17 October 2013
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Paediatric Committee (PDCO)

PDCO monthly report of opinions on paediatric investigation plans and other activities

09-11 October 2013

Opinions on paediatric investigation plans

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

- Alirocumab, from Sanofi-aventis recherche & développement, for the treatment of elevated cholesterol;
- Sodium benzylpenilloate / benzylpenicilloyl octa- L-lysine, from Diater Laboratorio de Diagnóstico y Aplicaciones Terapéuticas, S.A., for the diagnosis of beta-lactam allergy;
- Idelalisib, from Gilead Sciences International Limited, for the treatment of mature B-cell neoplasm.

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 an opinion for the following product:

After the re-examination of the positive opinion on a PIP adopted on 9 August 2013 for Human heterologous liver cells, from Cytonet GmbH & Co. KG, for the treatment of urea cycle disorders, the PDCO has granted a deferral for paediatric studies.

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.

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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:

- Synthetic double-stranded siRNA oligonucleotide directed against transthyretin mRNA, from Alnylam Pharmaceuticals, Inc., for the treatment of familial amyloid polyneuropathy;
- Metformin hydrochloride / rosuvastatin calcium, from GlaxoSmithKline Trading Services Limited, for the Treatment of type 2 diabetes mellitus concomitant with hypercholesterolaemia;
- Amlodipine (besylate) / perindopril (arginine) / atorvastatin (calcium trihydrate, from Les Laboratoires Servier, for the treatment of ischemic coronary artery disorders, treatment of hypertension and treatment of elevated cholesterol;
- Odanacatib / colecalciferol, from Merck Sharp & Dohme (Europe), Inc., for the treatment of osteoporosis;
- Lanreotide (acetate), from Ipsen Pharma, for the treatment of acromegaly, treatment of pituitary gigantism , treatment of gastrointestinal fistulae, treatment of metastases to peritoneum and treatment of pituitary neoplasms.

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:

- Dapagliflozin, from Bristol Myers Squibb / AstraZeneca EEIG, for the treatment of type 2 Diabetes Mellitus;
- Bilastine, from Faes Farma S.A., for the treatment of allergic rhinoconjunctivitis and treatment of urticaria;
- Beclometasone dipropionate / formoterol fumarate dihydrate, from Chiesi Farmaceutici S.p.A., for the treatment of asthma;
- Certolizumab pegol, from UCB Pharma S.A., for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis);
- Human normal immunoglobulin, from Kedrion S.p.A., for the treatment of Primary Immunodeficiency (PID);
- Travoprost, from Alcon Laboratories (UK) Ltd., for the treatment of glaucoma;
- Cysteamine hydrochloride, from Orphan Europe SARL, for the treatment of cystinosis;
- N. meningitidis serogroup A polysaccharide conjugated to tetanus toxoid / N. meningitidis serogroup C polysaccharide conjugated to tetanus toxoid / N. meningitidis serogroup W

polysaccharide conjugated to tetanus toxoid / N. meningitidis serogroup Y polysaccharide conjugated to tetanus toxoid, from GlaxoSmithKline Biologicals s.a, for the prevention of Meningococcal Disease;

- Delamanid, from Otsuka Frankfurt Research Institute GmbH, for the treatment of multi drug resistant tuberculosis;
- Tapentadol (hydrochloride), from Grünenthal GmbH, for the treatment of acute pain;
- Tapentadol (hydrochloride), from Grünenthal GmbH, for the treatment of chronic pain;
- Retigabine, from Glaxo Group Limited, for the treatment of epilepsy with partial onset seizures and treatment of Lennox-Gastaut Syndrome;
- Autologous cartilage derived cultured chondrocytes, from Genzyme Europe BV, for the treatment of cartilage disorders;
- Vandetanib, from AstraZeneca AB, for the treatment of medullary thyroid carcinoma;
- Insulin degludec, from Novo Nordisk A/S, for the treatment of type I diabetes mellitus and treatment of type II diabetes mellitus.

The PDCO adopted 1 opinion on the **refusal** of modifications to an agreed PIP for:

- Riociguat, from Bayer Pharma AG, for the treatment of pulmonary hypertension.

