15 December 2017
EMA/PDCO/844387/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

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

12 – 15 December 2017

Opinions on paediatric investigation plans

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

- Lucerastat, EMEA-002095-PIP01-16, from Idorsia Pharmaceuticals Deutschland GmbH, for the treatment of Fabry disease;
- Upadacitinib, EMEA-001741-PIP02-16, from AbbVie Ltd, for the treatment of ulcerative colitis;
- Recombinant *Clostridium difficile* toxoid A / recombinant *Clostridium difficile* toxoid B, EMEA-002112-PIP01-16, from Pfizer Ltd, for the prevention of *Clostridium difficile* infection (CDI);
- Glutamine (levoglutamide), EMEA-001996-PIP02-16, from Emmaus Medical Europe Ltd., for the treatment of sickle cell disease;
- Gilteritinib (as fumarate), EMEA-002064-PIP01-16, from Astellas Pharma Europe B.V., for the treatment of acute myeloid leukemia;
- 1,4-dihydro-1-[(2R)-2-(2-methoxyphenyl)-2-[(tetrahydro-2H-pyran-4-yl)oxy]ethyl]-α,α,5-trimethyl-6-(2-oxazolyl)-2,4-dioxo-thieno[2,3-d]pyrimidine-3(2H)-acetic acid, EMEA-002109-PIP01-16, from Gilead Sciences International Ltd., for the treatment of non-alcoholic steatohepatitis;
- Obiltoxaximab, EMEA-002144-PIP01-17, from SFL Regulatory Affairs Consulting Ltd., for the prevention of bacillary infection and treatment of bacillary infection;
- Maralixibat chloride, EMEA-001475-PIP03-17, from Shire Pharmaceuticals Ireland Limited, for the treatment of progressive familial intrahepatic cholestasis (PFIC);
- Chloroprocaine (hydrochloride), EMEA-000639-PIP03-16, from Sintetica GmbH, for the peripheral nerve block (local anesthesia by perineural injection);
- Dienogest / ethinyl estradiol, EMEA-002229-PIP01-17, from Exeltis France S. A., for prevention of pregnancy

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

An agency of the European Union

© European Medicines Agency, 2018. Reproduction is authorised provided the source is acknowledged.

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:

- Rosuvastatin calcium / acetylsalicylic acid, EMEA-002239-PIP01-17, from Adamed Sp. z o.o., for the prevention of cardiovascular events;
- Tucatinib, EMEA-002242-PIP01-17, from Cascadian Therapeutics Luxembourg S.A.R.L., for the treatment of breast malignant neoplasms;
- Recombinant human epidermal growth factor, EMEA-002258-PIP01-17, from Praxis Pharmaceuticals S.A, for the treatment of diabetic foot ulcer;

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

- Fluorocholine (18F), EMEA-002129-PIP02-17, from UJV Rez, a. s., for the visualisation of choline metabolism in malignant 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:

- Reslizumab, EMEA-001202-PIP02-13-M02, from Teva Pharmaceuticals Europe, for the treatment of asthma;
- Pembrolizumab, EMEA-001474-PIP02-16-M01, from Merck Sharp & Dohme (Europe), Inc., for the treatment of Hodgkin lymphoma;
- Posaconazole, EMEA-000468-PIP02-12-M04, from Merck Sharp & Dohme (Europe), Inc., for the prevention of invasive fungal infections and treatment of invasive fungal infections;
- Birch pollen extract (Betula verrucosa), EMEA-001879-PIP01-15-M01, from ALK Abelló A/S, for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Human normal immunoglobulin, EMEA-001797-PIP01-15-M01, from Octapharma Pharmazeutika Produktionsges.m.b.H, for the treatment of primary immunodeficiency;
- Ceftaroline fosamil, EMEA-000769-PIP01-09-M07, from Pfizer Limited, for the treatment of community acquired pneumonia and treatment of complicated skin and soft tissue infections;
- Tofacitinib, EMEA-000576-PIP01-09-M08, from Pfizer Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis);
- Artenimol / Piperaquine tetraphosphate, EMEA-000153-PIP01-07-M05, from Alfasigma SpA, for the treatment of uncomplicated malaria caused by *Plasmodium faciparum*;

