EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Human Medicines Development and Evaluation

Meeting highlights from the Paediatric Committee (PDCO)

04-06 August 2010

Opinions on paediatric investigation plans

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

- **Artemether / lumefantrine**, from Novartis Europharm Limited, in the therapeutic area of infectious diseases;
- **Influenza virus surface antigens (haemagglutinin and neuraminidase), inactivated, trivalent**, from Abbott Biologicals B.V., in the therapeutic area of infectious diseases;
- **Entecavir**, from Bristol-Myers Squibb Pharma EEIG, in the therapeutic area of infectious diseases;
- **Romiplostim**, from Amgen Europe B.V, in the therapeutic area of haematology-haemostaseology;
- **Rufinamide**, from Eisai Ltd, in the therapeutic area of neurology;
- **CAT-354, a neutralising human IgG4 monoclonal antibody with specificity for human interleukin-13 (IL-13)**, from MedImmune Ltd, in the therapeutic area of pneumology - allergology;
- **Glycinamide, L-cysteinyl-L-phenylalanyl-L-isoleucyl-6-oxo-L-lysyl-L-asparaginyl-L-cysteinyl-L-prolyl-N5-(1-methylethyl)-L-ornithyl-, cyclic(1 → 6)-disulfide acetate (FE 202158 acetate)**, from International PharmaScience Center, Ferring Pharmaceuticals A/S, in the therapeutic area of cardiovascular diseases;
- **Guanfacine hydrochloride**, from Shire Pharmaceutical Contracts Ltd, in the therapeutic area of psychiatry;
- **Mirabegron**, from Astellas Pharma Europe B.V., in the therapeutic area of uro-nephrology.

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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Adoption of an opinion following re-examination

The PDCO adopted one opinion after re-examination, on a request for modification of an agreed PIP.

A re-examination of the opinion can be requested by the applicant within 30 days following receipt of the opinion of the PDCO. The grounds for the re-examination should be based only on the original information and scientific data provided in the application that were previously available to the PDCO and on which the initial opinion was based. This may include new analysis of the same data or minor protocol amendments to a previously proposed study. Significant changes to the previous plan cannot be part of the re-examination process.

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:

- **(R)-3(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-cyclopentylpropanenitrilephosphate**, from Novartis Europharm Ltd, in the therapeutic area of oncology;
- **Copper [64 Cu] Chloride**, from Sparkle, in the therapeutic area of ophthalmology;
- **Pasireotide**, from Novartis Europharm Ltd, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- **Amlodipine camsylate / losartan potassium**, from Hanmi Europe Limited, in the therapeutic area of cardiovascular diseases;
- **Afamelanotide**, from Clinuvel (UK) Limited, in the therapeutic area of dermatology..

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 **midazolam (as hydrochloride)**, from ViroPharma SPRL, in the therapeutic area of neurology.

The PDCO adopted a positive opinion on compliance check for **nevirapine**, from Boehringer Ingelheim International GmbH, in the therapeutic area of infectious diseases.

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 4 applications were withdrawn during the late stages of the evaluation (30 days or less before opinion).

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. One expert was invited to the August meeting with a clinical expert in paediatric haematology and oncology, the PDCO discussed therapeutic settings in lymphoma to be studied for a potential paediatric use.

PDCO interactions

A CHMP assessor participated to the PDCO discussion on an opinion for an application in the therapeutic area of infectious diseases adopted by the PDCO.

Other issues

The PDCO welcomed the new member from Greece, Dr Lida Kalantzi, who has been nominated by the Greek Ministry of Health. The PDCO also welcomed the new alternate from Hungary Dr János Borvendég who was nominated together with Agnes Gyurasics, Hungarian member, by the CHMP.

The CHMP also nominated Carine de Beaufort, (CHMP alternate) as PDCO member, and Jacqueline Genoux-Hames (CHMP member), as new PDCO alternate, Luxembourg

The PDCO thanked Roxana Mustata and Tamas Mackay who are no longer members of the Committee.

The next meeting of the PDCO will be held on 08-09 September 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/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 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 '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 August 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	277	907[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	186	191	239	655 *(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	37	229 *(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	322	1283

Number of Paediatric Committee (PDCO) opinions	2008	2009	2010	Cumulative total
Positive on full waiver	48	67	37	161
Positive on PIP, including potential deferral	81	122	64	269
Negative opinions adopted	4	13	5	22
Positive opinions adopted on modification of a PIP	8	51	69	128
Negative opinions adopted on modification of a PIP	0	0	4	4
Positive opinions on compliance with a PIP	5	8	7	20
Negative opinions on compliance check with a PIP	0	1	0	1

[1] Of which 198 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	4
Uro-nephrology	3	5	1
Gastroenterology-hepatology	3	2	1
Pneumology-allergology	6	6	45
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	1
Haematology-haemostaseology	5	6	3
Otorhinolaryngology	1	1	3
Oncology	12	11	8
Dermatology	3	6	3
Vaccines	6	4	2
Ophthalmology	2	2	4
Anaesthesiology	1	1	1
Nutrition	1	0	0