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Human Medicines Division

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

24-27 March 2020

Opinions on paediatric investigation plans

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

- Livoletide, EMEA-002455-PIP01-18, from Millendo Therapeutics SAS, for the treatment of Prader-Willi syndrome;
- Cyclophosphamide, EMEA-002644-PIP01-19, from Accord Healthcare S.L.U., for the treatment of all malignant neoplasms;
- Imatinib, EMEA-002643-PIP01-19, Accord Healthcare S.L.U., for the treatment of acute lymphoblastic leukaemia and treatment of chronic myeloid leukaemia;
- Idasanutlin, EMEA-001489-PIP02-19, from Roche Registration GmbH, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue);
- Spesolimab, EMEA-002475-PIP02-19, from Boehringer Ingelheim International GmbH, for the prevention of generalised pustular psoriasis and treatment of generalised pustular psoriasis;
- Difelikefalin, EMEA-002565-PIP02-19, from Vifor Fresenius Medical Care Renal Pharma France, for the treatment of chronic kidney disease associated pruritus;
- Ibrexafungerp, EMEA-002535-PIP03-19, from SCYNEXIS, Inc., for the prevention of recurrent vulvovaginal candidiasis and for the treatment of vulvovaginal candidiasis.

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.

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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 31 January 2020 for Macimorelin, EMEA-001988-PIP01-16-M01, from Aeterna Zentaris GmbH, for the diagnosis of growth hormone deficiency, the PDCO adopted a revised positive opinion and agreed to changes to the paediatric investigational plan in the scope set out in the Annex I of the opinion.

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:

- Arfolitixorin, EMEA-002223-PIP01-19, from Isofol Medical AB, for the treatment of colorectal cancer;
- Rosuvastatin calcium/fenofibrate, EMEA-002743-PIP01-19, from Accord Healthcare S.L.U., for the treatment of mixed dyslipidaemia;
- Hydrocortisone (acetate)/ Benzocaine, EMEA-002739-PIP01-19, from Faes Farma, S.A., for the treatment of haemorrhoidal disease;
- Propan-2-yl 2-[5-(acryloylamino)-4-{[2-(dimethylamino)ethyl](methyl)amino}-2-methoxyanilino]-4-(1methyl-1H-indol-3-yl)pyrimidine-5-carboxylate (TAK-788) , EMEA-002716-PIP01-19, from Takeda Pharma A/S, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms);
- Tiragolumab, EMEA-002721-PIP01-19, from Roche Registration GmbH, for the treatment of lung carcinoma (small cell and non-small cell carcinoma);
- 18-(p-[131I]-iodophenyl)octadecyl phosphocholine, EMEA-002745-PIP01-19, from Cellectar Biosciences, Inc., for the treatment of multiple myeloma.

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:

