15 December 2011
EMA/PDCO/925174/2011
Paediatric Committee (PDCO)

PDCO monthly report of opinions on paediatric investigation plans

07-09 December 2011

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

- Treprostinil diethanolamine, from United Therapeutics Europe Ltd, in the therapeutic area of cardiovascular diseases;
- Methyl aminolevulinate hydrochloride, from Photocure ASA, in the therapeutic area of dermatology;
- Recombinant dimer of 6 kD early secretory antigenic target / recombinant 10 kD culture filtrate protein from Statens Serum Institut, in the therapeutic area of diagnostic;
- Elvitegravir, from Gilead Sciences International Limited, in the therapeutic area of infectious diseases;
- Bortezomib, from Janssen-Cilag International NV, in the therapeutic area of oncology;
- Cyclophosphamide, from Keocyt SAS, in the therapeutic area of oncology-haematology;
- N-{3-[5-(2-Amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzene sulfonamide, methanesulfonate salt (GSK2118436), from GlaxoSmithKline Trading Service Limited, in the therapeutic area of oncology;
- Morphine hydrochloride, from EPMC Pharma SPRL, in the therapeutic area of pain / neonatology - paediatric intensive care;
- Lebrikizumab, from Roche Products Limited, in the therapeutic area of pneumology – allergology;
- Atomoxetine hydrochloride, from Eli Lilly & Company, in the therapeutic area of psychiatry.
- Purified Tetanus Toxoid / Inactivated Type 1 Poliovirus (Mahoney) / Inactivated Type 2 Poliovirus (MEF-1) / Inactivated Type 3 Poliovirus (Saukett) / Purified Pertussis Toxoid (PT) / Haemophilus influenzae type b polysaccharide conjugated to tetanus protein / Purified Filamentous Haemagglutinin (FHA) / Hepatitis B Surface Antigen, recombinant (HBsAg) / Purified Diphtheria Toxoid (DTaP-IPV-HepB-PRP-T), from Sanofi pasteur, in the therapeutic area of vaccines;

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- Human Thrombin / Human Fibrinogen from Omrix Biopharmaceuticals SA, in the therapeutic area of other (haemorrhage resulting from a surgical procedure);
- Culture expanded autologous chondrocytes, from Fidia Advanced Biopolymers S.r.l., in the therapeutic area of other (orthopaedics).

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:

- Atorvastatin calcium / ezetimibe, from Merck Sharp & Dohme (Europe), Inc., in the therapeutic area of cardiovascular diseases;
- Anti-sclerostin human monoclonal antibody (AMG785), from Amgen Europe B.V, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Palonosetron / netupitant, from Helsinn Birex Pharmaceuticals Limited, in the therapeutic area of other / 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 confirmation of the current list of class waivers for conditions that do not affect children, or for classes of medicinal products to be used in specific conditions, and for which the requirement to submit a PIP can therefore be waived. The list of class waivers is updated at least once a year by the PDCO.

Adoption of a class waiver

The PDCO adopted an opinion on a class waiver for a class of medicinal products, used in the treatment of vulvar intraephitelial neoplasia. The Committee recommended that the requirement to submit clinical-trial data in all subsets of the paediatric population be waived for medicines belonging to this class and/or developed in this condition. This is because the condition does not occur in some or all of the paediatric populations.

The opinion is transformed into an Agency's decision.

The Agency already adopted decisions on a list of waivers in December 2011 for conditions that do not occur in children, or for products likely to be unsafe or ineffective in children. The list of waivers is regularly updated in light of the advance in knowledge and science in the paediatric field.

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 positive opinions on compliance checks for the following medicines:

- Darunavir, from Tibotec, in the therapeutic area of infectious disease;
- Etanercept, from Pfizer Limited, in the therapeutic area of dermatology / immunology-rheumatology-transplantation.

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 1 application was withdrawn during the late stages of the evaluation (30 days or less before opinion).

Other issues

The PDCO welcomed the new member from Greece, Professor Stefanos Mantagos, who has been nominated by the Greek National Organization for Medicines.

The PDCO welcomed the new alternate from Denmark, Dr Dorthe Meyer, who has been nominated by Danish Medicines Agency.

The next meeting of the PDCO will be held on 11-13 January 2012.

– 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 December 2011 PDCO meeting report

	2009 (January to December)	2010 (January to December)	2011 (January to current month)	Cumulative total (2007 to 2011)
Total number of validated PIP/waiver applications	273	326	187	1144[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	191	280	153	850 *(74%)*
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])*	72	43	33	268 *(24%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	10	4	1	26 *(2%)*
PIPs and full waiver indications covered by these applications	395	403	220	1584

Number of Paediatric Committee (PDCO) opinions	2009	2010	2011	Cumulative total
Positive on full waiver	67	52	45	221
Positive on PIP, including potential deferral	122	201	107	513
Negative opinions adopted	13	7	3	27
Positive opinions adopted on modification of a PIP	51	103	153	315
Negative opinions adopted on modification of a PIP	0	4	2	6
Positive opinions on compliance with a PIP	8	9	9	31
Negative opinions on compliance check with a PIP	1	0	0	1
Opinions adopted under Art. 14.2	0	2	0	2

[1] Of which 271 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	2009 *(%)*	2010 *(%)*	2011 *(Number of areas covered)**
Neurology	4	3	11
Uro-nephrology	5	2	4
Gastroenterology-hepatology	2	1	10
Pneumology-allergology	6	41	10
Infectious diseases	9	4	15
Cardiovascular diseases	9	8	21
Diagnostics	1	1	5
Endocrinology-gynaecology-fertility-metabolism	16	6	28
Neonatology-paediatric intensive care	2	0	0
Immunology-rheumatology-transplantation	6	5	13
Psychiatry	3	1	9
Pain	6	1	2
Haematology-haemostaseology	6	4	18
Otorhinolaryngology	1	3	2
Oncology	11	9	19
Dermatology	6	1	10
Vaccines	4	2	12
Ophthalmology	2	4	8
Anaesthesiology	1	2	1
Nutrition	0	0	0
Other			7

** One PIP can cover several therapeutic areas*