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Inspections, Human Medicines Pharmacovigilance and Committees Division

PDCO monthly report of opinions on paediatric investigation plans and other activities 12-14 October 2016

Opinions on paediatric investigation plans

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

- Galcanezumab, EMEA-001860-PIP03-16, from Eli Lilly and Company Limited, for the prevention of migraine headaches;
- Naldemedine tosylate, EMEA-001893-PIP01-15, from Shionogi Limited, for the treatment of opioid-induced constipation (OIC);
- Recombinant Fusion Protein Linking Coagulation Factor VIIa with Albumin (rVIIa-FP), EMEA-001886-PIP01-15, from CSL Behring GmbH, for the treatment of congenital Haemophilia A and B;
- Recombinant Fusion Protein Linking Coagulation Factor VIIa with Albumin (rVIIa-FP), EMEA-001886-PIP02-15, from CSL Behring GmbH, for the treatment of congenital Factor VII Deficiency;
- inebilizumab, EMEA-001911-PIP01-15, from MedImmune, LLC, for the treatment of neuromyelitis optica spectrum disorders.

The PDCO adopted an opinion on the **refusal** of a PIP and a waiver for 4H-pyrazolo[3,4-d]pyrimidin-4-one, 1,5-dihydro-6-(2-pyridinylmethyl)-1-(tetrahydro-2H-pyran-4-yl), EMEA-001742-PIP02-16, from Boehringer Ingelheim International GmbH, for the prevention of psychosis.

The PDCO adopted an opinion on the **refusal** of a PIP and a deferral Chlorhexidine gluconate / isopropyl alcohol, EMEA-002011-PIP01-16, from GAMA Healthcare Ltd, for the prevention of infections prior to invasive procedures.

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 does not represent a significant therapeutic benefit as the needs are already covered.

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The PDCO adopted an opinion on the **refusal** of a PIP and a deferral and a waiver for EMEA-001154-PIP02-15 for Antithrombin alfa, from GTC Biotherapeutics UK Limited, for the treatment of antithrombin deficiency.

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:

- Teprotumumab, EMEA-001973-PIP01-16, from River Vision Development Corporation, for the treatment of active thyroid eye disease;
- N-[5-(4-Bromophenyl)-6-[2-[(5-bromo-2-pyrimidinyl)oxy]ethoxy]-4-pyrimidinyl]-sulfamide, EMEA-001978-PIP01-16, from Actelion Registration Ltd., for the treatment of hypertension;
- Synthetic double-stranded siRNA oligonucleotide directed against p53 mRNA, EMEA-001993-PIP01-16, from Quark Pharmaceuticals Inc., for the prevention of delayed graft function (DGF) after kidney transplantation;

The PDCO adopted 1 opinion on the **refusal** of a request for waiver for:

- Terguride, EMEA-002015-PIP01-16, from medac Gesellschaft für klinische Spezialpräparate mbH, for the treatment of systemic sclerosis.

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:

- Tenofovir alafenamide / Emtricitabine / Bictegravir, EMEA-001766-PIP01-15-M01, from Gilead Sciences International Ltd., for the treatment of human immunodeficiency virus (HIV-1) infection;
- methoxyflurane, EMEA-000334-PIP01-08-M05, from Medical Developments UK Ltd, for the treatment of acute pain;
- fentanyl hydrocholoride, EMEA-001509-PIP01-13-M01, from Incline Therapeutics Europe Ltd., for the treatment of acute pain;
- Sunitinib, EMEA-000342-PIP01-08-M05, from Pfizer Limited, for the treatment of gastro-intestinal stromal tumour;

