European Medicines Agency

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PRESS RELEASE

Meeting highlights from the Paediatric Committee, 14-16 October 2009

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

- **Nomegestrol acetate and 17beta - estradiol**, from NV Organon (part of Schering Plough), in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- **Imatinib**, from Novartis Europharm Limited, in the therapeutic area of oncology;
- **Diphtheria toxoid, tetanus toxoid, inactivated poliovirus: type 2 (MEF-1 strain), inactivated poliovirus: type 3 (Saukett strain), inactivated poliovirus: type 1 (Mahoney strain), Bordetella pertussis antigens: filamentous haemagglutinin, pertactin, pertussis toxoid**, from GlaxoSmithKline Biologicals S.A, in the therapeutic area of vaccines;
- **Dasatinib**, from Bristol-Myers Squibb Pharma EEIG, in the therapeutic area of oncology;
- **Sildenafil citrate**, from Pfizer Limited, in the therapeutic area of cardiovascular diseases;
- **Exenatide**, from Eli Lilly and Company, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism.

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 (EMEA), 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:

- **Simvastatin / ramipril / acetyl salicylic acid**, from Ferrer Internacional, S.A., in the therapeutic area of cardiovascular diseases;
- **Saxagliptin / metformin**, from Bristol-Myers Squibb / AstraZeneca EEIG, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- **Fluorouracil / salicylic acid**, from Almirall Hermal GmbH, in the therapeutic area of dermatology;
- **Aliskiren hemifumarate / amlodipine besilate / hydrochlorothiazide**, from Novartis Europharm Ltd., in the therapeutic area of cardiovascular diseases;
- **Olmesartan medoxomil / amlodipine besilate / hydrochlorothiazide**, from Daiichi Sankyo Europe GmbH, in the therapeutic area of cardiovascular diseases.

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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.

Class waivers

The PDCO adopted an opinion on the confirmation of the current list of class waivers for conditions that do not affect children, or for classes of medicinal products to be used in specific conditions, and for which the requirement to submit a PIP can therefore be waived. The list of class waivers is updated at least once a year by the PDCO.

Adoption of a class waiver

The PDCO adopted an opinion on a condition class waiver for medicinal products for the treatment of laryngeal or nasal epithelial carcinoma, Fallopian tube carcinoma, peritoneal carcinoma, gastroenteropancreatic neuroendocrine tumours, ureteral carcinomas, vaginal and vulvar carcinoma. The Committee recommended that the requirement to submit clinical-trial data in all subsets of the paediatric population be waived for medicines belonging to this class and/or developed in this condition. This is because the conditions do normally not occur in some or all of the paediatric populations.

The opinion will be transformed into an EMEA decision.

The EMEA already adopted decisions on a list of waivers in April 2009 for conditions that do not occur in children, or for products likely to be unsafe or ineffective in children. The list of waivers is regularly updated in light of the advance in knowledge and science in the paediatric field.

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.

Opinion on compliance check

The PDCO adopted a positive opinion on compliance check for **Leucine / potassium acetate / cysteine / glutamic acid / praline / alanine / glycine / histidine / isoleucine / magnesium acetate tetrahydrate / olive oil, refined / methionine/ ornithine hcl / phenylalanine / tryptophan / valine/ taurine / tyrosine / sodium chloride / arginine / calcium chloride dihydrate / aspartic acid / serine / threonine / sodium glycerophosphate, hydrated / soya-bean oil, refined / lysine monohydrate / glucose monohydrate**, from Baxter World Trade SPRL in the therapeutic area of nutrition.

A compliance check is performed to verify that all the measures agreed in a PIP and reflected in the EMEA decision have been conducted in accordance with the decision, including the agreed timelines. Compliance 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 EMEA 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 eight applications, of which four were applications for modifications to an agreed PIP, were withdrawn during the late stages of the evaluation (30 days or less before opinion). The PDCO noted that a request for modification of an agreed PIP was withdrawn before the EMEA decision.

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. Two experts were invited to the October meeting with a clinical expert in paediatric intensive care and paediatric radiology. The PDCO discussed feasibility of performing studies in children with severe sepsis and the use of cardiac imaging techniques.

In addition three experts from the Paul Ehrlich Institute were invited to discuss the development of a "standard PIP" for allergen products for specific immunotherapy.

Informal meeting
On 1-2 October 2009, the PDCO held an informal meeting in Sweden, to review the work done and the processes put in place during its third year, and a joint meeting with the Committee for Orphan Medicinal Products (COMP). 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 issues
The PDCO welcomed the new alternate from Norway, Dr Ine Blankenberg Skottheim, who has been nominated by Norwegian Medicines Agency.
The PDCO thanked Ingvild Aaløkken for her work as she has resigned from the Committee.

The next meeting of the PDCO will be held on 11-13 November 2009.

– END –

Notes:

1. PDCO opinions on PIPs and waivers are transformed into EMEA decisions within the timeframe laid down by the Paediatric Regulation (Regulation (EC) No 1901/2006, as amended). The decisions can be found on the EMEA website at: http://www.emea.europa.eu/htms/human/paediatrics/decisions.htm
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 EEA, have to provide either the results of studies in children conducted in accordance with an approved PIP, or an EMEA decision on a waiver or on a deferral.
3. More information about the PDCO and the Paediatric Regulation is available in the 'Medicines for children' section of the EMEA website.
4. This meeting report, together with other information on the work of the EMEA, can be found on the EMEA website: http://www.emea.europa.eu

Enquiries only to: paediatrics@emea.europa.eu

Annex of the October 2009 PDCO meeting report

	2007 (August to December)	**2008** (January to December)	**2009** (January to current month)	**Cumulative total**
Total number of validated PIP/waiver applications	**85**	**271**	**238**	**594**[1]
Applications submitted for a product not yet authorised *(Article 7*[2]*)*	39	186	167	392 *(66%)*
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]*)*	45	75	62	182 *(31%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30*[2]*)*	1	10	9	20 *(3%)*
PIPs and full waiver indications covered by these applications	**202**	**395**	**312**	**909**

Number of Paediatric Committee (PDCO) opinions	**2007**	**2008**	**2009**	**Cumulative total**
Positive on full waiver	10	48	56	114
Positive on PIP, including potential deferral	2	81	110	193
Negative opinions adopted	0	4	12	16
Positive opinions adopted on modification of a PIP	0	8	38	46
Positive opinions on compliance with a PIP	0	5	7	12
Negative opinions on compliance with a PIP	0	0	1	1

[1] Of which 149 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	**2007** *(%)*	**2008** *(%)*	**2009** *(%)*
Neurology	12	6	4
Uro-nephrology	-	3	4
Gastroenterology-hepatology	9	3	5
Pneumology-allergology	8	6	6
Infectious diseases	12	8	9
Cardiovascular diseases	12	14	9
Diagnostics	-	1	1
Endocrinology-gynaecology-fertility-metabolism	19	15	17
Neonatology-paediatric intensive care	-	1	1
Immunology-rheumatology-transplantation	5	6	5
Psychiatry	5	3	2
Pain	1	3	6
Haematology-haemostaseology	1	5	6
Otorhinolaryngology	-	1	1
Oncology	11	12	11
Dermatology	1	3	6
Vaccines	2	6	4
Ophthalmology	1	2	2
Anaesthesiology	-	1	1
Nutrition	1	1	0