20 February 2014
EMA/PDCO/60726/2014
Paediatric Committee (PDCO)

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

12-14 February 2014

Opinions on paediatric investigation plans

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

- Adalimumab, from AbbVie Ltd., for the treatment of non-infectious uveitis;
- Herpes simplex 1 virus thymidine kinase and truncated low affinity nerve growth factor receptor transfected donor lymphocytes, from MolMed S.p.A., for the adjunctive treatment in haematopoietic cell transplantation;
- Nivolumab, from Bristol-Myers Squibb International Corporation, for the treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue);
- Allergoid preparation of Phleum pratense pollen extract, from Allergopharma GmbH & Co. KG, for the treatment of allergic rhinoconjunctivitis;
- Sirolimus, from Santen Incorporated, for the treatment of chronic non-infectious uveitis;
- Anti proprotein convertase subtilisin kexin type 9 humanized monoclonal antibody (PF-04950615), from Pfizer Limited, for the treatment of elevated cholesterol, treatment of mixed dyslipidaemia and prevention of cardiovascular events in patients with cardiovascular disease or cardiovascular disease risk equivalent;
- RNA,[2'-O-(2-methoxyethyl)](P-thio)(m5U- m5C-A- m5C-m5U-m5U-m5U- m5C-A-m5U-A-A-m5U-G- m5C-m5U-G-G) (ISIS 396443), from Isis Pharmaceuticals, for the treatment of spinal muscular atrophy;
- Anti-human interleukin 23 p19 humanised IgG1/Ig kappa monoclonal antibody, from Merck Sharp & Dohme (Europe), Inc., for the treatment of psoriasis;
- (E)-4-[(5-Phenyl-1,3,4-thiadiazol-2-yl)oxy]-1-azoniatricyclo[3.3.1.13,7] decane 3,4-dicarboxy-3-hydroxybutanoate hydrate (ABT-126), from AbbVie Ltd., for the treatment of schizophrenia;

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- Anti-PD1 humanized monoclonal antibody of the IgG4/kappa class (MK-3475), from Merck Sharp & Dohme (Europe), Inc, for the treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic and lymphoid tissue);
- Cyclic pyranopterin monophosphate (monohydrobromide dihydrate), from Alexion Europe SAS, for the treatment of molybdenum cofactor deficiency type A.

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:

- Following the re-examination of the negative opinion for a PIP with deferral and waiver adopted on 6 December 2013 for Azacitidine, from Celgene Europe Ltd, for the treatment of acute myeloid leukaemia and treatment of myelodysplastic syndrome (including juvenile myelomonocytic leukaemia), the PDCO revised its opinion and adopted a 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 medicine:

- Atropine sulphate/ dimethanesulfonate / avizafone hydrochloride, from Service de santé des armées, for the treatment of organophosphorus poisoning.

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:

- Concentrate of proteolytic enzymes in bromelain, from MediWound Germany GmbH, for the treatment of burns;

