European Medicines Agency

London,24 September 2009
Doc. Ref. EMEA/PDCO/570808/2009

Meeting highlights from the Paediatric Committee, 16-18 September 2009

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

- **Icatibant acetate**, from Jerini AG, in the therapeutic area of immunology-rheumatology-transplantation;
- **Fluticasone furoate / triphenylacetic acid - 4-{(1R)-2-[(6-{2-[(2,6-dichlorobenzyl)oxy]ethoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol (1:1)** , from Glaxo Group Limited , in the therapeutic area of pneumology – allergology;
- **Methoxyflurane**, from Voisin Consulting, in the therapeutic area of pain;
- **Ambrisentan**, from Glaxo Group Limited, in the therapeutic area of cardiovascular diseases;
- **Mannitol**, from Pharmaxis Pharmaceuticals Limited, in the therapeutic area of pneumology – allergology;
- **Bromocriptine mesilate**, from VeroScience EU Ltd, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- **Ticagrelor**, from AstraZeneca AB, in the therapeutic area of cardiovascular diseases;
- **C1 Inhibitor**, from ViroPharma SPRL, in the therapeutic area of immunology–rheumatology-transplantation;
- **Rivaroxaban**, from Bayer Schering Pharma AG, in the therapeutic area of cardiovascular diseases;
- **Pandemic influenza vaccine (H1N1) (split virion, inactivated, adjuvanted), containing antigen equivalent to Influenza A/California/7/2009 (Produced at GlaxoSmithKline Biologicals Quebec manufacturing site),** from GlaxoSmithKline Biologicals S.A., in the therapeutic area of vaccines*;
- **Pandemic influenza vaccine (H1N1) (split virion, inactivated, adjuvanted), containing antigen equivalent to Influenza A/California/7/2009 (Produced at GlaxoSmithKline Biologicals Dresden manufacturing site);** from GlaxoSmithKline Biologicals S.A., in the therapeutic area of vaccines*.

The PDCO adopted an opinion on the **refusal** of a PIP and a deferral and on the **granting** of a waiver for some subsets of the paediatric population, for **ulipristal (acetate)**, from PregLem S.A., 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 a subset 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.

*PIP approved under the accelerated procedure for evaluation of paediatric investigation plans for pandemic influenza vaccines during a pandemic (http://www.emea.europa.eu/pdfs/human/paediatrics/40577909en.pdf).

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On 1 September 2009 the Paediatric Committee adopted by written procedure an opinion agreeing on a paediatric investigation plan (PIP) for oseltamivir phosphate, from Roche Registration Ltd, in the therapeutic area of infectious diseases.

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.

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:

- **Ibuprofen / Famotidine**, from Horizon Therapeutics UK Limited, in the therapeutic area of pain;
- **Soluble yeast beta-1,3/1,6-glucan**, from Biotec Pharmacon ASA, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism.

The PDCO adopted 3 opinions on the **refusal** of a request for waiver for:

- **Chloroprocaine hydrochloride**, from Sintetica Italia S.r.l, in the therapeutic area of anaesthesiology;
- **Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerized, allergic extract of birch pollen**, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology;
- **Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerized, allergic extract of equal amounts of birch, alder and hazel pollen**, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.

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 **Purified diphtheria toxoid / Purified tetanus toxoid / Five component acellular pertussis [Purified Pertussis Toxoid (PT), Purified Filamentous Haemagglutinin (FHA), Purified Fimbriae Types 2 and 3 (FIM), and Purified Pertactin (PRN)] / Inactivated poliomyelitis vaccine (Vero) – Type 1 (Mahoney), Type 2 (MEF-1) and Type 3 (Saukett) / Purified polyribosylribitol phosphate capsular polysaccharide of Haemophilus influenzae type b covalently bound to Tetanus protein (PRP-T)** from Sanofi Pasteur MSD SNC, in the therapeutic area of vaccines.

A compliance check is performed to verify that all the measures agreed in a 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 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 EMEA 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 6 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. One expert was invited to the September meeting. With a clinical expert in paediatric immunology, the PDCO discussed the potential needs, utility and safety of replacement plasma products in paediatric immunology.

PDCO interactions
The Chair of the CMD(h) was invited to attend the September meeting to share with the PDCO their experiences on the assessment of paediatric data for medicinal products falling under Articles 45 and 46 of the Paediatric Regulation.

Cooperation with the FDA
At the September meeting, the PDCO welcomed a representative of the US Food and Drug Administration (FDA), who attended within the framework of the 'Principles of interaction between EMEA and FDA paediatric therapeutics'. According to the terms of these principles, EMEA staff may attend the FDA's Pediatric Implementation Team meetings and FDA staff may attend the EMEA'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 EMEA 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.

PDCO ad-hoc experts group meetings:

Epilepsy Expert group:
An expert group discussing aspects of development of antiepileptic medicinal products for children with particular focus on different patient populations, was convened with external experts from hospitals, academia and National Competent Authorities in order to identify the best possible research approaches for existing and new medications in the field. The meeting report will be published on the EMEA website at a later stage.

The next meeting of the PDCO will be held on 14-16 October 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

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Annex of the September 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**	**208**	**564**[1]
Applications submitted for a product not yet authorised (Article 7[2])	39	186	146	371 (66%)
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	53	173 (310%)
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation (Article 30[2])	1	10	9	20 (3%)
PIPs and full waiver indications covered by these applications	**202**	**395**	**273**	**870**

Number of Paediatric Committee (PDCO) opinions	**2007**	**2008**	**2009**	**Cumulative total**
Positive on full waiver	10	48	49	107
Positive on PIP, including potential deferral	2	81	104	187
Negative opinions adopted	0	4	12	16
Positive opinions adopted on modification of a PIP	0	8	32	40
Positive opinions on compliance with a PIP	0	5	6	11
Negative opinions on compliance with a PIP	0	0	1	1

[1] Of which 140 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	3
Uro-nephrology	-	3	4
Gastroenterology-hepatology	9	3	4
Pneumology-allergology	8	6	7
Infectious diseases	12	8	8
Cardiovascular diseases	12	14	9
Diagnostics	-	1	1
Endocrinology-gynaecology-fertility-metabolism	19	15	17
Neonatology-paediatric intensive care	-	1	1
Immunology-rheumatology-transplantation	5	6	6
Psychiatry	5	3	2
Pain	1	3	6
Haematology-haemostaseology	1	5	7
Otorhinolaryngology	-	1	1
Oncology	11	12	11
Dermatology	1	3	6
Vaccines	2	6	4
Ophthalmology	1	2	2
Anaesthesiology	-	1	1
Nutrition	1	1	0