European Medicines Agency

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Meeting highlights from the Paediatric Committee, 13-15 January 2010

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

- **Dalcetrapib**, from Roche Registration Limited, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism / cardiovascular diseases;
- **Tenofovir disoproxil (as fumarate)**, from Gilead Sciences International Limited, in the therapeutic area of infectious diseases;
- **Rupatadine fumarate**, from J. Uriach y Compañía, S.A, in the therapeutic area of dermatology / pneumology - allergology / oto-rhino-laryngology;
- **Expanded human autologous mesenchymal adult stem cells extracted from adipose tissue (CX-401)**, from Cellerix, S.A., in the therapeutic area of gastroenterology-hepatology;
- **Ecallantide (Recombinant Inhibitor of Human Plasma Kallikrein)**, from Dyax S.A., in the therapeutic area of other / dermatology / pneumology – allergology.

The PDCO adopted an opinion on the refusal of a PIP for **Duloxetine hydrochloride** from Eli Lilly & Company, in the therapeutic areas of psychiatry and pain. 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 is likely to be unsafe in all of the paediatric population.

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.

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:

- **Strontium ranelate**, from Les Laboratoires Servier, in the therapeutic area of immunology-rheumatology-transplantation.

The PDCO adopted 2 opinions on the **refusal** of a request for waiver for:

- **Lanthanum carbonate hydrate** , from Shire Pharmaceutical Contracts Ltd, in the therapeutic area of uro-nephrology;
- **Esomeprazole magnesium / acetylsalisylic acid**, from AstraZeneca AB, in the therapeutic area of gastroenterology-hepatology.

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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.

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 **Montelukast sodium** from Merck-Sharp & Dohme Ltd, in the therapeutic area of pneumology.

A compliance check is performed to verify that all the measures agreed in a PIP and reflected in the Agency's 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 Agency's Procedural advice for validation of a new marketing authorisation application or extension/variation application and compliance check with an agreed PIP.

From 2010 the European Medicines Agency will publish the outcome of the opinion on the final (full) compliance check for agreed Paediatric Investigation Plans in the "Decisions" webpage (http://www.ema.europa.eu/htms/human/paediatrics/decisions.htm).

This also applies to the already adopted opinions on final (full) compliance check.

Withdrawals
The PDCO noted that four applications were withdrawn during the late stages of the evaluation (30 days or less before opinion).

The PDCO also noted that an opinion adopted during the November 2009 PDCO meeting for **bevacizumab**, from Roche Registration Ltd., in the therapeutic area of oncology, has been withdrawn before the decision was adopted by the Agency.

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. A clinical expert in neonatology- infectious diseases was invited to the January meeting. The PDCO discussed bacterial sepsis of newborn children.

PDCO interactions
The Chair of the CHMP's PharmacoVigilance Working Party (PhVWP) attended the meeting of the PDCO and discussed common interactions in order to enhance the scientific collaboration between the two groups. Three additional presentations were also given by an EMEA Scientific Administrator, a PhVWP member and an external expert.

Other issues
The PDCO welcomed back the alternate from Bulgaria, Dr. Margarita Guizova.

The next meeting of the PDCO will be held on 17-19 February 2009.

– 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/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 Agency's 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 Agency's website.
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 of the January 2010 PDCO meeting report

	2008	2009	2010	Cumulative Total (2007-2010)
Total number of validated PIP/waiver applications	**271**	**273**	**39**	**668**[1]
Applications submitted for a product not yet authorised *(Article 7*[2]*)*	186	191	31	447 *(67%)*
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]*)*	75	72	7	199 *(30%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30*[2]*)*	10	10	1	22 *(3%)*
PIPs and full waiver indications covered by these applications	**395**	**395**	**49**	**1010**

Number of Paediatric Committee (PDCO) opinions	**2008**	**2009**	**2010**	**Cumulative total (2007-2010)**
Positive on full waiver	48	67	2	127
Positive on PIP, including potential deferral	81	122	5	210
Negative opinions adopted	4	13	2	19
Positive opinions adopted on modification of a PIP	8	51	11	70
Positive opinions on compliance with a PIP	5	8	1	14
Negative opinions on compliance check with a PIP	0	1	0	1

[1] Of which 161 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	**2008** *(%)*	**2009** *(%)*	**2010** *(%)*
Neurology	6	4	7
Uro-nephrology	3	5	-
Gastroenterology-hepatology	3	2	2
Pneumology-allergology	6	6	28
Infectious diseases	8	9	7
Cardiovascular diseases	14	9	9
Diagnostics	1	1	-
Endocrinology-gynaecology-fertility-metabolism	15	16	7
Neonatology-paediatric intensive care	1	2	-
Immunology-rheumatology-transplantation	6	6	7
Psychiatry	3	3	5
Pain	3	6	-
Haematology-haemostaseology	5	6	7
Otorhinolaryngology	1	1	2
Oncology	12	11	12
Dermatology	3	6	-
Vaccines	6	4	-
Ophthalmology	2	2	5
Anaesthesiology	1	1	2
Nutrition	1	0	