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Paediatric Committee (PDCO)

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

11-13 September 2013

Opinions on paediatric investigation plans

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

- Sofosbuvir / ledipasvir, from Gilead Sciences International Ltd., for the treatment of chronic hepatitis C;
- Clostridium difficile toxin A human monoclonal antibody / Clostridium difficile toxin B human monoclonal antibody, from Merck Sharp & Dohme (Europe), Inc, for the treatment of Clostridium difficile infection;
- Exon 45 specific phosphorothioate oligonucleotide, from Prosensa Therapeutics B.V., for the treatment of Duchenne muscular dystrophy;
- Exon 53 specific phosphorothioate oligonucleotide, from Prosensa Therapeutics B.V., for the treatment of Duchenne muscular dystrophy;
- Recombinant human tripeptidyl peptidase-1, from BioMarin Europe Limited, for the treatment of Neuronal Ceroid Lipofuscinosis type 2;
- Quilizumab, from Roche Registration Limited, for the treatment of asthma;
- Eptacog alfa (activated), from Baxter Innovations GmbH, for the treatment of congenital coagulation disorders;
- Tedizolid (phosphate), from Trius Therapeutics Inc., for the treatment of complicated skin and soft tissue infections;
- Autologous CD34+ cells transduced with lentiviral vector containing the human Wiskott Aldrich Syndrom Protein gene, from GENETHON, for the treatment of Wiskott-Aldrich syndrome.

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

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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:

- Amlodipine / atorvastatin, from Pharmaceutical Works Polpharma SA, for the treatment of hypertension and treatment of dyslipidaemia;
- Ezetimibe / atorvastatin, from Fontane Pharma GmbH, for the treatment of elevated cholesterol;
- Ezetimibe / rosuvastatin, from Fontane Pharma GmbH, for the treatment of elevated cholesterol;
- (4R,5R)-1-[[4-[[4-[3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenoxy]methyl]phenyl]methyl]-4-aza-1-azoniabicyclo[2.2.2]octane chloride, from Lumena Pharmaceuticals Inc, for the treatment of primary biliary cirrhosis.

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:

- Edoxaban (tosylate), from Daiichi Sankyo Development Limited, for the prevention of arterial thromboembolism, treatment of venous thromboembolism and prevention of venous thromboembolism;
- Regadenoson, from Rapidcan Pharma Solutions EU Limited, for the diagnosis of myocardial perfusion disturbances;
- Octocog alfa, from Bayer Pharma AG, for the treatment of hereditary factor VIII deficiency;
- Nitisinone, from Swedish Orphan Biovitrum International AB, for the treatment of tyrosinemia type 1;
- Rufinamide, from Eisai Limited, for the treatment of Lennox-Gastaut Syndrome;
- Melatonin, from RAD Neurim Pharmaceuticals EEC Ltd, for the treatment of insomnia;
- Lumacaftor, from Vertex Pharmaceuticals (Europe) Ltd., for the treatment of cystic fibrosis;
- Lebrikizumab, from Roche Products Limited, for the treatment of asthma;
- Delamanid, from Otsuka Frankfurt Research Institute GmbH, for the treatment of multi drug resistant tuberculosis;

- Dalbavancin, from Durata Therapeutics International B.V., for the treatment of skin and soft tissue infections;
- Ozenoxacin, from Ferrer Internacional S.A., for the Treatment of impetigo;
- Guanfacine (hydrochloride), from Shire Pharmaceuticals Contracts Ltd., for the treatment of attention deficit hyperactivity disorder (ADHD);
- Lurasidone (hydrochloride), from Takeda Pharma A/S, for the treatment of schizophrenia;
- Denosumab, from Amgen Europe B.V., for the treatment of bone loss associated with sex hormone ablative therapy, prevention of skeletal related events in patients with bone metastases, treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis) and treatment of giant cell tumour of bone;
- Everolimus, from Novartis Europharm Limited, for the prevention of rejection of transplanted kidney, prevention of rejection of transplanted heart and prevention of rejection of transplanted liver;
- Plerixafor, from Genzyme Europe B.V., for the myelosuppression caused by chemotherapy to treat malignant disorders, which requires an autologous haematopoietic stem cell transplant;
- Ivacaftor, from Vertex Pharmaceuticals Incorporated, for the treatment of cystic fibrosis;
- Diphtheria toxoid / Tetanus toxoid / Bordetella pertussis antigen: Pertussis toxoid / Bordetella pertussis antigen: Filamentous Haemagglutinin / Bordetella pertussis antigen: Pertactin / Inactivated poliovirus: type 1 (Mahoney strain) / Inactivated poliovirus: type 2 (MEF-1 strain) / Inactivated poliovirus: type 3 (Saukett strain), from GlaxoSmithKline Biologicals S.A., for the prevention of infectious diseases caused by Corynebacterium diphtheriae / Clostridium tetani / Bordetella pertussis / Poliovirus types 1, 2 and 3;
- Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) GlaxoSmithKline Biologicals: Purified antigen fractions of inactivated split virion Influenza A/Vietnam/1194/2004(H5N1) like strain used (NIBRG-14), from GlaxoSmithKline Biologicals S.A., for the prevention of influenza infection;
- Purified antigen fractions of inactivated split virion Influenza A/Indonesia/05/2005(H5N1) like strain used (PR8-IBCDC-RG2), from GlaxoSmithKline Biologicals S.A., for the prevention of influenza infection.

