29 May 2013
EMA/PDCO/310894/2013
Paediatric Committee (PDCO)

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

15-17 May 2013

Opinions on paediatric investigation plans

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

- Evacetrapib, from Eli Lilly and Company, for the treatment of hypercholesterolaemia and treatment of hypo-HDL-cholesterolaemia;
- Clostridium Botulinum neurotoxin type A (150 kD), free of complexing proteins, from Merz Pharmaceuticals GmbH, for the treatment of sialorrhoea;
- Dry extract from Betulae cortex, from Birken AG, for the treatment of skin injuries;
- Isavuconazonium (sulfate), from Astellas Pharma Europe B.V., for the treatment of Candida infections;
- Isavuconazonium (sulfate), from Astellas Pharma Europe B.V., for the treatment of invasive aspergillosis and treatment of mucormycosis;
- Cebranopadol, from Grünenthal GmbH, for the treatment of chronic pain;
- Estetrol / Drospirenone, from Estetra S.A., for oral contraception;
- Human fibrinogen / human thrombin, from ProFibrix BV, for the treatment of haemorrhage resulting from a surgical procedure;
- Metformin (hydrochloride), from EffRx Pharmaceuticals SA, for the treatment of polycystic ovary syndrome;
- Phenylephrine hydrochloride / ketorolac trometamol (OMS302), from Omeros Corporation, for lens therapeutic procedures;
- Glycopyrronium bromide, from Proveca Limited, for the treatment of sialorrhoea;
- Terbinafine hydrochloride, from Polichem SA, for the treatment of onychomycosis.

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

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:

- Ketoprofen / Omeprazole, from Conventia Healthcare LLP, for the treatment of pain;
- Ibrutinib, from Janssen-Cilag International N.V., for the treatment of mantle cell lymphoma;
- Ixazomib (citrate), from Takeda Global Research & Development Centre (Europe) Ltd, for the treatment of systemic light chain amyloidosis;
- Zolpidem tartrate, from Transcept Pharmaceuticals, Inc, for the treatment of insomnia;

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:

- Zoledronic acid, from Novartis Europharm Limited, for the treatment of osteoporosis and treatment of Paget's disease of the bone;
- Cysteamine hydrochloride, from Orphan Europe SARL, for the treatment of cystinosis;
- Selexipag, from Actelion Registration Ltd, for the treatment of pulmonary arterial hypertension;
- Adalimumab, from AbbVie Limited, for the treatment of ulcerative colitis;
- Ataluren (3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid), from PTC Therapeutics, Limited, for the treatment of cystic fibrosis;
- Icatibant acetate, from Shire Orphan Therapies GmbH, for the treatment of hereditary angioedema (HAE);
- Human coagulation Factor VIII / von Willebrand Factor, from CSL Behring, for the treatment of hereditary Factor VIII deficiency (Haemophilia A) and treatment of von Willebrand disease;
- Apremilast, from Celgene Europe Limited, for the treatment of psoriasis;
- Oseltamivir (phosphate), from Roche Registration Ltd, for the treatment and prevention of influenza;

- Canakinumab, from Novartis Europharm Limited, for the treatment of juvenile idiopathic arthritis, treatment of cryopyrin associated periodic syndromes (CAPS) including familial cold autoinflammatory syndrome (FCAS) / familial cold urticaria (FCU) / Muckle-Wells syndrome (MWS) and Neonatal-onset multisystem inflammatory disease (NOMID) / chronic infantile neurological, cutaneous, articular syndrome (CINCA);
- Voriconazole, from Pfizer Limited, for the treatment of invasive aspergillosis, treatment of candidaemia in non-neutropenic patients, treatment of fluconazole-resistant serious invasive candida infections (including C. krusei), treatment of serious fungal infections caused by Scedosporium spp. and Fusarium spp and Prevention of invasive fungal infections;

Withdrawals

The PDCO noted that 6 applications were withdrawn during the late stages of the evaluation (30 days or less before opinion).

Interaction with external experts

The PDCO has regular interactions with academic experts, with a view to bringing state-of-the-art knowledge to the PDCO scientific discussions. One expert was invited to the May meeting with a clinical expertise in paediatric haematology-oncology and haematopoietic stem cell transplantation (HSCT), the PDCO discussed the role of HSC transplants in children and the opportunities for improving disease- and transplant-related outcomes.

Committee interactions

One member of the Herbal Medicines Products Committee (HMPC) attended the May meeting of the PDCO bringing state-of-the-art knowledge to the PDCO scientific discussions as part of the collaboration between Committees.

Other matters

The PDCO welcomed the new member, George Savva, nominated to represent Cyprus.

The PDCO thanked Andreas Teloudes for his work following the end of his mandate.

The PDCO thanked Dorthe Meyer for her work as she has resigned from the Committee.

The PDCO welcomed Karl-Heinz Huemer in his new role as member and Christoph Male in his new role as alternate, nominated to represent Austria. The change of roles will take effect from July 2013 onward.

The next meeting of the PDCO will be held on 12-14 June 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 May 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	79	1401[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	153	149	69	1068 *(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	10	306 *(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	91	1893

Number of Paediatric Committee (PDCO) opinions	2011	2012	2013	Cumulative total (2007 to present)
Positive on full waiver	45	47	24	292
Positive on PIP, including potential deferral	107	87	54	654
Negative opinions adopted	3	3	1	31
Positive opinions adopted on modification of a PIP	153	165	65	545
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 365 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	4
Uro-nephrology	4	5	5
Gastroenterology-hepatology	10	8	6
Pneumology-allergology	10	9	3
Infectious diseases	15	19	9
Cardiovascular diseases	21	34	6
Diagnostics	5	3	2
Endocrinology-gynaecology-fertility-metabolism	28	27	9
Neonatology-paediatric intensive care	0	2	2
Immunology-rheumatology-transplantation	13	15	3
Psychiatry	9	0	3
Pain	2	9	2
Haematology-haemostaseology	18	9	9
Otorhinolaryngology	2	1	0
Oncology	19	19	15
Dermatology	10	14	5
Vaccines	12	2	2
Ophthalmology	8	5	1
Anaesthesiology	1	2	0
Nutrition	0	0	0
Other	7	16	5

** One PIP can cover several therapeutic areas*