- Telavancin hydrochloride, EMEA-000239-PIP01-08-M02, from Clinigen Healthcare Ltd, for the treatment of complicated skin and soft tissue infections (cSSTI) and treatment of nosocomial pneumonia;
- Naltrexone (hydrochloride) / bupropion (hydrochloride), EMEA-001373-PIP01-12-M02, from Orexigen Therapeutics Ireland Limited, for the treatment of obesity;
- Inotuzumab ozogamicin, EMEA-001429-PIP01-13-M01, from Pfizer Limited, for the treatment of acute lymphoblastic leukaemia;
- Semaglutide, EMEA-001441-PIP01-13-M01, from Novo Nordisk A/S, for the treatment of type 2 diabetes mellitus;
- linagliptin, EMEA-000498-PIP01-08-M06, from Boehringer Ingelheim International GmbH, for the treatment of type 2 diabetes mellitus;
- Eravacycline, EMEA-001555-PIP01-13-M02, from Tetraphase Pharmaceuticals, Inc., for the treatment of complicated intra-abdominal infection and treatment of urinary tract infection;
- Loxapine, EMEA-001115-PIP01-10-M05, from Ferrer Internacional, S.A., for the treatment of bipolar disorder and treatment of schizophrenia;
- Delta-9-tetrahydrocannabinol / Cannabidiol, EMEA-000181-PIP01-08-M03, from GW Pharma Ltd, for the treatment of spasticity;
- Migalastat (hydrochloride), EMEA-001194-PIP01-11-M02, from Amicus Therapeutics UK Ltd, for the treatment of Fabry disease;
- daclatasvir, EMEA-001191-PIP01-11-M02, from Bristol-Myers Squibb Pharma EEIG, for the treatment of chronic hepatitis C;
- Ceftobiprole medocaril (sodium), EMEA-000205-PIP02-11-M02, from Basilea Pharmaceutica International Ltd., for the treatment of pneumonia;
- Eribulin, EMEA-001261-PIP01-11-M03, from Eisai Europe Ltd, for the treatment of soft tissue sarcoma;
- Dobutamine (hydrochloride), EMEA-001262-PIP01-12-M02, from Proveca Limited, for the treatment of neonatal circulatory failure;
- Autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19, EMEA-001654-PIP01-14-M01, from Novartis Europharm Limited, for the treatment of B cell acute lymphoblastic leukaemia/lymphoblastic lymphoma;
- Elvitegravir / emtricitabine / tenofovir disoproxil (as fumarate) / cobicistat, EMEA-000970-PIP01-10-M01, from Gilead Sciences International Ltd, for the treatment of human immunodeficiency virus HIV-1 infection;
- Ambrisentan, EMEA-000434-PIP01-08-M04, from Glaxo Group Limited, for the treatment of pulmonary arterial hypertension;
- Empagliflozin, EMEA-000828-PIP01-09-M05, from Boehringer Ingelheim International GmbH, for the treatment of type 2 diabetes mellitus;
- Pixantrone, EMEA-000713-PIP02-10-M04, from CTI Life Sciences Limited, for the treatment of non-Hodgkin lymphoma;
- Tapentadol, EMEA-000018-PIP01-07-M12, from Grünenthal GmbH, for the treatment of acute pain;

- Autologous haematopoietic stem cells transduced with lentiviral vector Lenti-D encoding the human ATP-binding cassette, sub-family D (ALD), member 1 (ABCD1) from cDNA, EMEA-001244-PIP01-11-M01, from bluebird bio France, for the treatment of adrenoleukodystrophy;
- Bosutinib, EMEA-000727-PIP01-09-M02, from Pfizer Limited, for the treatment of chronic myeloid leukaemia (CML);
- Perampanel, EMEA-000467-PIP01-08-M08, from Eisai Europe Limited, for the treatment of treatment-resistant epilepsies.

The PDCO adopted an opinion on the **refusal** of modifications to an agreed PIP for the following application:

- Tapentadol, EMEA-000325-PIP01-08-M06, from Grünenthal GmbH, for the treatment of chronic pain.

Opinion on compliance check

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

- Hydrocortisone, EMEA-C-001283-PIP01-12, from DIURNAL LIMITED, for the treatment of adrenocortical insufficiency;
- Adalimumab, EMEA-C-000366-PIP05-12-M02, from AbbVie Ltd, for the treatment of non-infectious uveitis;
- Deferasirox, EMEA-C-001103-PIP01-10-M03, from Novartis Europharm Limited, for the treatment of chronic iron overload requiring chelation therapy.

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 2 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 8-11 November 2016.

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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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