19 January 2011
EMA/PDCO/9884/2011
Human Medicines Development and Evaluation

Paediatric Committee (PDCO) - meeting highlights

12-14 January 2011

Opinions on paediatric investigation plans

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

- Mipomersen sodium, from Genzyme Europe B.V., in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Bucelipase alfa, from Swedish Orphan Biovitrum Ab (publ), in the therapeutic area of gastroenterology-hepatology;
- Human coagulation factor X, from Bio Products Laboratory, in the therapeutic area of haematology-hemostaseology;
- (1R,2S)-6-bromo-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-1-naphthalenyl-beta-phenyl-3-quinolineethanol, (1R,2S)-6-bromo-alpha-[2-(dimethylamino)ethyl]-2-methoxy-alpha-1-naphthalenyl-beta-phenyl-3-quinolineethanol (2E)-2-butenedioate(1:1) (salt), from Tibotec BVBA, in the therapeutic area of infectious diseases;
- Bimatoprost, from Allergan Pharmaceuticals Ireland, in the therapeutic area of ophthalmology / dermatology;
- 2'-O-methyl-uridylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-cytidylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-adenosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-adenosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-guanosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-guanosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-adenosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-adenosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-guanosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-adenosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-uridylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-guanosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-guanosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-cytidylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-adenosylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-uridylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-uridylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-uridylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-cytidylyl-(3'→5' O,O-phosphorothioyl)-2'-O-methyl-uridine sodium

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salt (also known as exon 51 specific phosphorothioate oligonucleotide), from Glaxo Group Limited, in the therapeutic area of neurology;

- Laquinimod sodium, from Teva Pharma GmbH, in the therapeutic area of neurology;
- Monoclonal antibody against human CD30 covalently linked to the cytotoxin monomethylauristatin E, from Takeda Global Research and Development Centre (Europe), Ltd, in the therapeutic area of oncology.

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.

Adoption of an opinion following re-examination

The PDCO adopted opinions for the following products: `

- Following the re-examination of the positive opinion on a PIP adopted in 12 November 2010 for GLP-1 analogue linked to human IgG4 Fc-fragment (dulaglutide, LY2189265), from Eli Lilly & Company, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism, the PDCO adopted a revised positive opinion.

A re-examination of the opinion can be requested by the applicant within 30 days following receipt of the opinion of the PDCO. The grounds for the re-examination should be based only on the original information and scientific data provided in the application that were previously available to the PDCO and on which the initial opinion was based. This may include new analysis of the same data or minor protocol amendments to a previously proposed study. Significant changes to the previous plan cannot be part of the re-examination process.

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:

- Amlodipine besilate, atorvastatin L-lysine, from Gedeon Richter Plc, in the therapeutic area of cardiovascular diseases;
- (E)-4-(2-(6-(2-(2-(2-[18F]fluoroethoxy)ethoxy)ethoxy)pyridin-3-yl)vinyl)-N-methylbenzenamine, from Avid Radiopharmaceuticals Ireland Limited, in the therapeutic area of diagnostics;
- Testosterone, from Eli Lilly and Company Limited, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Romidepsin, from Celgene Europe Limited, in the therapeutic area of oncology;
- Lenalidomide, from Celgene Europe Limited, in the therapeutic area of oncology;
- Human Papilloma Virus Type 16 E6 071-095, Human Papilloma Virus Type 16 E6 085-109, Human Papilloma Virus Type 16 E7 001-035, Human Papilloma Virus Type 16 E6 019-050, Human Papilloma Virus Type 16 E6 109-140, Human Papilloma Virus Type 16 E7 022-056, Human Papilloma Virus Type 16 E6 001-032, Human Papilloma Virus Type 16 E6 041-065, Human

Papilloma Virus Type 16 E6 055-080, Human Papilloma Virus Type 16 E7 064-098, Human Papilloma Virus Type 16 E6 091-122, Human Papilloma Virus Type 16 E6 127-158, Human Papilloma Virus Type 16 E7 043-077, from ISA Therapeutics BV, 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.

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.

Withdrawals

The PDCO noted that two 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. Five experts were invited to the January meeting.

The PDCO discussed:

- Product-specific questions regarding treatment of hypercholesterolaemia with an expert with clinical expert in paediatric cardiology;
- Product-specific non-clinical and clinical questions for a number of PIP and waiver applications with four experts in the therapeutic area of paediatric oncology;

Other issues

The PDCO welcomed the new alternate from Romania, Dr Dana Gabriela Marin, who has been nominated by the Committee for Medicinal Products for Human Use, and the new alternate from France, Dr Sylvie Benchetrit, appointed by AFSSAPS.

The next meeting of the PDCO will be held on 16-18 February 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/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 January 2011 PDCO meeting report

	2009 (January to December)	2010 (January to December)	2011 (January to current month)	Cumulative total (2007 to 2010)
Total number of validated PIP/waiver applications	273	326	18	974[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	191	280	14	710 *(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])*	72	43	3	238 *(24%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	10	4	1	26 *(3%)*
PIPs and full waiver indications covered by these applications	395	403	21	1385

Number of Paediatric Committee (PDCO) opinions	2009	2010	2011	Cumulative total
Positive on full waiver	67	52	6	182
Positive on PIP, including potential deferral	122	201	8	414
Negative opinions adopted	13	7	0	24
Positive opinions adopted on modification of a PIP	51	103	11	173
Negative opinions adopted on modification of a PIP	0	4	0	4
Positive opinions on compliance with a PIP	8	9	0	22
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 220 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	1
Uro-nephrology	5	2	0
Gastroenterology-hepatology	2	1	2
Pneumology-allergology	6	41	2
Infectious diseases	9	4	1
Cardiovascular diseases	9	8	3
Diagnostics	1	1	0
Endocrinology-gynaecology-fertility-metabolism	16	6	3
Neonatology-paediatric intensive care	2	0	1
Immunology-rheumatology-transplantation	6	5	1
Psychiatry	3	1	1
Pain	6	1	0
Haematology-haemostaseology	6	4	1
Otorhinolaryngology	1	3	0
Oncology	11	9	2
Dermatology	6	1	1
Vaccines	4	2	1
Ophthalmology	2	4	0
Anaesthesiology	1	2	0
Nutrition	0	0	0
Other			1

** One PIP can cover several therapeutic areas*