- Ceftobiprole medocaril (sodium), from Basilea Pharmaceutica International Ltd., for the treatment of pneumonia;
- Golimumab, from Janssen Biologics B.V., for the treatment of ulcerative colitis;
- Glycerol phenylbutyrate, from Hyperion Therapeutics, Ltd, for the treatment of urea cycle disorders;
- Ivacaftor, from Vertex Pharmaceuticals Incorporated, for the treatment of cystic fibrosis;
- Entecavir, from Bristol-Myers Squibb Pharma EEIG, for the treatment of chronic hepatitis B;
- Oseltamivir (phosphate), from Roche Registration Ltd, for the treatment and prevention of influenza;
- Rivaroxaban, from Bayer Pharma AG, for the prevention of thromboembolic events and treatment of thromboembolic events;
- Human normal immunoglobulin, from Kedrion S.p.A., for the treatment of Primary Immunodeficiency (PID);
- Rupadatine fumarate, from J. Uriach y Compañía, S.A., for the treatment of allergic rhinitis and treatment of chronic idiopathic urticaria;
- Fidaxomicin, from Astellas Pharma Europe B.V., for the treatment of enterocolitis caused by Clostridium difficile;
- Ceftaroline fosamil, from AstraZeneca AB, for the treatment of complicated skin and soft tissue infections and treatment of community acquired pneumonia;
- Human normal immunoglobulin, from Kedrion S.p.A., for the treatment of Idiopathic thrombocytopenic purpura (ITP) and treatment of Primary Immunodeficiency (PID);
- Bimatoprost, from Allergan Pharmaceuticals Ireland, for the treatment of glaucoma and treatment of non-scarring hair loss;
- Laquinimod (sodium), from Teva Pharma GmbH, for the treatment of relapsing remitting multiple sclerosis;
- Sucroferric oxyhydroxide (mixture of iron (III)-oxyhydroxide, sucrose, starch) (PA21), from Vifor Fresenius Medical Care Renal Pharma, for the treatment of hyperphosphataemia;
- 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;
- Trametinib (dimethyl sulfoxide), from Glaxo Group Limited, for the treatment of melanoma and treatment of all conditions included in the category of malignant neoplasms (except melanoma, nervous system, haematopoietic and lymphoid tissue).

Opinion on compliance check

The PDCO adopted a positive opinion on (full) compliance check for Anagrelide hydrochloride, from Shire Pharmaceutical Contracts Limited, for the treatment of essential thrombocythaemia.

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.

Withdrawals

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

PDCO Membership

The PDCO thanked Julia Dunne for her work as she has resigned from the Committee.

The PDCO thanked Tadej Avcin for his work as he has resigned from the Committee.

The PDCO welcomed Angeliki Siapkara in her new role as member and Martina Riegl in her new role as alternate, nominated to represent United Kingdom.

The next meeting of the PDCO will be held on 19-21 March 2014.

– 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 February PDCO meeting report

	2012 (January to December)	2013 (January to December)	2014 (January to current month)	Cumulative total (2007 to present)
Total number of validated PIP/waiver applications	178	198	36	1556[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	149	176	33	1208 *(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])*	28	22	3	321 *(21%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	1	0	0	27 *(2%)*
PIPs and full waiver indications covered by these applications	218	225	39	2066

Number of Paediatric Committee (PDCO) opinions	2012	2013	2014	Cumulative total (2007 to present)
Positive on full waiver	47	52	9	329
Positive on PIP, including potential deferral	87	97	18	715
Negative opinions adopted	3	4	0	34
Positive opinions adopted on modification of a PIP	165	186	34	700
Negative opinions adopted on modification of a PIP	1	3	0	9
Positive opinions on compliance with a PIP	4	16	3	54
Negative opinions on compliance check with a PIP	0	1	0	2
Opinions adopted under Art. 14.2	0	0	0	2

[1] Of which 411 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	2012 *(Number of areas covered)**	2013 *(Number of areas covered)**	2014 *(Number of areas covered)**
Neurology	11	13	0
Uro-nephrology	5	9	1
Gastroenterology-hepatology	8	17	3
Pneumology-allergology	9	10	5
Infectious diseases	19	20	8
Cardiovascular diseases	34	21	5
Diagnostics	3	3	0
Endocrinology-gynaecology-fertility-metabolism	27	32	3
Neonatology-paediatric intensive care	2	3	0
Immunology-rheumatology-transplantation	15	11	2
Psychiatry	0	9	0
Pain	9	6	1
Haematology-haemostaseology	9	14	0
Otorhinolaryngology	1	3	0
Oncology	19	27	4
Dermatology	14	12	2
Vaccines	2	5	1
Ophthalmology	5	6	0
Anaesthesiology	2	0	0
Nutrition	0	0	0
Other	16	11	2

** One PIP can cover several therapeutic areas*