EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Paediatric Committee (PDCO)

PDCO monthly report of opinions on paediatric investigation plans

11-13 April 2012

Opinions on paediatric investigation plans

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

- Ixekizumab, from Eli Lilly & Company Limited, in the therapeutic area of immunology-rheumatology-transplantation;
- Agomelatine, from Les Laboratoires Servier, in the therapeutic area of psychiatry;
- Vonicog alfa, from BAXTER Innovations GmbH, in the therapeutic area of haematology-hemostaseology;
- Anti-BAFF monoclonal antibody (LY2127399) from Eli Lilly & Company Limited, in the therapeutic area of immunology-rheumatology-transplantation;
- Poly (oxy-1,2-ethanediyl), α-hydro-ω-methoxy-, 28B-ester with 28B-(N6-carboxy-L-Lysine)-29B-L-prolineinsulin (human) (LY 2605541), from Eli Lilly and Company, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Trisodium [3-((1S,3R)-1-biphenyl-4-ylmethyl-3-ethoxycarbonyl-1-butylcarbamoyl)propionate-(S)-3'-methyl-2'-(pentanoyl{2''-(tetrazol-5-ylate)biphenyl-4'-ylmethyl}amino)butyrate] hemipentahydrate, from Novartis Europharm Ltd., in the therapeutic area of cardiovascular diseases.

The PDCO adopted an opinion on the **refusal** of a PIP, including *waiver*, for bivalirudin, from The Medicines Company UK Limited, in the therapeutic area of cardiovascular diseases.

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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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:

- Nifedipine / candesartan (cilexetil), from Bayer Pharma AG, in the therapeutic area of cardiovascular diseases;
- Bimatoprost, from Allergan Pharmaceuticals Ireland, in the therapeutic area of dermatology;
- Glimepiride / atorvastatin (calcium), from GlaxoSmithKline Trading Services Limited, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism / cardiovascular diseases.

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

- Ranirestat, from Eisai Ltd, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism.

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. The PDCO adopted positive opinions, agreeing change(s), for the following products:

- 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;
- Human coagulation Factor VIII / von Willebrand Factor, from CSL Behring, in the therapeutic area of haematology-hemostaseology;
- Ferumoxytol, from AMAG Pharmaceuticals Inc., in the therapeutic area of haematology-hemostaseology;
- Belatacept, from Bristol-Myers Squibb Pharma EEIG, in the therapeutic area of immunology-rheumatology-transplantation;
- Bosentan, from Actelion Registration Ltd, in the therapeutic area of immunology-rheumatology-transplantation / cardiovascular diseases / pneumology - allergology;
- Dolutegravir, from ViiV Healthcare UK Ltd, in the therapeutic area of immunology-rheumatology-transplantation / gastroenterology-hepatology;
- Nalfurafine (hydrochloride), from Toray International U.K. Limited, in the therapeutic area of dermatology;
- L-Cysteinyl-L-prolyl-L-alanyl-L-valyl-L-lysyl-L-arginyl-L-aspartyl-L-valyl-L-aspartyl-L-leucyl-L-phenylalanyl-L-leucyl-L-threonine, hydrochloride 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-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-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-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-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-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, from Circassia Limited, in the therapeutic area of pneumology - allergology / oto-rhino-laryngology;

- Clevidipine butyrate, from The Medicines Company UK Ltd., in the therapeutic area of cardiovascular diseases;
- Ivabradine (hydrochloride), from Les Laboratorires Servier, in the therapeutic area of cardiovascular diseases;
- Voclosporin, from Lux Biosciences GmbH, in the therapeutic area of ophtalmology;
- Macitentan, from Actelion Registration Ltd, in the therapeutic area of cardiovascular diseases / immunology-rheumatology-transplantation / pneumology - allergology;

Withdrawals

The PDCO noted that one application was withdrawn during the late stages of the evaluation (30 days or less before opinion).

PDCO interactions

The Chair of the Blood Products Working Party (BPWP) and two members of the Advanced Therapies Committee (CAT) attended the April meeting of the PDCO bringing state-of-the-art knowledge to the PDCO scientific discussions as part of the collaboration between Committees.

Other issues

The PDCO welcomed the new member from the United Kingdom, Dr Julia Dunne, who has been nominated by Medicines and Healthcare products Regulatory Agency.

The PDCO also welcomed the alternate from Finland, Ann Marie Kaukonen, who has been nominated by the Finnish Medicines Agency.

The next meeting of the PDCO will be held on 14-16 May 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 April PDCO meeting report

	2010 (January to December)	2011 (January to December)	2012 (January to current month)	Cumulative total (2007 to present)
Total number of validated PIP/waiver applications	326	187	53	1197[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	280	153	38	888 *(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)*	43	33	15	283 *(24%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30)*	4	1	0	26 *(2%)*
PIPs and full waiver indications covered by these applications	403	220	60	**1644**

Number of Paediatric Committee (PDCO) opinions	2010	2011	2012	Cumulative total (2007 – Present)
Positive on full waiver	52	45	7	228
Positive on PIP, including potential deferral	201	107	23	**536**
Negative opinions adopted	7	3	2	29
Positive opinions adopted on modification of a PIP	103	153	46	361
Negative opinions adopted on modification of a PIP	4	2	0	6
Positive opinions on compliance with a PIP	9	9	1	32
Negative opinions on compliance check with a PIP	0	0	0	1
Opinions adopted under Art. 14.2	2	0	0	2

[1] Of which 286 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	2010 *(%)*	2011 *(Number of areas covered)**	2012 *(Number of areas covered)**
Neurology	3	11	2
Uro-nephrology	2	4	0
Gastroenterology-hepatology	1	10	1
Pneumology-allergology	41	10	4
Infectious diseases	4	15	5
Cardiovascular diseases	8	21	12
Diagnostics	1	5	0
Endocrinology-gynaecology-fertility-metabolism	6	28	7
Neonatology-paediatric intensive care	0	0	0
Immunology-rheumatology-transplantation	5	13	6
Psychiatry	1	9	0
Pain	1	2	0
Haematology-haemostaseology	4	18	3
Otorhinolaryngology	3	2	1
Oncology	9	19	6
Dermatology	1	10	5
Vaccines	2	12	2
Ophthalmology	4	8	2
Anaesthesiology	2	1	1
Nutrition	0	0	0
Other		7	3

** One PIP can cover several therapeutic areas*