EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

14 September 2011
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Monthly report

Paediatric Committee (PDCO)

7-9 September 2011

Opinions on paediatric investigation plans

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

- Selexipag, from Actelion Registration Ltd, in the therapeutic area of cardiovascular diseases.
- Secretin, from Repligen Europe Limited, in the therapeutic area of diagnostic;
- Lixivaptan, from Cardiokine Biopharma, LLC, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Lorcaserin, from Arena Pharmaceutical Enterprises Limited, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Recombinant fusion protein linking human coagulation factor IX with human albumin, from CSL Behring GmbH, in the therapeutic area of haematology-hemostaseology;
- Aciclovir, from BioAlliance Pharma, in the therapeutic area of infectious diseases;
- L-Seryl-L-arginyl-L-valyl-L-leucyl-L-aspartyl-glycyl-L-leucyl-L-valyl-L-methionyl-L-threonyl-L-threonyl-L-isoleucyl-L-seryl-L-seryl-L-seryl-L-lysine, acetate salt / L-Threonyl-L-alanyl-L-methionyl-L-lysyl-L-lysyl-L-isoleucyl-L-glutaminyl-L-aspartyl-L-cysteinyl-L-tyrosyl-L-valyl-L-glutamyl-L-asparaginyl-glycyl-L-leucyl-L-isoleucine, acetate salt / L-Lysyl-L-glutamyl-L-asparaginyl-L-alanyl-L-leucyl-L-seryl-L-leucyl-L-leucyl-L-aspartyl-L-lysyl-L-isoleucyl-L-tyrosyl-L-threonyl-L-seryl-L-prolyl-L-leucine, acetate salt / L-Arginyl-L-isoleucyl-L-leucyl-L-lysyl-L-asparaginyl-L-cysteinyl-L-valyl-L-aspartyl-L-alanyl-L-lysyl-L-methionyl-L-threonyl-L-glutamyl-L-glutamyl-L-aspartyl-L-lysyl-L-glutamic acid, acetate salt / L-Lysyl-L-alanyl-L-leucyl-L-prolyl-L-valyl-L-valyl-L-leucyl-L-glutamyl-L-asparaginyl-L-alanyl-L-arginyl-L-isoleucyl-L-leucyl-L-lysyl-L-asparaginyl-L-cysteinyl-L-valine, acetate salt / L-Glutamyl-L-glutaminyl-L-valyl-L-alanyl-L-glutaminyl-L-tyrosyl-L-lysyl-L-alanyl-L-leucyl-L-prolyl-L-valyl-L-valyl-L-leucyl-L-glutamyl-L-asparaginyl-L-alanine, acetate salt / L-Cysteinyl-L-prolyl-alanyl-L-valyl-L-lysyl-L-arginyl-L-aspartyl-

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L-valyl-L-aspartyl-L-leucyl-L-phenylalanyl-L-leucyl-L-threonine, acetate salt, from Circassia Limited, in the therapeutic area of pneumology-allergology;

- (1R, 4S, 5S, 6S)-4-[[(2s)-2-Amino-4-(methylthio)-1-oxobutyl]amino]-2-thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid,2,2-dioxide, monohydrate (LY2140023), from Eli Lilly and Company Limited, in the therapeutic area of psychiatry;
- Furosemide, from KidzPharma, Inc., 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.

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:

- Acetylsalicylic acid / clopidogrel (bisulphate), from TEVA Pharma B.V., in the therapeutic area of cardiovascular diseases;
- Metformin / (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;
- Linagliptin / (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-fertitily-metabolism;
- Pancreas powder, from Eurand Pharmaceuticals Limited, in the therapeutic area of gastroenterology-hepatology.
- Temsirolimus, from Wyeth Europa Ltd, in the therapeutic area of oncology;
- Brinzolamide / brimonidine (tartrate), from Alcon Laboratories (UK) Ltd, in the therapeutic area of ophthalmology;
- 4-[[9-[(3S)-tetrahydro-3-furanyl]-8-[(2,4,6-trifluorophenyl)amino]-9H-purin-2-yl]amino]-trans-cyclohexanol (CC-930), from Celgene Europe Limited, 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:

- Infliximab, from Janssen Biologics B.V., in the therapeutic area of immunology-rheumatology-transplantation / dermatology / gastroenterology-hepatology;
- Rizatriptan (benzoate), from Merck Sharp & Dohme (Europe) Inc, in the therapeutic area of pain.

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 September meeting, with a clinical expert in paediatric congenital venous malformations. The PDCO discussed<e.g. the potential needs, utility and safety of erythropoiesis-stimulating agents; with a clinical expert in paediatric oto-rhino-laryngology, the PDCO discussed specific infectious diseases.

Other issues

The PDCO welcomed the new alternate, Dr Gerard Nguyen, representing patients' organisations, who has been nominated by the European Commission.

The PDCO thanked Dr Karen Tornøe, alternate, for Denmark, for her outstanding work as she resigned from the Committee.

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

– 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 September 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	146	1103[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	191	280	117	814 *(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	28	263 *(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	171	1535

Number of Paediatric Committee (PDCO) opinions	2009	2010	2011	Cumulative total
Positive on full waiver	67	52	39	215
Positive on PIP, including potential deferral	122	201	78	484
Negative opinions adopted	13	7	3	27
Positive opinions adopted on modification of a PIP	51	103	115	277
Negative opinions adopted on modification of a PIP	0	4	1	5
Positive opinions on compliance with a PIP	8	9	5	27
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 261 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	8
Uro-nephrology	5	2	1
Gastroenterology-hepatology	2	1	8
Pneumology-allergology	6	41	7
Infectious diseases	9	4	10
Cardiovascular diseases	9	8	17
Diagnostics	1	1	5
Endocrinology-gynaecology-fertility-metabolism	16	6	25
Neonatology-paediatric intensive care	2	0	0
Immunology-rheumatology-transplantation	6	5	10
Psychiatry	3	1	6
Pain	6	1	1
Haematology-haemostaseology	6	4	13
Otorhinolaryngology	1	3	1
Oncology	11	9	16
Dermatology	6	1	6
Vaccines	4	2	9
Ophthalmology	2	4	6
Anaesthesiology	1	2	0
Nutrition	0	0	0
Other			5

** One PIP can cover several therapeutic areas*