21 May 2010
EMA/PDCO/323686/2010
Human Medicines Development and Evaluation

Meeting highlights from the Paediatric Committee, 19-21 May 2010

Opinions on paediatric investigation plans

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

- **Dapagliflozin**, from Bristol Myers Squibb /AstraZeneca EEIG, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- **Human normal immunoglobulin**, from Kedrion S.p.A., in the therapeutic area of immunology-rheumatology-transplantation / haematology-hemostaseology;
- **1-(4-{1-[(E)-4-Cyclohexyl-3-trifluoromethyl-benzyloxyimino]-ethyl}-2-ethyl-benzyl)-azetidine-3-carboxylic acid, (E)-but-2-enedioic acid (BAF 312)**, from Novartis Europharm Limited, in the therapeutic area of immunology-rheumatology-transplantation / neurology; (716)
- **N.meningitidis Outer Membrane Vesicles (OMV) from NZ 98/254 strain, N.meningitidis 287-953 purified antigen, N.meningitidis 961c purified antigen, N.meningitidis936-741 purified antigen**, from Novartis Vaccines and Diagnostics S.r.l., in the therapeutic area of vaccines;
- **Pneumococcal polysaccharide serotype 5 conjugated to Protein D (derived from non-typeable Haemophilus influenzae) carrier protein, Pneumococcal polysaccharide serotype 23F conjugated to Protein D (derived from non-typeable Haemophilus influenzae) carrier protein, Pneumococcal polysaccharide serotype 6B conjugated to Protein D (derived from non-typeable Haemophilus influenzae) carrier protein, Pneumococcal polysaccharide serotype 4 conjugated to Protein D (derived from non-typeable Haemophilus influenzae) carrier protein, Pneumococcal polysaccharide serotype 9V conjugated to Protein D (derived from non-typeable Haemophilus influenzae) carrier protein, Pneumococcal polysaccharide serotype 7F conjugated to Protein D (derived from non-typeable Haemophilus influenzae) carrier protein, Pneumococcal polysaccharide serotype 14 conjugated to Protein D (derived from non-typeable Haemophilus influenzae) carrier protein, Pneumococcal polysaccharide serotype 18C conjugated to tetanus toxoid carrier protein, Pneumococcal polysaccharide serotype 19F conjugated to diphtheria toxoid carrier protein, Pneumococcal polysaccharide serotype 1 conjugated to Protein D (derived from non-typeable**

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Haemophilus influenzae) carrier protein, from GlaxoSmithKline Biologicals S.A., in the therapeutic area of Vaccines;

- **Human papillomavirus type 6 l1 protein, human papillomavirus type 11 l1 protein, human papillomavirus type 45 l1 protein, human papillomavirus type 33 l1 protein, human papillomavirus type 16 l1 protein, human papillomavirus type 31 l1 protein, human papillomavirus type 18 l1 protein, human papillomavirus type 58 l1 protein, human papillomavirus type 52 l1 protein**, from Merck Sharp & Dohme (Europe), Inc., in the therapeutic area of vaccines;

The PDCO adopted an opinion on the **refusal** of a PIP for **tulobuterol free base**, from CSI GmbH, in the therapeutic area of pneumology - allergology. 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 condition, on the grounds that the specific medicinal product or class of medicinal products is likely to be ineffective or unsafe in part 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:

- **Diclofenac sodium/Omeprazole**, from Temmler Werke GmbH, in the therapeutic area of immunology-rheumatology-transplantation ;
- **MORAb-009 (Chimeric antibody to mesothelin)**, from Eisai Ltd, in the therapeutic area of oncology;

The PDCO adopted an opinion on the **refusal** of a request for waiver for:

- **Magnesium sulfate heptahydrate, sodium sulfate, potassium sulfate**, from Ipsen Pharma, in the therapeutic area of gastroenterology-hepatology;

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 **nomegestrol acetate / 17 beta - estradiol**, from N.V. Organon, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism.

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 2 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 May meeting. With a clinical expertise in the field of psychiatry, the PDCO discussed a treatment of alcohol dependence in adolescents.

PDCO interactions

The Chair of the CHMP's Blood Products Working Party (BPWP) with one of the member joined the meeting of PDCO via teleconference to discuss Paediatric Investigation Plans on immunoglobulins.

PDCO ad-hoc experts group meetings:

Reports on the PDCO expert groups held in 2009 have been published on the Agency's website: http://www.ema.europa.eu/htms/human/paediatrics/workshops.htm

The next meeting of the PDCO will be held on 9-11 June 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

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Annex of the May 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	209	838[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	186	191	185	601 *(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	22	214 *(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	244	1205

Number of Paediatric Committee (PDCO) opinions	2008	2009	2010	Cumulative total
Positive on full waiver	48	67	16	141
Positive on PIP, including potential deferral	81	122	40	245
Negative opinions adopted	4	13	4	21
Positive opinions adopted on modification of a PIP	8	51	43	102
Negative opinions adopted on modification of a PIP	0	0	1	1
Positive opinions on compliance with a PIP	5	8	4	17
Negative opinions on compliance check with a PIP	0	1	0	1

[1] Of which 184 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	53
Infectious diseases	8	9	3
Cardiovascular diseases	14	9	8
Diagnostics	1	1	1
Endocrinology-gynaecology-fertility-metabolism	15	16	6
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	2
Otorhinolaryngology	1	1	1
Oncology	12	11	5
Dermatology	3	6	2
Vaccines	6	4	2
Ophthalmology	2	2	3
Anaesthesiology	1	1	1
Nutrition	1	0	0