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PRESS RELEASE
Meeting highlights from the Paediatric Committee, 10-12 December 2008

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

- **Apixaban**, from Bristol Myers Squibb International Corp., in the therapeutic area of cardiovascular diseases;
- **Casopitant**, from Glaxo Group Limited, in the therapeutic area of oncology;
- **Ceftobiprole medocaril sodium**, from Janssen-Cilag International N.V., in the therapeutic area of infectious diseases;
- **Colistimethate sodium inhalation powder**, from Forest Laboratories Ltd., in the therapeutic area of infectious diseases;
- **Corifollitropin alfa,** from N.V. Organon, in the therapeutic area of endocrinology, gynaecology, fertility and metabolism;
- **Etravirine,** from Janssen-Cilag International NV, in the therapeutic area of infectious diseases;
- **Rosuvastatin calcium**, from AstraZeneca, in the therapeutic area of endocrinology, gynaecology, fertility and metabolism.

The PDCO adopted an opinion on the refusal of a PIP, including waiver and deferral, for **Human Papillomavirus type 16 L1 protein, Human Papillomavirus type 18 L1 protein**, from GlaxoSmithKline Biologicals, in the therapeutic area of vaccines. The PDCO granted, subsequently, a product-specific waiver for this medicine for all subsets of the paediatric population in the specified condition, on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

The PDCO adopted an opinion on the refusal of a PIP including a waiver for **Candesartan cilexetil**, from AstraZeneca AB and Takeda Global Research and Development Centre Ltd, in the therapeutic area of cardiovascular diseases, on the grounds that the proposed measures and timelines are not appropriate to ensure the generation of the necessary data determining the condition(s) in which the medicinal product may be used to treat the paediatric populations, are not appropriate to provide an adapted paediatric formulation, and are not expected to bring significant therapeutic benefit.

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 EMEA, or national competent authorities, as part of an application for a marketing authorisation for new medicines or for those 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 PIP modification
The PDCO adopted an opinion on the modification of an agreed PIP for **recombinant L-asparaginase**, from medac Gesellschaft für klinische Spezialpräparate, in the therapeutic area of

* Information concerning telmisartan/amlodipine besylate has been added: the PDCO adopted an opinion on a product-specific waiver.

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oncology, following the adoption of the PDCO opinion on the original PIP during its December 2007 meeting.

The PDCO adopted an opinion on the modification of an agreed PIP for **darunavir (as ethanolate)**, from Janssen-Cilag International NV, in the therapeutic area of infectious diseases, following the adoption of the PDCO opinion on the original PIP during its June 2008 meeting.

Modifications to an agreed PIP can be requested by the applicant when the plan is no longer appropriate or there are difficulties that render the plan unworkable.

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 besylate / valsartan, hydrochlorothiazide**, from Novartis Europharm Ltd., in the therapeutic area of cardiology;
- **Ibuprofen / paracetamol**, from Parexel Consulting, in the therapeutic area of pain;
- **Raltitrexed**, from Hospira UK Limited, in the therapeutic area of oncology;
- **Telmisartan / amlodipine besylate**, from Boehringer Ingelheim International GmbH, in the therapeutic area of cardiovascular diseases;
- **Valsartan / aliskiren hemifumarate**, from Novartis Europharm Ltd., in the therapeutic area of cardiology.

Waivers can be issued if there is evidence showing 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 does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

Interaction with EU medicines network
The second annual Paediatric Workshop for Clinical Assessors from national competent authorities was held at the EMEA on 21 November. The workshop fosters the collaboration between the EMEA and the national agencies, providing training to clinical assessors and paediatric contact points within each agency, particularly on the paediatric legislation and on the practical procedures for the evaluation of PIP/waiver applications.

The network of Paediatric networks
The first workshop of the networks, centres, and investigators of paediatric research will be held at the EMEA on 16 February 2009. The workshop aims at establishing the EMEA network as defined in the strategy adopted by its Management Board on 15 January 2008. It will address recognition criteria and quality standards of the networks. The PDCO will act as the scientific committee of this EMEA network.

Interaction with industry
A hearing of an EFPIA delegation took place during the meeting, in order to exchange views between industry and the PDCO after 18 months of experience. Several topics were discussed, including the general approach and the methodology followed by the PDCO for reaching an opinion, the level of interaction with the US-FDA, global development of paediatric medicines, further opportunities for industry interactions with the PDCO during the evaluation of applications, and the compliance check procedure.

The next meeting of the PDCO will be held on 7-9 January 2009.

-- ENDS --

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 July 2008, pharmaceutical companies that submit an application for a marketing authorisation for a medicine 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. This will also apply, from 26 January 2009, for medicines that are already authorised, and for which a company is submitting an application for an extension of indication, or for a new route of administration, or for a new pharmaceutical form.
3. More information about the PDCO and the Paediatric Regulation is available in the 'Medicines for children' section of the EMEA website.
4. This press release, together with other information on the work of the EMEA, can be found on the EMEA website: http://www.emea.europa.eu

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OVERVIEW OF PAEDIATRIC INVESTIGATION PLAN/WAIVER APPLICATIONS

	2007 (August to December)	**2008** (January to December)	**Cumulative Total**
Total number of validated PIP / waiver applications	**85**	**271**[1]	**356**[2]
Applications submitted for a product not yet authorised *(Article 7*[3]*)*	39	186	225 *(63%)*
Applications submitted for a product already authorised still under patent in view of a submission of a variation/extension for a new indication, pharmaceutical form or route of administration *(Article 8*[3]*)*	45	75	120 (*34%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30*[3]*)*	1	10	11 *(3%)*
PIPs and full waiver indications covered by these applications	**202**	**395**	**597**

Number of Paediatric Committee (PDCO) opinions	**2007**	**2008**	**Cumulative Total**
Positive on full waiver	10	48	58
Positive on PIPs including potential deferral	2	81	83
Negative opinions adopted	0	4	4
Positive opinions adopted on modification of the PIP	0	8	8
Positive opinion on compliance with PIP	0	5	5

[1] Figures including 11 December 2008 start of procedure.
[2] Of which 85 have been requests for full waiver.
[3] Applications submitted in accordance with this Article of Regulation (EC) No 1901/2006, as amended.

Areas covered by PIPs/waiver applications	2007 %	2008 %
Neurology	12	6
Uro-nephrology	-	3
Gastroenterology-hepatology	9	3
Pneumology-allergology	8	6
Infectious diseases	12	8
Cardiovascular diseases	12	14
Diagnostics	-	1
Endocrinology-gynaecology-fertility-metabolism	19	15
Neonatology-paediatric intensive care	-	1
Immunology-rheumatology-transplantation	5	6
Psychiatry	5	3
Pain	1	3
Haematology-haemostaseology	1	5
Otorhinolaryngology	-	1
Oncology	11	12
Dermatology	1	3
Vaccines	2	6
Ophthalmology	1	2
Anaesthesiology	-	1
Nutrition	1	1