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Human Medicines Development and Evaluation

Paediatric Committee (PDCO) - meeting report

08-10 December 2010

Opinions on paediatric investigation plans

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

- (2S,3R,4R,5S,6R)-2-(4-Chloro-3-{3-[(S)-(tetrahydrofuran-3-yl)oxy]-benzyl}-phenyl)-6-hydroxymethyltetrahydro-pyran-3,4,5-triol, from Boehringer Ingelheim International GmbH, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Lixisenatide, from Sanofi-Aventis R&D, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Ozenoxacin, from Ferrer Internacional, S.A, in the therapeutic area of infectious diseases;
- Amikacin Sulfate, from Transave, Inc., in the therapeutic area of infectious diseases / pneumology - allergology;
- Meropenem, from NeoMero Consortium, in the therapeutic area of neonatology - paediatric intensive care / infectious diseases;
- Pegloticase, from Savient Pharmaceuticals, Inc., in the therapeutic area of immunology-rheumatology-transplantation / oncology;
- Sotrastaurin acetate, from Novartis Europharm Ltd, in the therapeutic area of immunology-rheumatology-transplantation;
- Grass pollen allergen extract from Dactylis glomerata L., Anthoxanthum odoratum L., Lolium perenne L., Poa prantensis L. and Phleum pratense L. , from Stallergenes S.A., in the therapeutic area of pneumology - allergology;
- House dust mites allergen extract from Dermatophagoides pteronyssinus and Dermatophagoides farinae (50/50), from Stallergenes S.A., in the therapeutic area of pneumology - allergology;
- Rizatriptan benzoate, from Merck Sharp & Dohme (Europe) Inc., in the therapeutic area of pain.

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

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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:

- Indapamide, amlodipine besilate, perindopril arginine, from Les Laboratoires Servier, in the therapeutic area of cardiovascular disease;
- Nepafenac, from Alcon Laboratories (UK) Ltd, in the therapeutic area of ophthalmology;
- Tesamorelin, from Theratechnologies Inc, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism.

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

- Recombinant human granulocyte colony stimulating factor / recombinant human albumin fusion protein, from Teva Pharmaceuticals Europe B.V, in the therapeutic area of oncology.

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.

Class waivers

The PDCO adopted an opinion on the review of the current list of class waivers for medicinal products or classes of medicinal products to be used in specific conditions. The list of class waivers is updated at least once a year by the PDCO.

Adoption of a class waiver

The PDCO recommended that the requirement to submit the results of studies done in accordance with a PIP be waived, in all subsets of the paediatric population, for medicines developed for the following conditions, on the grounds that the diseases or conditions occur only in adult populations:

- Treatment of primary myelofibrosis;
- Treatment of diabetic macular oedema;
- Treatment of mesothelioma;
- Treatment of actinic keratosis.

The PDCO also discussed the following conditions, for which a class waiver was **not** adopted: treatment of leiomyoma of uterus, treatment of pituitary gigantism, treatment of secondary myelofibrosis, treatment of myelodysplastic syndrome and treatment of heredofamilial amyloidosis.

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 two positive opinions on compliance check for:

- Tretinoin / clindamycin phosphate, from Meda Pharma GmbH & Co. KG, in the therapeutic area of dermatology.
- Clopidogrel, from Sanofi Pharma Bristol-Myers Squibb SNC, in the therapeutic area of cardio vascular 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 five 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 in paediatric oncology and members of the EMA's paediatric oncology task force attended the December meeting. The PDCO discussed the intended interactions of the recently created European Network for Children with Cancer (ENCCA) with the regulatory network, as well as progress, and lack thereof, in availability of anti-cancer medicines for early paediatric trials and for authorised use.

Other issues

The PDCO elected two of its members, Dirk Mentzer and Paolo Rossi, to represent the Committee in the European paediatric research network at the EMA (EnprEMA).

The PDCO welcomed the appointment of Dr Nela Vilceanu as the new member from Romania. Dr Vilceanu, who was previously the Romanian alternate, has been nominated by the Committee for Medicinal Products for Human Use.

The next meeting of the PDCO will be held on 12-14 January 2011.

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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 December 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	326	956[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	186	191	280	696 *(73%)*
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	43	235 *(24%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	10	10	4	25 *(3%)*
PIPs and full waiver indications covered by these applications	395	364	403	1364

Number of Paediatric Committee (PDCO) opinions	2008	2009	2010	Cumulative total
Positive on full waiver	48	67	52	176
Positive on PIP, including potential deferral	81	122	201	406
Negative opinions adopted	4	13	7	24
Positive opinions adopted on modification of a PIP	8	51	103	162
Negative opinions adopted on modification of a PIP	0	0	4	4
Positive opinions on compliance with a PIP	5	8	9	22
Negative opinions on compliance check with a PIP	0	1	0	1
Opinions adopted under Art. 14.2	0	0	2	2

[1] Of which 214 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	3
Uro-nephrology	3	5	2
Gastroenterology-hepatology	3	2	1
Pneumology-allergology	6	6	41
Infectious diseases	8	9	4
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	5
Psychiatry	3	3	1
Pain	3	6	1
Haematology-haemostaseology	5	6	4
Otorhinolaryngology	1	1	3
Oncology	12	11	9
Dermatology	3	6	1
Vaccines	6	4	2
Ophthalmology	2	2	4
Anaesthesiology	1	1	2
Nutrition	1	0	0