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Meeting highlights from the Paediatric Committee, 14-16 July 2010

Opinions on paediatric investigation plans

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

- **Bosutinib (SKI-606),** from Wyeth Europa Limited, in the therapeutic area of oncology;
- **Recombinant human glutamic acid decarboxylase (rhGAD65)**, from Diamyd Medical AB, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- **Ceftaroline fosamil**, from AstraZeneca AB, in the therapeutic area of infectious diseases;
- **Emtricitabine / tenofovir disoproxil fumarate/ rilpivirine hydrochloride**, from Gilead Sciences International Limited, in the therapeutic area of infectious diseases;
- **Dexamethasone**, from Allergan Pharmaceuticals Ireland, in the therapeutic area of ophthalmology;
- **Chloroprocaine hydrochloride**, from Sintetica Italia S.r.l., in the therapeutic area of anaesthesiology;
- **Ivabradine hydrochloride**, from Les Laboratoires Servier, in the therapeutic area of cardiovascular diseases;
- **Clindamycin phosphate / tretinoin**, from MEDA Pharma GmbH & Co. KG, in the therapeutic area of dermatology.

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.

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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:

- **Telmisartan / hydrochlorothiazide**, from Boehringer Ingelheim International GmbH, in the therapeutic area of cardiovascular diseases;
- **Indapamide / amlodipine besilate**, from Les Laboratoires Servier, in the therapeutic area of cardiovascular diseases;
- **Perindopril erbumine / amlodipine besylate**, from Krka, d.d., Novo mesto, in the therapeutic area of cardiovascular diseases;
- **Valsartan / amlodipine besylate**, from Krka, d.d., Novo mesto, in the therapeutic area of cardiovascular diseases;
- **Vildagliptin / metformin hydrochloride,** from Novartis Europharm Limited, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- **Insulin glargine / lixisenatide**, from Sanofi-Aventis R&D, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- **Bazedoxifene / conjugated estrogens**, from Pfizer Ltd, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism.

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 **esomeprazole sodium**, from AstraZeneca AB, in the therapeutic area of gastroenterology-hepatology.

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.

Withdrawals

The PDCO noted that 3 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 July meeting. With a clinical expert in paediatric dermatology and an expert in paediatric cardiology, the PDCO discussed the paediatric needs and safety of topical calcineurin inhibitors, and the diagnosis of cardiac vascular and perfusion abnormalities.

PDCO interactions

A member of the CHMP participated in the PDCO meeting, to discuss an application in the therapeutic area of oncology and to contribute to a request for modification adopted by the PDCO.

A Member of the Committee on Herbal Medicinal Products (HMPC) has been nominated as an observer in the PDCO, and attended the meeting of PDCO to discuss the interactions with the HMPC, in order to enhance the scientific collaboration between the two committees.

Cooperation with US Food and Drug Administration (FDA)

At the July meeting, the PDCO welcomed two representatives of the US Food and Drug Administration (FDA), who attended within the framework of the 'Principles of interaction between the Agency and FDA paediatric therapeutics'. According to the terms of these principles, the Agency's staff may attend the FDA's Pediatric Implementation Team meetings and FDA staff may attend the Agency's Paediatric Committee meetings, to enable regulators from either agency to observe operational activities, and to optimise mechanisms and timing of information exchanges.

The objective of the cooperation between the Agency and FDA in the field of paediatric medicines is to facilitate the framework for global paediatric development plans, compatible for both agencies, with the aim of avoiding exposing children to unnecessary trials.

Priority list of off-patent medicines

Thanks to the Paediatric Regulation, funding of studies into off-patent medicinal products (i.e. those not covered by a patent or supplementary protection certificate) is available. This funding, provided through the EU Framework Programmes, should cover the development of off-patent medicinal products with a view to the submission of an application for a paediatric-use marketing authorisation.

In order to ensure that funds are directed into research of medicinal products with the highest need in the paediatric population, the PDCO has revised and, after public consultation, adopted the following priority list of off-patent products for which studies are required as a basis for call of the FP7 programme in 2011. The list will be published shortly on the EMA website.

Other issues

The PDCO welcomed the new member from Slovakia, Dr Vlasta Kákošová, who has been nominated by the Ministry of health of the Slovak Republic. Dr Jan Mazag, previously a member, has assumed duties as alternate to Dr Kákošová.

The Committee took note of the call for expression of interest for health professional and patient organisations representatives for the Paediatric Committee (PDCO) launched by the European Commission: http://ec.europa.eu/health/files/paediatrics/call_2010_06.pdf

The next meeting of the PDCO will be held on 04-06 August 2010.

– 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/ema/index.jsp?curl=pages/medicines/landing/pip_search.jsp&murl=menus/medicines/medicines.jsp&mid=WC0b01ac058001d129

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 European Union, 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 Regulatory section of the Agency's website: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000023.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800240cd

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 July 2010 PDCO meeting report

	2008 (January to December)	2009 (January to December)	2010 (January to current month)	Cumulative total (2007 to 2010)
Total number of validated PIP/waiver applications	271	273	257	886[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	186	191	225	641 *(72%)*
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	31	223 *(25%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	10	10	2	23 *(3%)*
PIPs and full waiver indications covered by these applications	395	395	301	1262

Number of Paediatric Committee (PDCO) opinions	2008	2009	2010	Cumulative total
Positive on full waiver	48	67	31	156
Positive on PIP, including potential deferral	81	122	55	260
Negative opinions adopted	4	13	5	22
Positive opinions adopted on modification of a PIP	8	51	62	121
Negative opinions adopted on modification of a PIP	0	0	4	4
Positive opinions on compliance with a PIP	5	8	5	18
Negative opinions on compliance check with a PIP	0	1	0	1

[1] Of which 195 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 (%)	2009 (%)
Neurology	6	4	4
Uro-nephrology	3	5	2
Gastroenterology-hepatology	3	2	1
Pneumology-allergology	6	6	46
Infectious diseases	8	9	4
Cardiovascular diseases	14	9	8
Diagnostics	1	1	1
Endocrinology-gynaecology-fertility-metabolism	15	16	5
Neonatology-paediatric intensive care	1	2	0
Immunology-rheumatology-transplantation	6	6	4
Psychiatry	3	3	2
Pain	3	6	2
Haematology-haemostaseology	5	6	3
Otorhinolaryngology	1	1	1
Oncology	12	11	7
Dermatology	3	6	3
Vaccines	6	4	2
Ophthalmology	2	2	4
Anaesthesiology	1	1	1
Nutrition	1	0	0