4 May 2016
EMA/PDCO/289960/2016
Procedure Management and Committees Support Division

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

27-29 April 2016

Opinions on paediatric investigation plans

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

- Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1), EMEA-001715-PIP01-14, from Seqirus S.r.l., for the prevention of influenza infection;
- Peanut flour, EMEA-001753-PIP02-15, from Cambridge Allergy Ltd, for the treatment of peanut allergy;
- Imipenem (monohydrate) / cilastatin (sodium) / relebactam, EMEA-001809-PIP01-15, from Merck Sharp & Dohme (Europe), Inc., for the treatment of Gram-negative bacterial infections;
- Recombinant humanized anti-MMP9 monoclonal antibody IgG4, EMEA-001813-PIP01-15, from Gilead Sciences International Ltd, for the treatment of ulcerative colitis and treatment of Crohn's disease;
- Methyl {(2S,3R)-1-[(2S)-2-{5-[(2R,5R)-1-{3,5-difluoro-4-[4-(4-fluorophenyl)piperidin-1-yl]phenyl}-5-(6-fluoro-2-{(2S)-1-[N-(methoxycarbonyl)-O-methyl-L-threonyl]pyrrolidin-2-yl}-1H-benzimidazol-5-yl)pyrrolidin-2-yl]-6-fluoro-1H-benzimidazol-2-yl}pyrrolidin-1-yl]-3-methoxy-1-oxobutan-2-yl}carbamate (ABT-530) / (3aR,7S,10S,12R,21E,24aR)-7-tert-butyl-N-[(1R,2R)-2-(difluoromethyl)-1-{[(1-methylcyclopropyl)sulfonyl] carbamoyl}cyclopropyl]-20,20-difluoro-5,8-dioxo-2,3,3a,5,6,7,8,11,12,20,23,24a-dodecahydro-1H,10H-9,12-methanocyclopenta[18,19][1,10,17,3,6] trioxadiazacyclononadecino[11,12-b]quinoxaline-10-carboxamide, EMEA-001832-PIP01-15, from AbbVie Ltd, for the treatment of chronic hepatitis C;
- Bexagliflozin, EMEA-001841-PIP01-15, from Theracos Sub, LLC., for the treatment of type 2 diabetes mellitus.

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

The PDCO adopted an opinion on the **refusal** of a PIP, including a waiver and deferral, for Pimavanserin, EMEA-001688-PIP02-15, from ACADIA Pharmaceuticals Inc., for the treatment of schizophrenia and other psychotic disorders.

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:

- Ibuprofen / Tramadol, EMEA-001887-PIP01-15, from FARMALIDER, S.A., for the treatment of pain;
- Imetelstat, EMEA-001910-PIP01-15, from Janssen-Cilag International N.V, for the treatment of myelofibrosis;
- Olmesartan (medoxomil)/Rosuvastatin (calcium), EMEA-001914-PIP01-15, from Daewoong Pharmaceutical Co., Ltd., for the treatment of hypertension, treatment of dyslipidaemia and prevention of cardiovascular events;
- Ciclosporin, EMEA-001916-PIP01-15, from Laboratoires Théa, for the treatment of keratoconjunctivitis sicca.

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:

- Liraglutide, EMEA-000128-PIP02-09-M02, from Novo Nordisk A/S, for the treatment of obesity;
- Eltrombopag, EMEA-000170-PIP01-07-M04, from Novartis Europharm Limited, for the treatment of Idiopathic Thrombocytopenia Purpura (ITP);
- Raltegravir, EMEA-000279-PIP01-08-M05, from Merck Sharp & Dohme (Europe), Inc., for the treatment of Human Immunodeficiency Virus (HIV-1) infection;
- Darbepoetin alfa, EMEA-000329-PIP02-09-M05, from Amgen Europe B.V., for the treatment of anaemia due to chronic disorders;

- Secukinumab, EMEA-000380-PIP02-09-M03, from Novartis Europharm Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, spondyloarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Melatonin, EMEA-000440-PIP02-11-M04, from RAD Neurim Pharmaceuticals EEC Ltd, for the treatment of insomnia;
- Sodium sulphate / potassium sulphate / magnesium sulphate heptahydrate, EMEA-000816-PIP02-10-M01, from Ipsen Pharma, for the diagnostic of organic and/or functional bowel diseases;
- Clostridium Botulinum neurotoxin type A (150 kD), free of complexing proteins, EMEA-001039-PIP01-10-M02, from Merz Pharmaceuticals GmbH, for the treatment of muscle spasticity, treatment of dystonia and treatment of muscle-induced wrinkles;
- Clostridium Botulinum neurotoxin type A (150 kD), free of complexing proteins, EMEA-001039-PIP02-12-M02, from Merz Pharmaceuticals GmbH, for the treatment of sialorrhoea;
- Alemtuzumab, EMEA-001072-PIP01-10-M02, from Genzyme Europe B.V., for the treatment of multiple sclerosis;
- Efmorocotocog alfa, EMEA-001114-PIP01-10-M03, from Biogen Idec Ltd, for the treatment of hereditary factor VIII deficiency;
- Naloxegol, EMEA-001146-PIP01-11-M02, from AstraZeneca AB, for the treatment of opioid-induced constipation;
- Ferric citrate (coordination complex), EMEA-001213-PIP02-12-M02, from Keryx Biopharmaceuticals, Inc., for the treatment of hyperphosphataemia;
- Tolvaptan, EMEA-001231-PIP02-13-M03, from Otsuka Pharmaceutical Europe Ltd., for the treatment of dilutional hyponatraemia and treatment of polycystic kidney disease;
- Retosiban, EMEA-001359-PIP01-12-M03, from GlaxoSmithKline Trading Services Limited, for the treatment of spontaneous preterm labour;
- Ibrutinib, EMEA-001397-PIP03-14-M01, from Janssen-Cilag International N.V., for the treatment of mature B-cell neoplasm;
- Atrasentan (hydrochloride), EMEA-001666-PIP01-14-M01, from AbbVie, Ltd, for the treatment of nephropathy.

The PDCO adopted 1 opinion on the **refusal** of modifications to an agreed PIP for:

- Tafluprost, EMEA-001187-PIP01-11-M03, from Santen Oy, for the treatment of glaucoma.

Adoption of an opinion following re-examination

The PDCO adopted opinions for the following product:

- Following the re-examination of the positive opinion on a modification of a Paediatric Investigation Plan adopted on 26 February 2016 for Coagulation Factor VIIa (Recombinant), EMEA-001203-PIP02-14-M01, from LFB SA, for the treatment of congenital coagulation disorders and treatment of acquired haemophilia, 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.

Opinion on compliance check

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

- Maraviroc, EMEA-C-000020-PIP01-07-M05, from ViiV Healthcare UK Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Tobramycin, EMEA-C-000184-PIP02-14, from Novartis Europharm Ltd., for the treatment of pseudomonas aeruginosa pulmonary infection/colonisation in patients with cystic fibrosis;
- Ciclosporin, EMEA-C-000575-PIP01-09-M03, from SANTEN OY, for the treatment of keratoconjunctivitis sicca and treatment of vernal keratoconjunctivitis.

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 PDCO thanked Witkowska-Ożogowska for her work at the end of her mandate as alternate for Poland.

The PDCO thanked Maria Grazia Valsecchi as she has resigned from the Committee.

The next meeting of the PDCO will be held on 25-27 May 2016.

– 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=)