European Medicines Agency

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Meeting highlights from the Paediatric Committee, 4-6 February 2009

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

- **3-[5-(2-fluoro-phenyl)-[1, 2, 4]oxadiazole-3-yl]- benzoic acid,** from PTC Therapeutics Inc, in the therapeutic area of neurology;
- **Cannabidiol, delta-9-tetrahydrocannabinol**, from GW Pharma Ltd, in the therapeutic area of neurology;
- **Clevidipine butyrate**, from The Medicines Company, in the therapeutic area of cardiovascular diseases;
- **Cysteamine hydrochloride**, from Orphan Europe SARL, in the therapeutic area of ophthalmology;
- **Fluticasone propionate/formoterol fumarate**, from Mundipharma Research Ltd, in the therapeutic area of pneumology;
- **Glucose monohydrate**, from Cblaya & Mhuguet S.L., in the therapeutic area of pain;
- **Golimumab**, from Centocor B.V., in the therapeutic area of immunology;
- **Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A/H1N1, Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A/H3N2, Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B**, from Novartis Vaccines and Diagnostics S.r.l., in the therapeutic area of vaccines;
- **Maribavir**, from ViroPharma SPRL, in the therapeutic area of infectious diseases;
- **Nilotinib**, from Novartis Europharm Ltd, in the therapeutic area of oncology;
- **Tapentadol hydrochloride**, from Grünenthal GmbH, in the therapeutic area of pain;
- **Tobramycin**, from Novartis Europharm Ltd, in the therapeutic area of pneumology;
- **Tocilizumab,** from Roche Registration Ltd, in the therapeutic area of immunology.

Following re-examination, the PDCO adopted two opinions on the **refusal** of a PIP, including waiver and deferral, for **Candesartan cilexetil** in the therapeutic area of cardiovascular diseases, one from Takeda Global Research and development Centre (Europe) Ltd, and one from Astra Zeneca.

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 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:

- **17-allylamino-17-demethoxygeldanamycin hydroquinone hydrochloride**, from Voisin Consulting SARL, in the therapeutic area of oncology;
- **Bisoprolol fumarate**, from ASA Pharma Plc, in the therapeutic area of cardiovascular diseases

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The PDCO adopted four opinions on the **refusal** of a request for waiver for:

- **Dirucotide acetate**, from Eli Lilly and Company, in the therapeutic area of neurology;
- **Melatonin**, from RAD Neurim Pharmaceuticals EEC Ltd, in the therapeutic area of neurology;;
- **Dexamethasone,** from Allergan Pharmaceuticals Ireland, in the therapeutic area of ophthalmology;
- **(2S)-N-{4-[(Z)-amino(methoxyimino)methyl]benzyl}-1-{(2R)-2-[3-chloro-5-(difluoromethoxy) phenyl]-2-hydroxyethanoyl}-azetidine-2-carboxamide, benzenesulfonic acid salt** from AstraZeneca AB, in the therapeutic area of cardio-vascular diseases.

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 does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

Opinion on Compliance check

The PDCO adopted a positive opinion on compliance check for **Losartan Potassium** from Merck Sharp & Dohme (Europe) Inc., in the therapeutic area of cardiovascular diseases.

A compliance check is a verification that all the measures agreed in a paediatric investigation plan (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 to obtain the rewards and incentives provided for in Articles 36 to 38 of the paediatric regulation.

Before the submission of compliance check applicants are encouraged to consult the EMEA Procedural advice for validation of new marketing authorisation application - extension/variation application and compliance check with an agreed PIP.

Opinions on modifications to an agreed PIP

The PDCO also adopts every month opinions on Modifications to an agreed PIP that can be requested by the applicant, when the plan is no longer appropriate or when there are difficulties that render the plan unworkable.

Interaction with external experts

The PDCO has regular interaction with academic experts with a view to bringing state-of-the-art knowledge to the PDCO scientific discussions. Two experts were invited to the February meeting: with a clinical expert in paediatric oncology the PDCO discussed the potential needs, utility and safety of erythropoiesis-stimulating agents; with a clinical expert in paediatric oto-rhino-laryngology. the PDCO discussed specific infectious diseases

PDCO interactions

A hearing of an European Vaccine Manufacturers (EVM) 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 on PIPs for flu vaccines, including vaccines against pandemic flu. The Chair of the Vaccines Working Party (VWP) of the CHMP attended the hearing.

The Chair of the CHMP's Scientific Advice Working Party (SAWP) attended the meeting of the PDCO and discussed with the PDCO the interactions with the SAWP, in order to enhance the scientific collaboration between the two groups.

The next meeting of the PDCO will be held on 4-6 March 2009.

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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 of 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 to the February 2009 PDCO meeting report

	2007 (August to December)	**2008** (January-December)	**2009**- (January-February)	**Cumulative Total**
Total number of validated PIP / waiver applications	**85**	**271**[1]	**30**	**386**[2]
Applications submitted for a product not yet authorised *(Article 7*[3]*)*	39	186	19	244 *(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	10	130 (*34%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30*[3]*)*	1	10	1	*12 (3%)*
PIPs and full waiver indications covered by these applications	**202**	**395**	**43**	**640**

Number of Paediatric Committee (PDCO) opinions	**2007**	**2008**	**2009**	**Total**
Positive on full waiver	10	48	11	69
Positive on PIPs including potential deferral	2	81	26	109
Negative Opinions adopted	0	4	5	9
Positive Opinions adopted on Modification of the PIP	0	8	2	10
Positive opinion on Compliance with PIP	0	5	1	6

[1] Figures including 5 February 2009 start of procedure
[2] Of which 91 are 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 (%)	2009 (%)
Neurology	12	6	3
Uro-nephrology	-	3	3
Gastroenterology-hepatology	9	3	3
Pneumology-allergology	8	6	3
Infectious diseases	12	8	17
Cardiovascular diseases	12	14	3
Diagnostics	-	1	3
Endocrinology-gynaecology-fertility-metabolism	19	15	36
Neonatology-paediatric intensive care	-	1	0
Immunology-rheumatology-transplantation	5	6	3
Psychiatry	5	3	3
Pain	1	3	7
Haematology-haemostaseology	1	5	3
Otorhinolaryngology	-	1	0
Oncology	11	12	7
Dermatology	1	3	3
Vaccines	2	6	3
Ophthalmology	1	2	0
Anaesthesiology	-	1	0
Nutrition	1	1	0