- Lumacaftor / ivacaftor, EMEA-001582-PIP01-13-M07, from Vertex Pharmaceuticals (Europe) Limited, for the treatment of cystic fibrosis;
- Linagliptin, EMEA-000498-PIP01-08-M07, from Boehringer Ingelheim International GmbH, for the treatment of type 2 diabetes mellitus;
- Empagliflozin, EMEA-000828-PIP01-09-M06, from Boehringer Ingelheim International GmbH, for the treatment of type 2 diabetes mellitus;
- Tenofovir alafenamide (as fumarate), EMEA-001584-PIP01-13-M03, from Gilead Sciences International Ltd., for the treatment of chronic viral hepatitis B;
- N-[(1,3-dicyclohexyl-6-hydroxy-2,4-dioxo-1,2,3,4-tetrahydro-5-pyrimidinyl)carbonyl]glycine, EMEA-001452-PIP01-13-M01, from GlaxoSmithKline Trading Services Limited, for the treatment of anaemia due to chronic disorders;
- Conestat alfa, EMEA-000367-PIP01-08-M07, from Pharming Group N.V., for the treatment of hereditary angioedema (HAE);
- Burosumab, EMEA-001659-PIP01-15-M03, from Ultragenyx Pharmaceutical Inc., for the treatment of X-linked hypophosphatemia;
- L-asparaginase encapsulated in erythrocytes, EMEA-000341-PIP02-09-M05, from ERYTECH pharma S.A., for the treatment of acute lymphoblastic leukaemia;
- Ixekizumab, EMEA-001050-PIP01-10-M03, from Eli Lilly & Company Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis) and treatment of psoriasis;
- Sitagliptin, EMEA-000470-PIP01-08-M10, from Merck Sharp and Dohme (Europe), Inc., for the treatment of type 2 diabetes mellitus;
- Tedizolid (phosphate), EMEA-001379-PIP01-12-M03, from Merck Sharp & Dohme (Europe) Inc., for the treatment of acute bacterial skin and skin structure infections;
- Baricitinib, EMEA-001220-PIP01-11-M02, from Eli Lilly and Company Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Recombinant *Neisseria meningitidis* group B NHBA fusion protein / recombinant *Neisseria meningitidis* group B NadA protein / recombinant *Neisseria meningitidis* group B fHbp fusion protein / Outer Membrane Vesicles (OMV) from *Neisseria meningitidis* group B strain NZ98/254 measured as amount of total protein containing the PorA P1.4, EMEA-000139-PIP01-07-M02, from GSK Vaccines S.r.l., for the prevention of meningococcal meningitis;
- Atazanavir (sulphate) / cobicistat, EMEA-001465-PIP01-13-M02, from Bristol-Myers Squibb Pharma EEIG, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Lacosamide, EMEA-000402-PIP02-11-M05, from UCB Pharma S.A., for the treatment of epilepsy with partial onset seizures;
- Regadenoson, EMEA-000410-PIP01-08-M02, from Rapidscan Pharma Solutions EU Limited, for the diagnosis of myocardial perfusion disturbances;
- Matrix applied characterised autologous cultured chondrocytes, EMEA-000979-PIP01-10-M02, from Vericel Denmark ApS, for the treatment of cartilage disorders

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

- Gadolinium, [α3,α6,α9-tris[3-[(2,3-dihydroxypropyl)amino]-3-oxopropyl]-3,6,9,15-tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene-3,6,9-triacetato(3-)-κN3,κN6,κN9,κN15,κO3,κO6,κO9]-(P03277), EMEA-001949-PIP01-16-M01, from GUERBET, for the detection and visualisation of areas with disruption of the blood brain barrier and/or abnormal vascularity for diagnostic purposes;
- Midostaurin, EMEA-000780-PIP01-09-M04, from Novartis Europharm Ltd, for the treatment of acute myeloid leukaemia, treatment of malignant mastocytosis and treatment of mast cell leukaemia;

Opinion on compliance check

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

- Clostridium Botulinum neurotoxin type A (150 kD), free from complexing proteins, EMEA-C-001039-PIP01-10-M02, from Merz Pharmaceuticals GmbH, for the treatment of muscle spasticity, treatment of dystonia and treatment of muscle-induced wrinkles;

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

- Dasatinib, EMEA-C-000567-PIP01-09-M04, from Bristol-Myers Squibb Pharma EEIG, for the treatment of Philadelphia chromosome (BCR-ABL translocation)-positive chronic myeloid leukaemia and treatment of Philadelphia chromosome (BCR-ABL translocation)-positive acute lymphoblastic leukaemia

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

The PDCO also noted that the application leading to the opinion adopted during the November PDCO meeting for Cannabidiol / delta-9-tetrahydrocannabinol, from GW Pharma Ltd, for the treatment of spasticity, has been withdrawn before the decision was issued by the Agency.

Other matters

The PDCO thanked Marianne Orholm from Denmark for her work as she has resigned from the Committee.

The next meeting of the PDCO will be held on 23 – 26 January 2018.

– 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=)