- Ivacaftor, EMEA-000335-PIP01-08-M14, from Vertex Pharmaceuticals (Ireland) Ltd, for the treatment of cystic fibrosis;
- Isoflurane, EMEA-002320-PIP01-17-M01, from Sedana Medical AB, for the sedation of mechanically ventilated patients;
- Crisaborole, EMEA-002065-PIP01-16-M02, from Pfizer Europe MA EEIG, for the treatment of atopic dermatitis;
- Afatinib, EMEA-001596-PIP02-17-M02, from Boehringer Ingelheim International GmbH, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms) and treatment of malignant neoplasms of the central nervous system;
- Tezavaftor / ivacaftor, EMEA-001640-PIP01-14-M06, from Vertex Pharmaceuticals (Europe) Ltd., for the treatment of cystic fibrosis;
- Alicaforsen (sodium salt), EMEA-002060-PIP02-17-M01, from Atlantic Healthcare Europe B.V., for the treatment of pouchitis;
- Setmelanotide, EMEA-002209-PIP01-17-M01, from Rhythm Pharmaceuticals, Inc, for the treatment of appetite and general nutrition disorders;
- Dimethyl fumarate, EMEA-000832-PIP01-10-M05, from Biogen Idec Ltd., for the treatment of multiple sclerosis;
- Influenza virus surface antigens - A/turkey/Turkey/1/05 (H5N1), EMEA-000599-PIP01-09-M07, from Seqirus S.r.l., for the prevention of influenza;
- Volanesorsen, EMEA-001915-PIP01-15-M02, from Akcea Therapeutics, for the treatment of familial chylomicronemia syndrome;
- Romosozumab, EMEA-001075-PIP04-15-M02, from UCB Pharma S.A., for the treatment of osteoporosis;
- 2-iminobiotin, EMEA-001070-PIP01-10-M02, from Neurophyxia BV, for the treatment of perinatal asphyxia;
- Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted), EMEA-001830-PIP01-15-M02, from Seqirus S.r.l., for the prevention of influenza infection;
- Gilteritinib (as fumarate), EMEA-002064-PIP01-16-M02, from Astellas Pharma Europe B.V., for the treatment of acute myeloid leukaemia;
- Tofacitinib, EMEA-000576-PIP03-12-M03, from Pfizer Europe MA EEIG, for the treatment of ulcerative colitis;
- Talimogene laherparepvec, EMEA-001251-PIP01-11-M04, from Amgen Europe B.V., for the treatment of solid malignant non-CNS tumours;
- Roxadustat, EMEA-001557-PIP01-13-M04, from Astellas Pharma Europe B.V., for the treatment of anaemia due to chronic disorders;
- Avalglucosidase alfa, EMEA-001945-PIP01-16-M02, from Genzyme Europe B.V., for the treatment of Pompe disease;
- Dulaglutide, EMEA-000783-PIP01-09-M05, from Eli Lilly and Company, for the treatment of type 2

diabetes mellitus;

- Pitolisant, EMEA-001176-PIP01-11-M04, from BIOPROJET PHARMA, for the treatment of narcolepsy;
- Rolapitant, EMEA-001768-PIP02-15-M03, from Tesaro Bio Netherlands B.V., for the prevention of nausea and vomiting;
- Methoxyflurane, EMEA-000334-PIP01-08-M09, from Medical Developments UK Ltd, for the treatment of acute pain.

Opinion on compliance check

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

- Mometasone (furoate monohydrate) / olopatadine (hydrochloride) (GSP 301 NS), EMEA-C-002514-PIP01-18, from Glenmark Pharmaceuticals Europe Ltd., for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Romiplostim, EMEA-C-000653-PIP01-09-M05, from Amgen Europe B.V., for the treatment of immune thrombocytopenia (idiopathic thrombocytopenic purpura) and treatment of disease-related thrombocytopenia in myelodysplastic syndrome;
- Lonafarnib, EMEA-C-002516-PIP01-18, from EigerBio Europe Limited, for the treatment of Hutchinson-Gilford Progeria Syndrome (HGPS) and treatment of Progeroid Laminopathies.

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).

New meeting dates adopted

The PDCO meeting dates for September 2020 and 2021 were updated and adopted during the February 2020 meeting. These dates are important for applicants in planning the submission of applications for PIPs, requests for waivers, requests for modification of an agreed PIP, and requests for compliance checks. The dates are published on the Agency's website at: https://www.ema.europa.eu/en/documents/other/pdco-meeting-dates-2019-2020-2021_en.pdf

Other matters

The PDCO welcomed the new member from Czech Republic, Dr Lucie Kraváčková.

The PDCO thanked Dr Tereza Bažantová for her work as she has resigned from the Committee.

The PDCO revised the submission deadlines for paediatric procedures (https://www.ema.europa.eu/en/human-regulatory/research-development/paediatric-medicines/paediatric-investigation-plans/paediatric-investigation-plans-templates-forms-submission-dates). The submission deadlines were revised in order to remove restrictions and allow all type of submissions throughout the year.

The next meeting of the PDCO will be held on 28-30 April 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: 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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