21 July 2017
EMA/PDCO/473581/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

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

18 – 21 July 2017

Opinions on paediatric investigation plans

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

- Selonsertib, EMEA-001868-PIP03-16, from Gilead Sciences International Ltd., for the Treatment of non-alcoholic steatohepatitis (NASH);
- Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor, EMEA-002010-PIP01-16, from Kite Pharma EU B.V., for the Treatment of mature B-cell neoplasms;
- Lefamulin, EMEA-002075-PIP01-16, from Nabriva Therapeutics AG, for the Treatment of community-acquired pneumonia;
- Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor, EMEA-001862-PIP01-15, from Kite Pharma EU B.V., for the Treatment of acute lymphoblastic leukaemia;
- fenfluramine hydrochloride, EMEA-001990-PIP01-16, from Zogenix International Ltd, for the Treatment of Dravet syndrome;
- Atacicept, EMEA-002004-PIP01-16, from Merck KGaA, for the Treatment of systemic lupus erythematosus;
- Autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19, EMEA-001654-PIP02-17, from Novartis Europharm Limited, for the treatment of mature B-cell neoplasms;

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

- Fluticasone (propionate), EMEA-002140-PIP01-17, from Teva Pharmaceuticals Europe B.V., for the treatment of asthma;

For this medicine the PDCO granted a product-specific waiver on its own motion for all subsets of the

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

paediatric population in the specified condition, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

- Human normal immunoglobulin, EMEA-002163-PIP01-17, from Kedrion S.p.A., for the treatment of primary immunodeficiency;

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 over existing treatments for paediatric patients.

- Salmeterol (xinafoate) / fluticasone (propionate), EMEA-002177-PIP01-17, from Teva Pharmaceuticals Europe B.V., for the treatment of asthma;

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 over existing treatments for paediatric patients.

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:

- Litoxetine (benzoate), EMEA-002151-PIP01-17, from Ixaltis SA, for the Bladder and urethral symptoms (including incontinence);
- Burosumab, EMEA-001659-PIP02-16, from Ultragenyx Pharmaceutical Inc., for the treatment of tumor-induced osteomalacia;
- Human normal immunoglobulin, EMEA-002084-PIP01-16, from ProMetic BioTherapeutics Ltd., for the treatment of primary immunodeficiency;
- Human normal immunoglobulin, EMEA-002092-PIP01-16, from Biotest AG, for the treatment of primary immunodeficiency (PID) and for the Treatment of idiopathic thrombocytopenic purpura (ITP);
- Daratumumab, EMEA-002152-PIP02-17, from Janssen-Cilag International N.V., for the treatment of mature B-cell neoplasms;

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 / cobicistat / darunavir, EMEA-001825-PIP01-15-M01, from Janssen-Cilag International NV, for the Treatment of human immunodeficiency virus type-1 (HIV-1) infection;
- Lipegfilgrastim, EMEA-001019-PIP01-10-M04, from UAB "Sicor Biotech", for the Prevention of chemotherapy-induced febrile neutropenia and Treatment of chemotherapy-induced neutropenia;
- exenatide, EMEA-000689-PIP01-09-M07, from AstraZeneca AB, for the Treatment of type 2 diabetes mellitus;
- mepolizumab, EMEA-000069-PIP02-10-M08, from GlaxoSmithKline Trading Services, for the Treatment of asthma;
- Tilmanocept, EMEA-001255-PIP01-11-M02, from Norgine BV, for the Visualisation of lymphatic drainage of solid malignant tumours for diagnostic purposes;
- Brivaracetam, EMEA-000332-PIP01-08-M12, from UCB Pharma S.A., for the Treatment of epilepsy with partial onset seizures, Treatment of neonatal seizures and treatment of paediatric epilepsy syndromes;
- Autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19, EMEA-001654-PIP01-14-M02, from Novartis Europharm Limited, for the Treatment of B cell acute lymphoblastic leukaemia/lymphoblastic lymphoma;
- Trametinib (trametinib dimethyl sulfoxide), EMEA-001177-PIP01-11-M04, from Novartis Europharm Limited, for the Treatment of solid malignant tumours (excluding melanoma) and treatment of melanoma;
- elbasvir / grazoprevir, EMEA-001604-PIP01-13-M03, from Merck Sharp & Dohme (Europe), Inc., for the Treatment of chronic hepatitis C;
- Dabrafenib (dabrafenib mesilate), EMEA-001147-PIP01-11-M05, from Novartis Europharm Limited, for the Treatment of melanoma and Treatment of solid malignant tumours (excluding melanoma);
- Fidaxomicin, EMEA-000636-PIP01-09-M06, from Astellas Pharma Europe B.V., for the Treatment of enterocolitis caused by Clostridium difficile;
- Tenofovir disoproxil (fumarate), EMEA-000533-PIP01-08-M07, from Gilead Sciences International Ltd, for the Treatment of chronic viral hepatitis B and Treatment of human immunodeficiency virus (HIV-1) infection;
- cobicistat / darunavir, EMEA-001280-PIP01-12-M01, from Janssen-Cilag International NV, for the Treatment of HIV-1 infection;
- Human Fibrinogen, EMEA-001208-PIP01-11-M03, from Octapharma Pharmazeutika Produktionsges. m. b. H, for the Treatment of congenital fibrinogen deficiency;
- Sunitinib malate, EMEA-000342-PIP01-08-M06, from Pfizer Limited, for the Treatment of gastro-intestinal stromal tumour;

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

- lurasidone hydrochloride, EMEA-001230-PIP01-11-M03, from Sunovion Pharmaceuticals Ltd., for the Treatment of schizophrenia;

Opinion on compliance check

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

- vigabatrin, EMEA-C-000717-PIP02-13-M02, from ORPHELIA Pharma SA, for the Treatment of epilepsy;

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.

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 19 May 2017 for CYSTEAMINE HYDROCHLORIDE, EMEA-000322-PIP01-08-M05, from ORPHAN EUROPE SARL, for the treatment of corneal cystine crystal deposits in cystinosis, the PDCO adopted a revised positive opinion and agreed to the changes regarding the measures of the paediatric investigation plan and the timelines of the deferral in the scope set out in the Annex I of this opinion, and refusing the changes to the waiver.

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 6 applications were withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure).

Other matters

The PDCO welcomed the new member and alternate from Lithuania Sigita Burokiene and Goda Vaitkeviciene. The PDCO thanked Jorrit Gerritsen and Tsveta Schyns-Liharska for their work at the end of their mandate.

The next meeting of the PDCO will be held on 15 – 18 August 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

Enquiries to: AskEMA
(http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/landing/ask_ema_landing_page.jsp&mid=)