European Medicines Agency

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PRESS RELEASE
Meeting highlights from the Paediatric Committee, 28-30 April 2009

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

- **Azilsartan medoxomil**, from Takeda Global Research and Development Centre (Europe) Ltd, in the therapeutic area of cardiovascular diseases;
- **Etanercept**, from Wyeth Europa Limited, in the therapeutic area of immunology–rheumatology-transplantation;
- **Esomeprazole magnesium trihydrate / esomeprazole sodium**, from AstraZeneca AB, in the therapeutic area of gastroenterology-hepatology;
- **Carisbamate**, from Janssen Cilag International NV, in the therapeutic area of neurology;
- **Adalimumab**, from Abbott Laboratories Ltd, in the therapeutic area of immunology–rheumatology-transplantation;
- **Human papillomavirus1 Type 6 L1 protein / human papillomavirus1 Type 11 L1 protein / human papillomavirus1 Type 16 L1 protein / human papillomavirus1 Type 18 L1 protein**, from Sanofi Pasteur MSD SNC, in the therapeutic area of vaccines;
- **Human papillomavirus1 Type 6 L1 protein / human papillomavirus1 Type 11 L1 protein / human papillomavirus1 Type 16 L1 protein / human papillomavirus1 Type 18 L1 protein**, from Merck Sharp & Dohme (Europe) Inc., in the therapeutic area of vaccines;
- **Ciprofloxacin hydrochloride / dexamethasone** , from Alcon Pharma GmbH, in the therapeutic area of oto-rhino-laryngology;
- **1H-Purine-2,6-dione, 8-[(3R)-3-amino-1-piperidinyl]-7-(2-butyn-1-yl)-3,7-dihydro-3-methyl-1-[(4-methyl-2-quinazolinyl)methyl]- (BI-1356)**, from Boehringer Ingelheim International GmbH, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism.

The PDCO adopted an opinion on the **refusal** of a PIP, for **Dienogest / ethinylestradiol (as betadex clathrate) / L-5-methyltetrahydrofolic acid, calcium salt)**, from Bayer Schering Pharma AG, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism. The PDCO subsequently granted on its own motion a product-specific waiver for this medicine for all subsets of the paediatric population in the specified conditions, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

The PDCO adopted an opinion on the **refusal** of a PIP for **Nε141-[2-(2-(2,3-(mPeg(20000)yloxy)propyloxycarbonylamino)ethyloximino)ethyl] hGH**, from Novo Nordisk A/S, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism. The PDCO subsequently granted on its own motion a product-specific waiver for this medicine for all subsets of the paediatric population in the specified condition, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 86 13
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

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:

- **Triamcinolone acetonide**, from Alcon Pharma GmbH, in the therapeutic area of ophthalmology;
- **Pravastatin sodium / fenofibrate**, from Laboratoires SMB s.a., in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- **Human plasma proteins**, from Octapharma Pharmazeutika Produktionsges.m.b.H, in the therapeutic area of haematology-hemostaseology;
- **Recombinant human anti-Rhesus D monoclonal antibody)**, from LFB Biotechnologies, in the therapeutic area of immunology;
- **Aliskiren hemifumarate / amlodipine besilate**, from Novartis Europharm Ltd., in the therapeutic area of cardiovascular diseases;
- **Cladribine**, from Merck KGaA, in the therapeutic area of neurology;
- **Clazosentan,** from Actelion Registration Ltd., in the therapeutic area of neurology.

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

- **Human autologous mesenchymal adult stem cells extracted from adipose tissue**, from Cellerix, S.A., in the therapeutic area of gastroenterology-hepatology.

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.

Adoption of an opinion following re-examination
The PDCO adopted opinions for the following products:

- Following the re-examination of the positive opinion on a PIP adopted in 6 February 2009 for **3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid**, from PTC Therapeutics, Inc., in the therapeutic area of neurology, the PDCO maintained a positive opinion, with amendment of some measures of the paediatric investigation plan;
- Following the re-examination of the negative opinion for a waiver adopted 6 March 2009 for **Bromfenac sodium sesquihydrate**, from Croma Pharma GmbH, the PDCO revised its opinion and adopted a positive opinion for a waiver in the therapeutic area of ophthalmology.

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 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. This month the PDCO adopted one positive opinion on the modification of an agreed PIP.

Withdrawals
The PDCO noted that 2 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. Two experts were invited to the April (28-30) meeting, in the fields of ophthalmology and endocrinology.

Other issues
The PDCO welcomed the new alternate member from Portugal, Dr Hugo Braga Tavares, who has been nominated by INFARMED, the National Authority of Medicines and Health Products of Portugal.
The PDCO thanked Dominique Giocanti for her work as she has resigned from the Committee.

The next meeting of the PDCO will be held on 27-29 May 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 28-30 April 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**	**103**	**459**[1]
Applications submitted for a product not yet authorised *(Article 7*[2]*)*	39	186	67	292 *(64%)*
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	29	149 *(32%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30*[2]*)*	1	10	7	18 *(4%)*
PIPs and full waiver indications covered by these applications	**202**	**395**	**145**	**742**

Number of Paediatric Committee (PDCO) opinions	**2007**	**2008**	**2009**	**Cumulative total**
Positive on full waiver	10	48	27	85
Positive on PIP, including potential deferral	2	81	60	143
Negative opinions adopted	0	4	8	12
Positive opinions adopted on modification of a PIP	0	8	8	16
Positive opinions on compliance with a PIP	0	5	2	7

[1] Of which 110 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	2
Uro-nephrology	-	3	4
Gastroenterology-hepatology	9	3	3
Pneumology-allergology	8	6	5
Infectious diseases	12	8	7
Cardiovascular diseases	12	14	5
Diagnostics	-	1	1
Endocrinology-gynaecology-fertility-metabolism	19	15	25
Neonatology-paediatric intensive care	-	1	1
Immunology-rheumatology-transplantation	5	6	7
Psychiatry	5	3	3
Pain	1	3	3
Haematology-haemostaseology	1	5	5
Otorhinolaryngology	-	1	0
Oncology	11	12	15
Dermatology	1	3	6
Vaccines	2	6	5
Ophthalmology	1	2	3
Anaesthesiology	-	1	0
Nutrition	1	1	0