25 July 2016
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Procedure Management and Committees Support Division

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

20-22 July 2016

Opinions on paediatric investigation plans

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

- Autologous cartilage derived cultured chondrocytes, EMEA-001823-PIP01-15, from TETEC AG, for the treatment of cartilage disorders;
- Elafibranor, EMEA-001857-PIP01-15, from Genfit SA, for the treatment of non-alcoholic fatty liver disease (NAFLD) including non-alcoholic steatohepatitis (NASH);
- Eculizumab, EMEA-000876-PIP07-15, from Alexion Europe SAS, for the prevention of delayed graft function after solid organ transplantation;
- Cathine hydrochloride, EMEA-001909-PIP01-15, from Schuck GmbH, for the treatment of obesity;
- derivative of 4H-pyrazolo[3,4-d]pyrimidin-4-one, EMEA-001742-PIP01-14, from Boehringer Ingelheim International GmbH, for the treatment of schizophrenia;

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

- Angiotensin II, EMEA-001912-PIP01-15, from La Jolla Pharmaceutical Company, Inc., for the treatment of catecholamine-resistant hypotension associated with distributive shock.

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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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:

- Amlodipine besylate / perindopril erbumine / indapamide, EMEA-001948-PIP01-16, from Zentiva, k.s., for the treatment of hypertension;
- Ezetimibe / Rosuvastatin (calcium), EMEA-001941-PIP01-16, from Adamed sp z o.o., for the treatment of hypercholesterolaemia;
- Allogeneic human neural stem cells genetically modified to express c-MycER^{TAM}, a c-Myc and modified oestrogen receptor fusion protein (CTX0E03), EMEA-001969-PIP01-16, from ReNeuron Ltd, for the treatment of cerebral infarction;
- (S)-lactic acid, EMEA-001953-PIP01-16, from YES Pharmaceutical Development Services GmbH, for the prevention of pregnancy;
- Lesinurad / allopurinol, EMEA-001952-PIP01-16, from AstraZeneca AB, for the treatment of hyperuricemia;
- Macitentan / tadalafil, EMEA-001961-PIP01-16, from Actelion Registration Ltd., for the treatment of pulmonary arterial hypertension;
- Humanized IgG1, kappa anti-serum amyloid A and anti-AL amyloid antibody, EMEA-001962-PIP01-16, from Prothena Therapeutics Limited, for the treatment of systemic light chain amyloidosis.

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:

- Brexpiprazole, EMEA-001185-PIP01-11-M03, from Otsuka Europe Development and Commercialisation Ltd, Zweigniederlassung Frankfurt am Main, for the treatment of schizophrenia;
- Evolocumab, EMEA-001268-PIP01-12-M03, from Amgen Europe B.V., for the treatment of elevated cholesterol and treatment of mixed dyslipidaemia;
- Lanthanum carbonate hydrate, EMEA-000637-PIP02-10-M05, from Shire Pharmaceutical Contracts Ltd, for the treatment of hyperphosphataemia;
- piperaquine tetraphosphate / dihydroartemisinin, EMEA-000153-PIP01-07-M04, from Sigma-Tau SpA, for the treatment of uncomplicated malaria caused by Plasmodium falciparum;
- Lubiprostone, EMEA-000245-PIP01-08-M03, from Sucampo Pharma Europe Ltd., for the treatment of

constipation;

- Fingolimod (hydrochloride), EMEA-000087-PIP01-07-M04, from Novartis Europharm Limited, for the treatment of multiple sclerosis;
- Vedolizumab, EMEA-000645-PIP01-09-M04, from Takeda Pharma A/S, for the treatment of Crohn's disease and treatment of ulcerative colitis;
- Linaclotide, EMEA-000927-PIP01-10-M03, from Allergan Pharmaceuticals International Limited, for the treatment of functional constipation;
- Ixekizumab, EMEA-001050-PIP01-10-M02, from Eli Lilly & Company Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis).

Opinion on compliance check

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

- Levamisole (hydrochloride), EMEA-C-001885-PIP01-15-M01, from ACE Pharmaceuticals BV, for the treatment of glomerulonephritis and nephrotic syndrome.

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.

Withdrawals

The PDCO noted that 1 application was withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure).

Other matters

The PDCO welcomed Maaike van Dartel in her new role representing the Netherlands as member.

The PDCO thanked Hendrik van den Berg at the end of his mandate as member for the Netherlands.

The PDCO welcomed Sara Galluzzo the new member nominated to represent Italy.

The PDCO thanked Paolo Rossi and Francesca Rocchi for their work as member and, respectively, as alternate, leaving the committee at the end of their mandates.

The PDCO welcomed Johanna Wernsperger the new alternate nominated to represent Austria.

The PDCO thanked Christoph Male at the end of his mandate as alternate for Austria.

The PDCO welcomed Jorrit Gerritsen nominated by the European Commission to represent Doctors' organisations as alternate.

The next meeting of the PDCO will be held on 17-19 August 2016.

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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