EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 June 2013
EMA/356485/2013
Paediatric Committee (PDCO)

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

12-14 June 2013

Opinions on paediatric investigation plans

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

- Ferric citrate, from Keryx Biopharmaceuticals, Inc., for the treatment of hyperphosphataemia;
- 3-[[4-[(1S)-1-[4-(4-tert-butylphenyl)-3,5-dimethyl-phenoxy]-4,4,4-trifluorobutyl]benzoyl]amino]propanoic acid, from Eli Lilly and Company, for the treatment of type 2 diabetes mellitus;
- Alpha tocotrienol quinone, from Edison Orphan Pharma BV, for the treatment of Leigh syndrome;
- Mifepristone, from Corcept Therapeutics Incorporated, for the treatment of hypercortisolism (Cushing's syndrome) of endogenous origin;
- Recombinant Varicella Zoster Virus (VZV) glycoprotein E antigen, from GlaxoSmithKline Biologicals SA, for the prevention of VZV reactivation;
- Glucarpidase; from BTG International Ltd; for the treatment of methotrexate toxicity.

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:

7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 77523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

© European Medicines Agency, 2013. Reproduction is authorised provided the source is acknowledged.

- Lopinavir / lamivudine / ritonavir / zidovudine, from AbbVie Limited, for the treatment of human immunodeficiency virus, type 1 (HIV 1) infection;
- Capsici acris extractum spissum normatum, from Momaja s.r.o., for the treatment of painful peripheral neuropathy;
- Pegylated proline-interferon alpha-2b, from AOP Orphan Pharmaceuticals AG, for the treatment of polycythaemia vera;
- Clopidogrel (hydrogen sulphate) / acetylsalicylic acid, from Billev Pharma ApS, for the prevention of cardiovascular disease;
- Amlodipine / ramipril, from Adamed Sp. z o.o., for the treatment of hypertension.

The PDCO adopted one opinion on the **refusal** of a request for waiver for esketamine; from Janssen-Cilag International N.V.; for the treatment of major depressive disorder.

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:

- Colistimethate sodium, from Forest Laboratories UK Limited, for the treatment of Pseudomonas aeruginosa pulmonary infection/colonisation in patients with cystic fibrosis;
- Etravirine, from Janssen-Cilag International N.V, for the treatment of Human Immunodeficiency Virus Infection;
- Rivaroxaban, from Bayer Pharma AG, for the prevention of thromboembolic events and treatment of thromboembolic events;
- Perampanel, from Eisai Europe Limited, for the treatment of treatment-resistant epilepsies (localisation-related or generalised epilepsies and age-related epilepsy syndromes);
- C1 inhibitor, from ViroPharma SPRL, for the treatment of C1 inhibitor deficiency;
- Tofacitinib, from Pfizer Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis);
- Tofacitinib, from Pfizer Limited, for the treatment of psoriasis;
- Sildenafil, from Pfizer Limited, for the treatment of pulmonary arterial hypertension;
- 2'-O-methyl-uridylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-cytidylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-adenosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-adenosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-guanosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-guanosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-adenosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-adenosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-guanosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-adenosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-uridylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-guanosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-

guanosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-cytidylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-adenosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-uridylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-uridylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-uridylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-cytidylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-uridine sodium salt (exon 51 specific phosphorothioate oligonucleotide), from Glaxo Group Limited, for the treatment of Duchenne muscular dystrophy;

- Purified antigen fractions of inactivated split virion Influenza virus type A, H1N1 / Influenza virus type A, H3N2 / Influenza virus type B, Victoria lineage / Influenza virus type B, Yamagata lineage, from GlaxoSmithKline Biologicals S.A., for the prevention of influenza infection;
- Human normal immunoglobulin, from Bio Products Laboratory Limited, for the treatment of primary immunodeficiency as model for replacement therapy and treatment of idiopathic thrombocytopenic purpura as model for immunomodulation;
- Cobicistat, from Gilead Sciences International Limited, for the treatment of human immunodeficiency virus type-1 (HIV-1) infection;
- Laquinimod (sodium), from Teva Pharma GmbH, for the treatment of relapsing remitting multiple sclerosis.

Opinion on compliance check

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

- Influenza Virus Type A, H1N1 / Influenza Virus Type A, H3N2 / Influenza Virus Type B, Yamagata lineage / Influenza Virus Type B, Victoria lineage, from MedImmune Limited, for the prevention of influenza infection;
- Recombinant L-asparaginase; from medac Gesellschaft für klinische Spezialpräparate mbH; for the treatment of acute lymphoblastic leukaemia and treatment of lymphoblastic lymphoma;

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 3 applications were withdrawn during the late stages of the evaluation (30 days or less before opinion).

Other matters

The PDCO thanked for their work and dedication following the end of their mandate to Johannes Taminiau (The Netherlands), Vlasta Kakosova and Jan Mazag (Slovakia) and Marta Granström (Sweden).

The PDCO also thanked Janez Jazbec (Slovenia) for his commitment and hard work as he resigned from the Committee.

The next meeting of the PDCO will be held on 17-19 July 2013.

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 only to: paediatrics@ema.europa.eu

Annex of the June 2013 PDCO meeting report

	2011 (January to December)	2012 (January to December)	2013 (January to current month)	Cumulative total (2007 to present)
Total number of validated PIP/waiver applications	187	178	95	1417[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	153	149	84	1083 *(76%)*
Applications submitted for a product already authorised and still under patent, in view of a submission of a variation/extension for a new indication, pharmaceutical form or route of administration *(Article 8[2])*	33	28	11	307 *(22%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	1	1	0	27 *(2%)*
PIPs and full waiver indications covered by these applications	220	218	108	1910

Number of Paediatric Committee (PDCO) opinions	2011	2012	2013	Cumulative total (2007 to present)
Positive on full waiver	45	47	29	297
Positive on PIP, including potential deferral	107	87	60	660
Negative opinions adopted	3	3	2	32
Positive opinions adopted on modification of a PIP	153	165	78	558
Negative opinions adopted on modification of a PIP	2	1	2	8
Positive opinions on compliance with a PIP	9	4	6	41
Negative opinions on compliance check with a PIP	0	0	0	1
Opinions adopted under Art. 14.2	0	0	0	2

[1] Of which 371 have been requests for a full waiver.
[2] Applications submitted in accordance with the referenced article of Regulation (EC) No 1901/2006, as amended.

Areas covered by PIPs/waiver applications	2011 *(Number of areas covered)**	2012 *(Number of areas covered)**	2013 *(Number of areas covered)**
Neurology	11	11	6
Uro-nephrology	4	5	5
Gastroenterology-hepatology	10	8	8
Pneumology-allergology	10	9	3
Infectious diseases	15	19	10
Cardiovascular diseases	21	34	10
Diagnostics	5	3	2
Endocrinology-gynaecology-fertility-metabolism	28	27	12
Neonatology-paediatric intensive care	0	2	2
Immunology-rheumatology-transplantation	13	15	3
Psychiatry	9	0	5
Pain	2	9	2
Haematology-haemostaseology	18	9	9
Otorhinolaryngology	2	1	0
Oncology	19	19	17
Dermatology	10	14	5
Vaccines	12	2	3
Ophthalmology	8	5	2
Anaesthesiology	1	2	0
Nutrition	0	0	0
Other	7	16	6

** One PIP can cover several therapeutic areas*