The following product(s) was/were granted a product-specific waiver in replacement of an agreed PIP:

- Pegloticase, from Savient Pharmaceuticals, Inc., for the treatment of hyperuricaemia and prevention of hyperuricaemia[1].

Opinion on compliance check

The PDCO adopted a positive opinion on (full) compliance check for Split influenza virus, inactivated containing antigen equivalent to A/California/7/2009 (H1N1)-like strain (A/California/7/2009 (NYMC X-179A)), non-adjuvanted, from Sanofi Pasteur SA, for the prevention of Influenza infection.

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.

[1] Previously published as a modification to an agreed PIP.

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.

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. One expert was invited to the September meeting with a clinical expertise in paediatric ophthalmology, the PDCO discussed the potential need for and safety of anti VEGF (Vascular Endothelial Growth Factor) agents. A further expert was involved in a discussion of paediatric pharmacology of an anti-cancer medicinal product.

Election of the Chair and vice Chair of the PDCO

The European Medicines Agency's Paediatric Committee (PDCO) elected Dirk Mentzer as its new Chair at its September 2013 meeting. Henk van den Berg has been elected as the Committee's new Vice-chair. Both have been elected for a three-year term.

A paediatrician by training, Dr Mentzer is currently Head of the Pharmacovigilance Unit at the Paul-Ehrlich Institut in Frankfurt, Germany. Dr van den Berg is a consultant in paediatric haematology / oncology at the Medicines Evaluation Board in Utrecht, the Netherlands. Both have been members of the PDCO since it was established in 2007.

At the meeting, Drs Mentzer and van den Berg and the Committee thanked Daniel Brasseur, outgoing chair of the PDCO, for his exceptional leadership of the PDCO over the past six years, and said that they looked forward to working with him in his new capacity as a member of the Committee for Medicinal Products for Human Use (CHMP).

The main role of the PDCO is to assess the content of paediatric investigation plans (PIPs) and adopt opinions on them. This includes the assessment of applications for a full or partial waiver and assessment of applications for deferrals.

Other matters

The PDCO welcomed the new alternate for Germany, Dr Immanuel Barth.

The next meeting of the PDCO will be held on 09-11 October 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 September 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	149	1471[2]
Applications submitted for a product not yet authorised *(Article 7[3])*	153	149	132	1131 *(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[3])*	33	28	17	313 *(21%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[3])*	1	1	0	27 *(2%)*
PIPs and full waiver indications covered by these applications	220	218	171	1973

Number of Paediatric Committee (PDCO) opinions	2011	2012	2013	Cumulative total (2007 to present)
Positive on full waiver	45	47	41	309
Positive on PIP, including potential deferral	107	87	84	684
Negative opinions adopted	3	3	3	33
Positive opinions adopted on modification of a PIP	153	165	135	615
Negative opinions adopted on modification of a PIP	2	1	2	8
Positive opinions on compliance with a PIP	9	4	9	44
Negative opinions on compliance check with a PIP	0	0	0	1
Opinions adopted under Art. 14.2	0	0	0	2

[2] Of which 388 have been requests for a full waiver.
[3] 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	6
Gastroenterology-hepatology	10	8	12
Pneumology-allergology	10	9	6
Infectious diseases	15	19	15
Cardiovascular diseases	21	34	18
Diagnostics	5	3	3
Endocrinology-gynaecology-fertility-metabolism	28	27	23
Neonatology-paediatric intensive care	0	2	2
Immunology-rheumatology-transplantation	13	15	6
Psychiatry	9	0	7
Pain	2	9	3
Haematology-haemostaseology	18	9	9
Otorhinolaryngology	2	1	1
Oncology	19	19	24
Dermatology	10	14	9
Vaccines	12	2	4
Ophthalmology	8	5	5
Anaesthesiology	1	2	0
Nutrition	0	0	0
Other	7	16	10

** One PIP can cover several therapeutic areas*