a CRISPR-edited erythroid enhancer region of the BCL11A gene, EMEA-002730-PIP03-21, from Vertex Pharmaceuticals (Ireland) Limited, for the treatment of sickle cell disease;
- Autologous CD34+ hematopoietic stem cells with a CRISPR-edited erythroid enhancer region of the BCL11A gene, EMEA-002730-PIP04-21, from Vertex Pharmaceuticals (Ireland) Limited, for the treatment of beta-thalassemia intermedia and major;
- Leniolisib, EMEA-002989-PIP01-21, from Pharming Group N.V., for the treatment of activated phosphoinositide 3-kinase delta syndrome (APDS);
- Exebacase, EMEA-002947-PIP01-20, from ContraFect Corporation, for the treatment of *Staphylococcus aureus* bacteraemia;
- Tosatoxumab, EMEA-002506-PIP03-21, from Aridis Pharmaceuticals Inc, for the treatment of *Staphylococcus aureus* pneumonia;
- Vatiquinone, EMEA-001238-PIP03-21, from PTC Therapeutics International, for the treatment of Friedreich's ataxia;
- 2'-O-(2-methoxyethyl) modified antisense oligonucleotide targeting glial fibrillary acidic protein pre-mRNA (ION373), EMEA-002822-PIP01-20, from Ionis Pharmaceuticals, for the treatment of Alexander disease;
- Repotrectinib, EMEA-002635-PIP02-21, from Premier Research SLU, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic neoplasms);
- Molnupiravir, EMEA-002940-PIP02-21; from Merck Sharp & Dohme (Europe), Inc.; for the prevention of coronavirus disease 2019 (COVID-19);

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

- Plitidepsin, EMEA-000095-PIP02-21; Pharma Mar, S.A.; for the treatment of coronavirus disease 2019 (COVID-19). 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 unsafe.

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 opinions for the following products:

- Following the re-examination of the positive opinion on a modification to an agreed PIP adopted on 10 September 2021 for EMEA-002893-PIP01-20-M01, 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 from MODERNA BIOTECH SPAIN, S.L.; for the prevention of coronavirus disease 2019 (COVID-19), the PDCO adopted a revised positive opinion and agreed to the changes regarding the measures in the scope set out in the Annex I of the opinion;
- Following the re-examination of the negative opinion on a full waiver adopted on 10 September 2021 for EMEA-003037-PIP01-21, perflubutane from GE Healthcare AS, for diagnostic evaluation of focal hepatic lesions, the PDCO recommended to maintain its opinion and refuse the granting of a product-specific waiver for all subsets of the paediatric population and the above mentioned condition(s) as it does not meet the grounds detailed in Article 11(1) of Regulation (EC) No 1901/2006.

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:

- Secukinumab, EMEA-000380-PIP08-21, from Novartis Europharm Limited, for the treatment of vasculitides;
- Paracetamol / acetylcysteine / phenylephrine, EMEA-003091-PIP01-21, from HEXAL AG, for the treatment of upper respiratory tract infections;
- Humanised IgG2k Fc-modified bispecific antibody against CD3 and BCMA (PF-06863135), EMEA-

003083-PIP01-21, from Pfizer Europe MA EEIG, for the treatment of multiple myeloma;

- Efgartigimod alfa - EMEA-002597-PIP07-21, from argenx for the condition treatment of pemphigus;

The PDCO adopted 0 opinions on the **refusal** of a request for waiver.

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:

- Nemolizumab, EMEA-001624-PIP01-14-M04, from Galderma International S.A.S, for the treatment of atopic dermatitis;
- Romosozumab, EMEA-001075-PIP04-15-M04, from UCB Pharma S.A., for the treatment of osteoporosis;
- Alirocumab, EMEA-001169-PIP01-11-M05, from Sanofi-aventis Recherche & Développement, for the treatment of elevated cholesterol;
- Estetrol / drospirenone, EMEA-001332-PIP01-12-M05, from Estetra SRL, for the prevention of pregnancy;
- Tirzepatide, EMEA-002360-PIP01-18-M01, from Eli Lilly and Company Ltd, for the treatment of type 2 diabetes mellitus;
- Vedolizumab, EMEA-000645-PIP01-09-M08, from Takeda Pharma A/S, for the treatment of Crohn's disease and treatment of ulcerative colitis;
- Crizanlizumab, EMEA-002141-PIP01-17-M03, from Novartis Europharm Limited, for the treatment of sickle cell disease;
- Giroctocogene fitelparvovec, EMEA-002724-PIP01-19-M02, from Pfizer Europe MA EEIG, for the treatment of haemophilia A;
- Tozinameran, EMEA-002861-PIP02-20-M03, from BioNTech Manufacturing GmbH, for the prevention of coronavirus disease 19 (COVID-19);
- Fully human IgG1 RB-1 YTE anti-RSV F monoclonal antibody (MK-1654), EMEA-002755-PIP01-19-M01, from Merck Sharp & Dohme (Europe), Inc., for the prevention of lower respiratory tract infection caused by respiratory syncytial virus;
- Fenfluramine (hydrochloride), EMEA-001990-PIP01-16-M04, from Zogenix International Ltd, for the treatment of Dravet syndrome;
- Risdiplam, EMEA-002070-PIP01-16-M06, from Roche Registration GmbH, for the treatment of spinal muscular atrophy;
- Eribulin, EMEA-001261-PIP01-11-M07, from Eisai GmbH, for the treatment of soft tissue sarcoma;

- Pembrolizumab, EMEA-001474-PIP02-16-M02, from Merck Sharp & Dohme (Europe), Inc., for the treatment of Hodgkin lymphoma;
- Avelumab, EMEA-001849-PIP02-15-M04, from Merck Healthcare KGaA, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms), treatment of malignant neoplasms of lymphoid tissue and treatment of malignant neoplasms of the central nervous system;
- Lisocabtagene maraleucel, EMEA-001995-PIP01-16-M03, from Bristol-Myers Squibb Pharma EEIG, for the treatment of B-lymphoblastic leukaemia/lymphoma and treatment of mature B-cell neoplasms;
- Palovarotene, EMEA-001662-PIP01-14-M05, from Ipsen Pharma, for the treatment of fibrodysplasia ossificans progressiva;
- Alpelisib, EMEA-002016-PIP03-19-M01, from Novartis Europharm Limited, for the treatment of PIK3CA related overgrowth spectrum;
- Nedosiran (DCR-PHXC), EMEA-002493-PIP01-18-M03, from Dicerna Ireland Limited, for the treatment of primary hyperoxaluria;
- COVID-19 Vaccine (ChAdOx1-S [recombinant]), EMEA-002862-PIP01-20-M02, from AstraZeneca AB, for the prevention of coronavirus disease 2019 (COVID-19);

Opinion on compliance check

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

- No item

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.

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. Opinions of the Paediatric Committee (PDCO) on PIPs and waivers lead to 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

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