Opinion on compliance check

The PDCO adopted positive opinions on (full) compliance check for:

- Human normal immunoglobulin, from Octapharma Pharmazeutika Produktionsges.m.b.H, for the treatment of primary immunodeficiency as model for replacement therapy and treatment of idiopathic thrombocytopenic purpura as model for immunomodulation;
- Valganciclovir hydrochloride, from Roche Registration Limited, for the prevention of infection due to cytomegalovirus in solid organ transplant recipients and treatment of infection due to cytomegalovirus in immunocompromised patients;
- Rosuvastatin (calcium), from AstraZeneca AB, for the treatment of primary hypercholesterolaemia, treatment of homozygous familial hypercholesterolaemia, treatment of primary combined (mixed) dyslipidaemia and prevention of cardiovascular events.

The PDCO adopted 1 opinion on the **refusal** of a (full) compliance check for:

- Rupatadine fumarate, from J. Uriach y Compañía, S.A., for the treatment of allergic rhinitis and treatment of chronic idiopathic urticaria.

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. Full compliance with all studies/measured contained in the PIP 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.

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.

Withdrawals

The PDCO noted that 8 applications were withdrawn during the late stages of the evaluation (30 days or less before opinion).

Committee interactions

The first PDCO/COMP workshop was organised on 9 October 2013, to discuss scientific and regulatory aspects on conditions for rare diseases.

Cooperation with other Agencies

At the October meeting, the PDCO welcomed Dr Nao Tsuchida from the National Center for Child Health and Development (NCCHD) in Japan as representative of the Pharmaceuticals and Medical Devices Agency (PMDA), Japan.

Election of the Chair and vice Chair of the PDCO

The PDCO thanked Hendrik van den Berg as he has resigned as the Committee's Vice-chair. A new election will be organised during the next meeting.

Other matters

The PDCO welcomed Birka Lehmann in her new role as a member nominated to represent Germany.

The PDCO welcomed Stefan Grosek in his new role as a member nominated to represent Slovenia.

The next meeting of the PDCO will be held on 06-08 November 2013.

– END –

Notes:

1. 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.

2. 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

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 October 2013 PDCO meeting report

	2011 (January to December)	2012 (January to December)	2013 (January to current month)	Cumulative total (2007 to present)
Total number of validated PIP/waiver applications	187	178	164	1486[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	153	149	145	1144 *(77%)*
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])*	33	28	19	315 *(21%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	1	1	0	27 *(2%)*
PIPs and full waiver indications covered by these applications	220	218	188	1990

Number of Paediatric Committee (PDCO) opinions	2011	2012	2013	Cumulative total (2007 to present)
Positive on full waiver	45	47	46	314
Positive on PIP, including potential deferral	107	87	87	687
Negative opinions adopted	3	3	3	33
Positive opinions adopted on modification of a PIP	153	165	154	634
Negative opinions adopted on modification of a PIP	2	1	3	9
Positive opinions on compliance with a PIP	9	4	12	47
Negative opinions on compliance check with a PIP	0	0	1	2
Opinions adopted under Art. 14.2	0	0	0	2

[1] Of which 389 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	2011 *(Number of areas covered)**	2012 *(Number of areas covered)**	2013 *(Number of areas covered)**
Neurology	11	11	9
Uro-nephrology	4	5	7
Gastroenterology-hepatology	10	8	13
Pneumology-allergology	10	9	7
Infectious diseases	15	19	16
Cardiovascular diseases	21	34	18
Diagnostics	5	3	3
Endocrinology-gynaecology-fertility-metabolism	28	27	27
Neonatology-paediatric intensive care	0	2	2
Immunology-rheumatology-transplantation	13	15	10
Psychiatry	9	0	7
Pain	2	9	5
Haematology-haemostaseology	18	9	10
Otorhinolaryngology	2	1	1
Oncology	19	19	26
Dermatology	10	14	10
Vaccines	12	2	4
Ophthalmology	8	5	5
Anaesthesiology	1	2	0
Nutrition	0	0	0
Other	7	16	11

** One PIP can cover several therapeutic areas*