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

14-16 May 2012

Opinions on paediatric investigation plans

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

- Ulimorelin, from Norgine Ltd, in the therapeutic area of gastroenterology-hepatology;
- Tafluprost, from Merck Sharp & Dohme (Europe), Inc., in the therapeutic area of ophthalmology;
- Azithromycin (monohydrate), from Ixodes AG, in the therapeutic area of infectious diseases / dermatology;
- Odanacatib, from Merck Sharp & Dohme (Europe), Inc., in the therapeutic area of immunology-rheumatology-transplantation;
- Cabozantinib (S)-malate, from Exelixis, Inc., in the therapeutic area of oncology;
- Ponatinib, from Ariad Pharma, Ltd., in the therapeutic area of oncology;
- Lumacaftor, from Voisin Consulting SARL, in the therapeutic area of pneumology – allergology;
- Melatonin, from RAD Neurim Pharmaceuticals EEC Ltd, in the therapeutic area of neurology;
- Albiglutide, from GlaxoSmithKline LLC, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Golimumab, from Janssen Biologics B.V., in the therapeutic area of immunology-rheumatology-transplantation / gastroenterology-hepatology.

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.

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Adoption of an opinion following re-examination

The PDCO adopted an opinion for the following product:

- Following the re-examination of the positive opinion on a PIP adopted on 9 March 2012 for Liraglutide, from Novo Nordisk A/S, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism, 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.

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:

- Amlodipine (besilate) / valsartan, from Synthon B.V., in the therapeutic area of cardiovascular diseases;
- Alisporivir, from Novartis Europharm Ltd, in the therapeutic area of infectious diseases;
- Masitinib (mesylate), from AB Science, 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:

- Liraglutide, from Novo Nordisk A/S, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Rivaroxaban, from Bayer Pharma AG, in the therapeutic area of cardiovascular diseases;
- Tadalafil, from Eli Lilly and Company Limited, in the therapeutic area of cardiovascular diseases;
- Tenofovir (disoproxil fumarate), from Gilead Sciences International Limited, in the therapeutic area of infectious diseases;
- Ozenoxacin, from Ferrer Internacional, S.A., in the therapeutic area of infectious diseases;
- Perampanel, from Eisai Ltd, in the therapeutic area of neurology;
- (3aR,4S,7aR)-Octahydro-4-hydroxy-4-[(3-methylphenyl)ethynyl]-1H-indole-1-carboxylic acid methyl ester (AFQ056), from Novartis Europharm Ltd, in the therapeutic area of neurology;

- Ipilimumab, from Bristol-Myers Squibb Pharma EEIG, in the therapeutic area of oncology;
- Tiotropium bromide (monohydrate), from Boehringer Ingelheim International GmbH, in the therapeutic area of pneumology – allergology;
- Modified grass pollen extract, from Allergy Therapeutics (UK) Ltd., in the therapeutic area of pneumology – allergology;
- Asenapine (maleate), from N.V. Organon, in the therapeutic area of psychiatry;
- Cinacalcet hydrochloride, from Amgen Europe B.V., in the therapeutic area of uro-nephrology;
- Canakinumab, from Novartis Europharm Limited, in the therapeutic area of immunology-rheumatology-transplantation;
- Bimatoprost, from Allergan Pharmaceuticals Ireland, in the therapeutic area of ophthalmology / dermatology.

Withdrawals

The PDCO noted that four applications, of which three were requests of modifications to agreed PIPs, were withdrawn during the late stages of the evaluation (30 days or less before opinion).

PDCO interactions

A hearing with the European Allergen Manufacturer Group (EAMG) delegation took place during the meeting, in order to exchange views with the PDCO. Specific issues of the Standard PIP for Allergen Specific Immunotherapy were discussed at the meeting. The PDCO members acknowledged the concerns raised by the EAMG and invited manufacturers and experts to suggest alternate study designs which would allow generating robust data demonstrating both short and long-term efficacy.

A member of the Advanced Therapies Committee (CAT) attended the April 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 a new observer from Croatia, Dr Igor Francetic, who has been nominated by Ministry of Heath of the Republic of Croatia.

The PDCO thanked Timothy Chambers for his work as he has resigned from the Committee.

The next meeting of the PDCO will be held on 06-08 June 2012.

The European Medicines Agency will not host meetings during the month of July due to the Olympic Games taking place in London. The PDCO plenary, 04-06 July 2012, will be held at the Paul-Ehrlich-Institute in Langen, Germany.

– END –

Notes:

1. 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

2. 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.

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 I of the May 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	75	1219[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	280	153	57	907 *(74%)*
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	18	286 *(24%)*
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	98	1682

Number of Paediatric Committee (PDCO) opinions	2010	2011	2012	Cumulative total (2007 to present)
Positive on full waiver	52	45	10	231
Positive on PIP, including potential deferral	201	107	33	546
Negative opinions adopted	7	3	2	29
Positive opinions adopted on modification of a PIP	103	153	61	376
Negative opinions adopted on modification of a PIP	4	2	0	6
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 293 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	4
Uro-nephrology	2	4	2
Gastroenterology-hepatology	1	10	2
Pneumology-allergology	41	10	4
Infectious diseases	4	15	9
Cardiovascular diseases	8	21	15
Diagnostics	1	5	0
Endocrinology-gynaecology-fertility-metabolism	6	28	10
Neonatology-paediatric intensive care	0	0	1
Immunology-rheumatology-transplantation	5	13	6
Psychiatry	1	9	0
Pain	1	2	2
Haematology-haemostaseology	4	18	3
Otorhinolaryngology	3	2	1
Oncology	9	19	11
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*