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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

21-24 March 2017

Opinions on paediatric investigation plans

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

- 3,6-diamino-2,5-bis{N-[(1R)-1-carboxy-2-hydroxyethyl]carbamoyl}pyrazine, EMEA-001983-PIP01-16, from MediBeacon Inc., for the monitoring of renal function;
- Avacopan, EMEA-002023-PIP01-16, from ChemoCentryx, Ltd., for the treatment of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis.

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

- Recombinant modified human growth hormone, EMEA-001152-PIP02-16, from Richardson Associates Regulatory Affairs Ltd, for the treatment of growth hormone deficiency.

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 and that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

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:

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- Small interfering RNA targeting human TRPV1, EMEA-002061-PIP01-16, from Sylentis SAU, for the treatment of dry eye disease;
- Ramipril / Indapamide, EMEA-002081-PIP01-16, from Pharmaceutical Works Polpharma SA, for the treatment of hypertension;
- Nintedanib, EMEA-001006-PIP03-16, from Boehringer Ingelheim International GmbH, for the Treatment of adenocarcinoma of the colon and rectum, treatment of lung carcinoma (small cell and non-small cell carcinoma) and treatment of mesothelioma;
- Mepolizumab, EMEA-000069-PIP05-16, from GSK Trading Services Limited, for the treatment of nasal polyposis;
- Erdafitinib, EMEA-002042-PIP01-16, from Janssen-Cilag International NV, for the treatment of urothelial carcinoma.

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:

- Dopamine hydrochloride, EMEA-001105-PIP01-10-M03, from BrePco Biopharma Limited, for the treatment of vascular hypotensive disorders;
- Doravirine / lamivudine / tenofovir disoproxil fumarate, EMEA-001695-PIP01-14-M01, from Merck Sharp & Dohme (Europe), Inc., for the treatment of human immunodeficiency virus type 1 (HIV-1) infection;
- 3-[[5-chloro-1-[3-(methylsulfonyl)propyl]-1H-indol-2-yl]methyl]-1-(2,2,2-trifluoroethyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridine-2-one, EMEA-001838-PIP01-15-M01, from Janssen-Cilag International NV, for the treatment of lower respiratory tract disease caused by human respiratory syncytial virus (RSV);
- Tapentadol, EMEA-000018-PIP01-07-M13, from Grünenthal GmbH, for the treatment of acute pain;
- Doravirine, EMEA-001676-PIP01-14-M01, from Merck Sharp & Dohme (Europe), Inc., for the treatment of human immunodeficiency virus type 1 (HIV-1) infection;
- Melatonin, EMEA-000440-PIP02-11-M05, from RAD Neurim Pharmaceuticals EEC Ltd, for the treatment of insomnia;
- Ponatinib, EMEA-001186-PIP01-11-M01, Incyte Biosciences UK Ltd., for the treatment of chronic myeloid leukaemia and treatment of acute lymphoblastic leukaemia.

Opinion on compliance check

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

- Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with lentiviral vector that encodes for the human Wiskott Aldrich Syndrome (WAS) cDNA sequence, EMEA-C-001792-PIP01-15, from GlaxoSmithKline Trading Services Ltd, for the treatment of Wiskott Aldrich Syndrome.

The PDCO adopted a negative opinion on (full) compliance check for:

- Darbepoetin alfa, EMEA-C-000329-PIP02-09-M05, from Amgen Europe B.V., for the treatment of anaemia due to chronic 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/measured 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.

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 of an agreed PIP adopted on 27 January 2017 for fingolimod (hydrochloride), EMEA-000087-PIP01-07-M05, from Novartis Europharm Limited, for the treatment of multiple sclerosis, the PDCO adopted a revised positive opinion.
- Following the re-examination of the positive opinion on a modification of an agreed PIP adopted on 27 January 2017 for dupilumab, EMEA-001501-PIP01-13-M04, from Regeneron Pharmaceuticals, Inc, for the treatment of atopic dermatitis, the PDCO adopted a revised positive 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.

Withdrawals

The PDCO noted that 2 applications were withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure).

Committee interactions

In a joint presentation and discussion representatives from 2 national multispecialty networks together with the current president of EUCROF (European CRO Federation) informed the committee about the roles and tasks of CROs and those of networks. As there is some overlap, the need for clear definitions and communication between sponsors and CROs/networks, of who does what would help avoiding duplication of work. It is planned to put this topic on the agenda of next year's annual Enpr-EMA workshop.

Other matters

The next meeting of the PDCO will be held on 18-21 April 2017.

– 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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