13 February 2013
EMA/PDCO/92072/2013
Paediatric Committee (PDCO)

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

06-08 February 2013

Opinions on paediatric investigation plans

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

- Clonidine (hydrochloride), from Therakind Limited, for the sedation;
- Etoxybamide, from Dr. Franz Köhler Chemie GmbH, for the sedation;
- Anacetrapib, from Merck Sharp & Dohme (Europe), Inc., for the treatment of hypercholesterolaemia and prevention of cardiovascular events in patients with hypercholesterolaemia;
- Pegylated human recombinant factor VIII (BAX 855), from Baxter Innovations GmbH, for the treatment of congenital factor VIII deficiency;
- Oritavancin (diphosphate), from The Medicines Company, for the treatment of skin and subcutaneous tissue bacterial infections;
- Vancomycin, from Fondazione PENTA Onlus, for the treatment of bacterial sepsis;
- Sarilumab, from sanofi-aventis recherche & développement, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Baricitinib, from Eli Lilly & Company Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Autologous CD34+ Cells Transduced ex-vivo with Retroviral Vector (GIADAI) Containing Human Adenosine Deaminase Gene from cDNA, from Glaxo Group Ltd, for the treatment of severe combined immunodeficiency due to adenosine deaminase deficiency;
- Gabapentin, from Pharm SRL, for the treatment of chronic pain;
- Asfotase alfa, from Alexion Europe SAS, for the treatment of hypophosphatasia.

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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:

- Bisoprolol / amlodipine, from Krka, d.d., Novo mesto, for the treatment of hypertension and treatment of ischaemic coronary artery disorders;
- Hexaminolevulinate, from Photocure ASA, for the treatment of cervical dysplasia and diagnosis of bladder cancer;
- Alendronic acid / colecalciferol, from TEVA Pharma B.V., for the treatment of osteoporosis;
- Lutetium [177 Lu], from I.D.B. Radiopharmacy B.V., as radiolabelling agent;
- Sialic acid, from Ultragenyx Pharmaceutical Inc., for the treatment of distal myopathy, Nonaka type (Hereditary Inclusion Body Myopathy).

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:

- Saxagliptin, from Bristol Myers Squibb / AstraZeneca EEIG, for the treatment of type 2 diabetes mellitus;
- Ambrisentan, from Glaxo Group Limited, for the primary and secondary pulmonary hypertension;
- Vedolizumab, from Takeda Global Research & Development Centre (Europe) Ltd, for the treatment of Crohn's disease and treatment of ulcerative colitis;
- Everolimus, from Novartis Europharm Limited, for the prevention of rejection of transplanted kidney, prevention of rejection of transplanted heart and prevention of rejection of transplanted liver;
- Belimumab, from Glaxo Group Limited, for the treatment of systemic lupus erythematosus;
- Dalbavancin, from Durata Therapeutics, Inc., for the treatment of skin and soft tissue infections;
- Elvitegravir, from Gilead Sciences International Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;

- Mepolizumab, from Glaxo Group Limited, for the treatment of asthma;
- Beclometasone dipropionate / formoterol fumarate dihydrate, from Chiesi Farmaceutici S.p.A., for the treatment of asthma;
- Retigabine, from Glaxo Group Limited, for the treatment of epilepsy with partial onset seizures, and treatment of lennox-gastaut syndrome;
- Brivaracetam, from UCB Pharma SA, for the treatment of paediatric epilepsy syndromes, treatment of neonatal seizures, treatment of epilepsy with partial onset seizures and treatment of generalised epilepsy;
- Aprepitant, from Merck Sharp & Dohme Ltd., for the prevention of nausea and vomiting;
- Bimatoprost, from Allergan Pharmaceuticals Ireland, for the treatment of glaucoma and treatment of non-scarring hair loss;
- Tapentadol (hydrochloride), from Grünenthal GmbH, in the treatment of acute pain;
- Guanfacine (hydrochloride), from Shire Pharmaceuticals Contracts Ltd., for the treatment of attention deficit hyperactivity disorder (ADHD).

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

- Everolimus, from Novartis Europharm Limited, for the treatment of subependymal giant cell astrocytoma and treatment of angiomyolipoma.

Opinion on compliance check

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

- Paliperidone / paliperidone palmitate, from Janssen-Cilag International NV, for schizophrenia and schizoaffective disorder;
- Propranolol hydrochloride, from Pierre Fabre Dermatologie, for the treatment of haemangioma.

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).

The PDCO also noted that an opinion adopted during the January PDCO meeting for Tolvaptan, from Otsuka Pharmaceutical Europe Ltd., for the treatment of hyponatraemia, treatment of autosomal dominant polycystic kidney disease (ADPKD) and treatment of autosomal recessive polycystic kidney disease (ARPKD), has been withdrawn before the decision was adopted by the Agency.

Committee interactions

The PDCO adopted an opinion on a List of Questions issued by the CHMP to the PDCO on an ongoing assessment of Votubia in the field of neurology / oncology.

Two members of the Advanced Therapies Committee (CAT) attended the February meeting of the PDCO by teleconference bringing state-of-the-art knowledge to the PDCO scientific discussions as part of the collaboration between Committees.

Other matters

The next meeting of the PDCO will be held on 13-15 March 2013.

– 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 only to: paediatrics@ema.europa.eu

Annex of the February 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	28	1350[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	153	149	26	1025 *(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	2	298 *(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	32	1834

Number of Paediatric Committee (PDCO) opinions	2011	2012	2013	Cumulative total (2007 to present)
Positive on full waiver	45	47	13	281
Positive on PIP, including potential deferral	107	87	24	624
Negative opinions adopted	3	3	1	31
Positive opinions adopted on modification of a PIP	153	165	28	508
Negative opinions adopted on modification of a PIP	2	1	2	8
Positive opinions on compliance with a PIP	9	4	4	39
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 348 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	1
Uro-nephrology	4	5	1
Gastroenterology-hepatology	10	8	2
Pneumology-allergology	10	9	1
Infectious diseases	15	19	4
Cardiovascular diseases	21	34	3
Diagnostics	5	3	2
Endocrinology-gynaecology-fertility-metabolism	28	27	5
Neonatology-paediatric intensive care	0	2	2
Immunology-rheumatology-transplantation	13	15	1
Psychiatry	9	0	1
Pain	2	9	0
Haematology-haemostaseology	18	9	1
Otorhinolaryngology	2	1	0
Oncology	19	19	2
Dermatology	10	14	3
Vaccines	12	2	1
Ophthalmology	8	5	0
Anaesthesiology	1	2	0
Nutrition	0	0	0
Other	7	16	2

** One PIP can cover several therapeutic areas*