EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Paediatric Committee (PDCO)

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

06-08 June 2012

Opinions on paediatric investigation plans

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

- Serelaxin, from Novartis Europharm Ltd., in the therapeutic area of cardiovascular disease;
- Ethanol, from Orfagen, in the therapeutic area of dermatology;
- Migalastat (hydrochloride), from Glaxo Group Limited, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Apremilast, from Celgene Europe Limited, in the therapeutic area of immunology-rheumatology-transplantation;
- Potassium (chloride) / magnesium (sulphate heptahydrate) / procaine (hydrochloride) / xylitol, from Swiss Cardio Technologies AG, in the therapeutic area of cardiac surgery;
- Brexpiprazole, from Otsuka Frankfurt Research Institute GmbH, in the therapeutic area of psychiatry;
- Lurasidone (hydrochloride), from Takeda Global Research & Development Centre (Europe) Ltd., in the therapeutic area of psychiatry;
- Trivalent, seasonal, recombinant influenza hemagglutinin vaccine, from Protein Sciences Europa, in the therapeutic area of vaccines / infectious diseases.

Adoption of an opinion following re-examination

The PDCO adopted opinions for the following products:

- Following the re-examination of the negative opinion for a full waiver adopted 13 April 2012 for ranirestat, from Eisai Ltd, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism, the PDCO maintained its opinion and adopted a negative opinion for full waiver.

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- Following the re-examination of the negative opinion for a PIP and waiver adopted 13 April 2012 for bivalirudin, from The Medicines Company UK Limited, in the therapeutic area of cardiovascular disease, the PDCO maintained its opinion and adopted a negative opinion for PIP with Deferral.

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.

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:

- Ezetimibe / simvastatin, from MSD-SP Limited, in the therapeutic area of cardiovascular diseases;
- Ezetimibe, from from MSD-SP Limited, in the therapeutic area of cardiovascular diseases;
- Tafluprost / timolol, from Santen Oy, in the therapeutic area of ophthamology;

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

- Tivantinib, from Daiichi Sankyo Development Limited, in the therapeutic area of oncology.

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:

- Propranolol hydrochloride, from Pierre Fabre Dermatologie, in the therapeutic area of dermatology;
- Bilastine, from Faes Farma S.A., in the therapeutic area of dermatology / pneumology - allergology / oto-rhino-laryngology;
- Velaglucerase alfa, from Shire Pharmaceuticals Ireland Limited, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Romiplostim, from Amgen Europe B.V., in the therapeutic area of haematology-hemostaseology;
- Human coagulation Factor VIII / von Willebrand Factor, from CSL Behring, in the therapeutic area of haematology-hemostaseology;
- Nonacog alfa (recombinant coagulation factor IX), from Baxter Innovations GmbH, in the therapeutic area of haematology-hemostaseology;
- Turoctocog alfa, from Novo Nordisk A/S, in the therapeutic area of haematology-hemostaseology;

- Abatacept, from Bristol-Myers Squibb Pharma EEIG, in the therapeutic area of immunology-rheumatology-transplantation;
- Human normal immunglobulin, from Baxter Innovations GmbH, in the therapeutic area of immunology-rheumatology-transplantation;
- Human normal immunglobulin, from Octapharma Pharmazeutika Produktionsges.m.b.H, in the therapeutic area of immunology-rheumatology-transplantation/ haematology-hemostaseology;
- Voriconazole, from Pfizer Limited, in the therapeutic area of infectious diseases;
- Lopinavir / ritonavir, from Abbott Laboratories Limited, in the therapeutic area of infectious diseases;
- Tobramycin, from Novartis Europharm Limited, in the therapeutic area of infectious diseases / pneumology - allergology;
- Aprepitant, from Merck Sharp & Dohme Ltd., in the therapeutic area of oncology;
- Fosaprepitant, from Merck Sharp & Dohme Ltd., in the therapeutic area of oncology;
- Ivacaftor, from Vertex Pharmaceuticals Incorporated, in the therapeutic area of other (congenital, hereditary, and neonatal diseases and abnormalities);
- Sildenafil, from Pfizer Limited, in the therapeutic area of other (Pulmonary vascular disease);
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extract from the pollen of Betula alba, from Leti Pharma GmbH, in the therapeutic area of pneumology - allergology;
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extract of birch, alder and hazel pollen, from Leti Pharma GmbH, in the therapeutic area of pneumology - allergology;
- Aripiprazole, from Otsuka Pharmaceutical Europe Ltd, in the therapeutic area of psychiatry;
- Purified antigen fractions of inactivated split virion Influenza H5N1, from GlaxoSmithKline Biologicals S.A., in the therapeutic area of vaccines;
- Purified antigen fractions of inactivated split virion Influenza A/Indonesia/5/05/ (H5N1), from GlaxoSmithKline Biologicals S.A., in the therapeutic area of vaccines.

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

- Zoledronic acid, from Novartis Europharm Limited, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism.

Withdrawals

The PDCO noted that two 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 June meeting with a clinical expertise in paediatric oncology and haematology, the PDCO discussed aspects of paediatric medical needs and of clinical trial designs.

Informal meeting

On 24-25 May 2012, the PDCO held an informal meeting in Denmark to review the work done and the processes put in place during its sixth year. The PDCO discussed improvements in the functioning of the PDCO, in particular timelines, summary reports, interactions with experts, learned societies and industry, and priorities in the implementation of the Paediatric Regulation.

Other matters

The next meeting of the PDCO will be held on 04-06 July 2012 in Langen, Germany.

– 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

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Annex of the June2012 PDCO meeting report

	2010 (January to December)	2011 (January to December)	2012 (January to current month)	Cumulative total (2007 to present)
Total number of validated PIP/waiver applications	326	187	88	1232[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	280	153	68	918 *(75%)*
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])*	43	33	20	288 *(23%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	4	1	0	26 *(2%)*
PIPs and full waiver indications covered by these applications	403	220	111	1695

Number of Paediatric Committee (PDCO) opinions	2010	2011	2012	Cumulative total (2007 to present)
Positive on full waiver	52	45	13	234
Positive on PIP, including potential deferral	201	107	41	554
Negative opinions adopted	7	3	3	30
Positive opinions adopted on modification of a PIP	103	153	83	398
Negative opinions adopted on modification of a PIP	4	2	1	7
Positive opinions on compliance with a PIP	9	9	1	32
Negative opinions on compliance check with a PIP	0	0	0	1
Opinions adopted under Art. 14.2	2	0	0	2

[1] Of which 298 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	2010 *(%)*	2011 *(Number of areas covered)**	2012 *(Number of areas covered)**
Neurology	3	11	5
Uro-nephrology	2	4	2
Gastroenterology-hepatology	1	10	2
Pneumology-allergology	41	10	5
Infectious diseases	4	15	12
Cardiovascular diseases	8	21	18
Diagnostics	1	5	0
Endocrinology-gynaecology-fertility-metabolism	6	28	11
Neonatology-paediatric intensive care	0	0	1
Immunology-rheumatology-transplantation	5	13	8
Psychiatry	1	9	0
Pain	1	2	2
Haematology-haemostaseology	4	18	5
Otorhinolaryngology	3	2	1
Oncology	9	19	12
Dermatology	1	10	5
Vaccines	2	12	2
Ophthalmology	4	8	3
Anaesthesiology	2	1	1
Nutrition	0	0	0
Other		7	6

** One PIP can cover several therapeutic areas*