24 July 2013
EMA/435730/2013
Paediatric Committee (PDCO)

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

17-19 July

Opinions on paediatric investigation plans

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

- Glycerol phenylbutyrate (GPB), from Hyperion Therapeutics, Ltd., for the treatment of urea cycle disorders;
- Budesonide, from Activaero GmbH, for the treatment of asthma;
- Glibenclamide, from AMMTeK, for the treatment of neonatal diabetes mellitus;
- Cangrelor tetrasodium salt, from The Medicines Company UK Ltd., for the prevention of non-site specific embolism and thrombosis;
- Daclizumab, from Biogen Idec Ltd, for the treatment of multiple sclerosis;
- Retosiban, from Glaxo Group Limited, for the treatment of labour onset and length abnormalities;
- Thrombomodulin alfa, from Asahi Kasei Pharma America Corporation, for the treatment of sepsis;
- Naltrexone (hydrochloride) / bupropion (hydrochloride), from Orexigen Therapeutics, Inc., for the treatment of obesity;

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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 77523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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:

- Risedronate sodium / colecalciferol, from Pharma Patent Kft., for the treatment of osteoporosis;
- Mifepristone, from Laboratorios Litaphar, S.A., for the treatment of leiomyoma of uterus;
- Pomalidomide, from Celgene Europe Ltd, for the treatment of post-essential thrombocythaemia myelofibrosis and treatment of post-polycythaemia vera myelofibrosis;

The PDCO adopted 1 opinion on the **refusal** of a request for waiver for:

- Acotiamide, from Zeria Pharmaceutical Co Ltd, for the treatment of functional dyspepsia;

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:

- Ipilimumab, from Bristol-Myers Squibb Pharma EEIG, for the treatment of solid malignant tumours excluding melanoma;
- Modified grass pollen extract, from Allergy Therapeutics (UK) Limited, for the treatment of allergic rhinitis due to pollen and treatment of acute atopic conjunctivitis;
- Alipogene tiparvovec, from uniQure biopharma B.V., for the treatment of hyperchylomicronaemia;
- Tocilizumab, from Roche Registration Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis);
- Rilpivirine (hydrochloride), from Janssen-Cilag International NV, for the treatment of Human Immunodeficiency Virus (HIV-1) infection;
- Solifenacin (succinate), from Astellas Pharma Europe B.V., for the treatment of idiopathic overactive bladder;
- Solifenacin (succinate), from Astellas Pharma Europe B.V., for the treatment of neurogenic detrusor overactivity;
- Rupadatine fumarate, from J. Uriach y Compañía, S.A., for the treatment of allergic rhinitis and treatment of chronic idiopathic urticaria;
- Mirabegron, from Astellas Pharma Europe B.V., for the treatment of idiopathic overactive bladder and treatment of neurogenic detrusor overactivity;
- Human Papillomavirus Type 6 L1 protein / Human Papillomavirus Type 11 L1 protein / Human Papillomavirus Type 16 L1 protein / Human Papillomavirus Type 18 L1 protein / Human

Papillomavirus Type 31 L1 protein / Human Papillomavirus Type 33 L1 protein / Human Papillomavirus Type 45 L1 protein / Human Papillomavirus Type 52 L1 protein / Human Papillomavirus Type 58 L1 protein, from Sanofi Pasteur MSD SNC, for the prevention of infection by human papillomavirus;

- Exenatide, from Bristol-Myers Squibb / AstraZeneca EEIG, for the treatment of type 2 diabetes mellitus;
- Eslicarbazepine (acetate), from BIAL - Portela & Ca, SA, for the treatment of epilepsy with partial onset seizures;
- Recombinant fusion protein consisting of human coagulation factor IX attached to the Fc domain of human IgG1 (rFIXFc), from Biogen Idec Ltd, for the treatment of hereditary factor IX deficiency;
- Elvitegravir, from Gilead Sciences International Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;
- 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, for the treatment of perennial allergic rhinitis;
- Fibrinogen concentrate / Thrombin preparation / Aprotinin / Calcium chloride, from Kedrion S.p.A., for the treatment of haemorrhage resulting from a surgical procedure and prevention of haemorrhage resulting from a surgical procedure;
- Recombinant fusion protein consisting of Human Coagulation Factor VIII attached to the Fc domain of Human IgG1 (rFVIIIFc), from Biogen Idec Ltd, for the treatment of hereditary factor VIII deficiency;
- Loxapine, from Alexza UK, Limited, for the treatment of schizophrenia and treatment of bipolar disorder;
- Pitolisant (hydrochloride), from Bioprojet Pharma, for the treatment of narcolepsy;
- Levofloxacin (hemihydrate), from Aptalis Pharma SAS, for the treatment of cystic fibrosis;
- Chimeric anti-disialoganglioside (GD2) monoclonal antibody (NSC764038), from United Therapeutics Europe Limited, in the treatment of neuroblastoma;

Withdrawals

The PDCO noted that 1 application was withdrawn during the late stages of the evaluation (30 days or less before opinion).

Other matters

The PDCO welcomed Sylvie Benchetrit in her new role as a member nominated to represent France, Marta Granström in her new role as an alternate nominated to represent Denmark, Marina Dimov Di Giusti in her new role as a member nominated to represent Croatia, Melinda Sobor in her new role as a CHMP alternate nominated to represent Hungary, Jana Lass in her new role as an alternate nominated to represent Estonia and Ninna Gullberg in her new role as an alternate nominated to represent Sweden.

The PDCO thanked Gerard Pons (France) for his work and dedication following the end of his mandate.

The next meeting of the PDCO will be held on 7-9 August 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 July 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	114	1436[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	153	149	100	1099 *(76%)*
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)*	33	28	14	310 *(22%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30)*	1	1	0	27 *(2%)*
PIPs and full waiver indications covered by these applications	220	218	128	1930

Number of Paediatric Committee (PDCO) opinions	2011	2012	2013	Cumulative total (2007 to present)
Positive on full waiver	45	47	32	300
Positive on PIP, including potential deferral	107	87	69	669
Negative opinions adopted	3	3	3	33
Positive opinions adopted on modification of a PIP	153	165	99	579
Negative opinions adopted on modification of a PIP	2	1	2	8
Positive opinions on compliance with a PIP	9	4	6	41
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 376 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	6
Uro-nephrology	4	5	5
Gastroenterology-hepatology	10	8	10
Pneumology-allergology	10	9	4
Infectious diseases	15	19	12
Cardiovascular diseases	21	34	13
Diagnostics	5	3	2
Endocrinology-gynaecology-fertility-metabolism	28	27	15
Neonatology-paediatric intensive care	0	2	2
Immunology-rheumatology-transplantation	13	15	4
Psychiatry	9	0	5
Pain	2	9	2
Haematology-haemostaseology	18	9	9
Otorhinolaryngology	2	1	0
Oncology	19	19	20
Dermatology	10	14	6
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*