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Paediatric Committee (PDCO)

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

7-9 August 2013

Opinions on paediatric investigation plans

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

- Idursulfase, from Shire Human Genetic Therapies AB, for the treatment of Mucopolysaccharidosis II (Hunter syndrome);
- Vorapaxar, from Prevention of arterial thromboembolism, for the Merck Sharp & Dohme (Europe), Inc;
- Iron as iron maltol (iron(III)-maltol complex), from Iron Therapeutics (UK) Ltd., for the treatment of iron deficiency anaemia (IDA);
- Tolvaptan, from Otsuka Pharmaceutical Europe Ltd., for the treatment of dilutional hyponatraemia and treatment of polycystic kidney disease
- Deleobuvir, from Boehringer Ingelheim International GmbH, for the treatment of chronic viral hepatitis C;
- Sapropterin Dihydrochloride, from Merck KGaA, for the treatment of hyperphenylalaninemia;

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:

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- Perindopril (erbumine) / Amlodipin (besylate), from Zentiva k.s., for the treatment of hypertension;
- Ramipril / amlodipine (besilate), from GlaxoSmithKline Trading Services Limited, for the treatment of hypertension;
- Valsartan / atorvastatin, from GlaxoSmithKline Trading Services Limited, for the treatment of hypertension and treatment of elevated cholesterol;
- Metformin / rosuvastatin, from Fontane Pharma GmbH, for the treatment of type 2 diabetes mellitus concomitant with hypercholesterolaemia;
- Calcium (citrate) / colecalciferol, from Pharma Patent Kft., for the prevention of calcium and vitamin D3 deficiency and treatment of calcium and vitamin D3 deficiency;

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:

- Human heterologous liver cells, from Cytonet GmbH & Co. KG, for the treatment of urea cycle disorders;
- Mepolizumab, from Glaxo Group Limited, for the treatment of asthma;
- Apixaban, from Bristol-Myers Squibb / Pfizer EEIG, for the treatment of venous thromboembolism;
- Azilsartan medoxomil, from Takeda Global Research and Development Centre (Europe) Ltd, for the treatment of hypertension;
- Fluticasone furoate / triphenylacetic acid - 4-{(1R)-2-[(6-{2-[(2,6-dichlorobenzyl)oxy]ethoxy}hexyl) amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol, from Glaxo Group Limited, for the treatment of asthma;
- Teduglutide, from Nycomed Danmark ApS, for the treatment of short bowel syndrome;
- Belimumab, from Glaxo Group Limited, for the treatment of systemic lupus erythematosus;
- Decitabine, from Janssen-Cilag International NV, for the treatment of acute myeloid leukaemia;
- Valganciclovir, 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;
- Nonacog beta pegol, from Novo Nordisk A/S, for the treatment of hereditary factor IX deficiency;
- Sonidegib, from Novartis Europharm Limited, for the treatment of medulloblastoma;
- Insulin peglispro, from Eli Lilly and Company, for the treatment of type 1 diabetes mellitus and treatment of type 2 diabetes mellitus;
- Odanacatib, from Merck Sharp & Dohme (Europe), Inc., for the treatment of osteoporosis;

- Dabrafenib (mesilate), from GlaxoSmithKline Trading Service Limited, for the treatment of melanoma and treatment of solid malignant tumours (excluding melanoma);
- 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 SA, for the prevention of infections caused by Corynebacterium diphtheriae, Clostridium tetani, Bordetella pertussis, poliovirus types 1, 2 and 3, Haemophilus influenzae type b and Hepatitis B virus;

Opinion on compliance check

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

- Voriconazole, from Pfizer Limited, for the treatment of invasive aspergillosis, treatment of candidaemia in non-neutropenic patients, treatment of fluconazole-resistant serious invasive candida infections (including C. krusei), treatment of serious fungal infections caused by Scedosporium spp. and Fusarium spp. and prevention of invasive fungal infections;
- Palivizumab, from AbbVie Ltd, for the prevention of serious lower respiratory tract disease

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.

Other matters

The PDCO welcomed Maaike van Dartel in her new role as an alternate nominated to represent The Netherlands.

The PDCO thanked Dobrin Konstantinov for his work as he resigned from the Committee.

The next meeting of the PDCO will be held on 11-13 September 2013.

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 August 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	129	1451[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	153	149	113	1112 *(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	16	312 *(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	150	1952

Number of Paediatric Committee (PDCO) opinions	2011	2012	2013	Cumulative total (2007 to present)
Positive on full waiver	45	47	37	305
Positive on PIP, including potential deferral	107	87	75	675
Negative opinions adopted	3	3	3	33
Positive opinions adopted on modification of a PIP	153	165	114	594
Negative opinions adopted on modification of a PIP	2	1	2	8
Positive opinions on compliance with a PIP	9	4	8	43
Negative opinions on compliance check with a PIP	0	0	0	1
Opinions adopted under Art. 14.2	0	0	0	2

[1] Of which 383 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	7
Uro-nephrology	4	5	5
Gastroenterology-hepatology	10	8	11
Pneumology-allergology	10	9	4
Infectious diseases	15	19	13
Cardiovascular diseases	21	34	16
Diagnostics	5	3	3
Endocrinology-gynaecology-fertility-metabolism	28	27	20
Neonatology-paediatric intensive care	0	2	2
Immunology-rheumatology-transplantation	13	15	6
Psychiatry	9	0	7
Pain	2	9	2
Haematology-haemostaseology	18	9	9
Otorhinolaryngology	2	1	0
Oncology	19	19	22
Dermatology	10	14	7
Vaccines	12	2	4
Ophthalmology	8	5	5
Anaesthesiology	1	2	0
Nutrition	0	0	0
Other	7	16	8

** One PIP can cover several therapeutic areas*

*** Tables have been updated*