EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Paediatric Committee (PDCO)

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

04-06 July 2012

Opinions on paediatric investigation plans

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

- Apremilast, from Celgene Europe Limited, in the therapeutic area of dermatology;
- Naloxegol, from AstraZeneca AB, in the therapeutic area of gastroenterology-hepatology;
- Human fibrinogen, from Octapharma GmbH, in the therapeutic area of haematology-hemostaseology;
- Eculizumab, from Alexion Europe SAS, in the therapeutic area of immunology-rheumatology-transplantation;
- Olokizumab, from UCB Pharma S.A., in the therapeutic area of immunology-rheumatology-transplantation;
- Asunaprevir, from Bristol-Myers Squibb International Corporation, in the therapeutic area of infectious diseases;
- Daclatasvir, from Bristol-Myers Squibb International Corporation, in the therapeutic area of infectious diseases;
- Peginterferon lambda-1a, from Bristol-Myers Squibb International Corporation, in the therapeutic area of infectious diseases;
- Misoprostol, from Ferring Pharmaceuticals A/S, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Pitolisant, from Bioprojet Pharma, in the therapeutic area of neurology;
- Pegylated human interferon beta-1a, from Biogen Idec Ltd., in the therapeutic area of neurology;

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- N-[6-(cis-2,6-Dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy) [1,1'-biphenyl]-3-carboxamide diphosphate, from Novartis Europharm Limited, in the therapeutic area of oncology;
- MAGE-A3 recombinant protein, from GlaxoSmithKline Biologicals s.a, in the therapeutic area of oncology;
- Ex-vivo expanded human autologous epithelium containing stem cells, from Chiesi Farmaceutici S.p.A., in the therapeutic area of ophthalmology;
- Indacaterol (acetate) / mometasone (furoate), from Novartis Europharm Limited, in the therapeutic area of pneumology – allergology.

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 opinions for the following products:

- Following the re-examination of the positive opinion on a modification of an agreed PIP adopted on 08 June 2012 for turoctocog alfa, from Novo Nordisk A/S, in the therapeutic area of haematology-hemostaseology, the PDCO adopted a revised 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 medicines:

- Sitagliptin / atorvastatin, from Merck Sharp & Dohme (Europe), Inc., in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Autologous tumour-derived immunoglobulin idiotype coupled to keyhole limpet haemocyanin, from Biovest Europe Ltd., in the therapeutic area of oncology;
- [N-((2S,3R,3aS,3´R,4a´R,6S,6a´R,6b´S,7aR,12a´S,12b´S,Z)-3,6,11´,12b´-tetramethyl-2´,3a,3´,4,4´,4a´,5,5´,6,6´,6a´,6b´,7,7a,7´,8´,10´,12´,12a´,12b´-icosahydro-1´H,3H-spiro[furo[3,2-b]pyridine-2,9´-naphtho[2,1-a]azulene]-3´-yl)methanesulfonamide hydrochloride], from Voisin Consulting, in the therapeutic area of oncology;
- Rosuvastatin / ezetimibe, from EGIS Pharmaceuticals PLC, in the therapeutic area of cardiovascular diseases;

- Amlodipine (besilate) / lisinopril (dihydrate) / rosuvastatin (calcium), from Gedeon Richter Plc., in the therapeutic area of cardiovascular diseases;
- Recombinant human antibody against activin type IIB receptors, from Novartis Europharm Limited, in the therapeutic area of neurology;
- Co-crystal of rac-tramadol HCl / celecoxib, from Laboratorios del Dr. Esteve S.A., in the therapeutic area of pain.

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:

- Fibrinogen (human plasma-derived), from LFB Biotechnologies, in the therapeutic area of haematology-hemostaseology;
- Catridecacog, from Novo Nordisk A/S, in the therapeutic area of haematology-hemostaseology;
- Tocilizumab, from Roche Registration Limited, in the therapeutic area of immunology-rheumatology-transplantation;
- Human normal immunoglobulin, from LFB Biotechnologies, in the therapeutic area of immunology-rheumatology-transplantation;
- Oseltamivir (phosphate), from Roche Registration Ltd, in the therapeutic area of infectious diseases
- Emtricitabine / rilpivirine (hydrochloride) / tenofovir (disoproxil fumarate) [FTC/RPV/TDF], from Gilead Sciences International Limited, in the therapeutic area of infectious diseases;
- Pazopanib, from Glaxo Group Limited, in the therapeutic area of oncology.
- Human fibrinogen / human thrombin, from Omrix Biopharmaceuticals NV/SA, in the therapeutic area of other (haemostasis);
- Lubiprostone, from Sucampo Pharma Europe Ltd, in the therapeutic area of other / gastroenterology-hepatology;
- Beclometasone dipropionate / formoterol fumarate dihydrate, from Chiesi Farmaceutici S.p.A., in the therapeutic area of pneumology - allergology;
- Amikacin (sulfate), from Insmed Incorporated, in the therapeutic area of infectious diseases / pneumology - allergology;
- Pneumococcal Polysaccharide Serotype 1 – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 3 – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 4 – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 5 – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 6A – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 6B – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 7F – Diphtheria CRM197 Conjugate / Pneumococcal

Polysaccharide Serotype 9V – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 14 – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 18C – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 19A – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 19F – Diphtheria CRM197 Conjugate / Pneumococcal Polysaccharide Serotype 23F – Diphtheria CRM197 Conjugate, from Pfizer Limited, in the therapeutic area of vaccines;

- Pneumococcal polysaccharide serotype 1 conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 4 conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 5 conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 6B conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 7F conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 9V conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 14 conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein / pneumococcal polysaccharide serotype 18C conjugated to tetanus toxoid / pneumococcal polysaccharide serotype 19F conjugated to diphtheria toxoid / pneumococcal polysaccharide serotype 23F conjugated to protein D (derived from non-typeable haemophilus influenzae) carrier protein, from GlaxoSmithKline Biologicals S.A., in the therapeutic a area of vaccines

Withdrawals

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

The PDCO also noted that an opinion after re-examination adopted during the June PDCO meeting for ranirestat, from Eisai Ltd, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism, has been withdrawn before the decision was adopted by the Agency.

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 July meeting with a clinical expertise in paediatric oncological surgery, with whom the PDCO discussed the potential needs, utility and safety of diagnostic medicines.

Other matters

The next meeting of the PDCO will be held on 15-17 August 2012.

– 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

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Annex of the July PDCO meeting report

	2010 (January to December)	2011 (January to December)	2012 (January to current month)	Cumulative total (2007 to present)
Total number of validated PIP/waiver applications	326	187	102	1246[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	280	153	81	931 *(75%)*
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])*	43	33	21	289 *(23%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	4	1	0	26 *(2%)*
PIPs and full waiver indications covered by these applications	403	220	127	1711

Number of Paediatric Committee (PDCO) opinions	2010	2011	2012	Cumulative total (2007 to present)
Positive on full waiver	52	45	20	241
Positive on PIP, including potential deferral	201	107	56	569
Negative opinions adopted	7	3	3	30
Positive opinions adopted on modification of a PIP	103	153	96	411
Negative opinions adopted on modification of a PIP	4	2	1	7
Positive opinions on compliance with a PIP	9	9	1	32
Negative opinions on compliance check with a PIP	0	0	0	1
Opinions adopted under Art. 14.2	2	0	0	2

[1] Of which 304 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	2010 *(%)*	2011 *(Number of areas covered)**	2012 *(Number of areas covered)**
Neurology	3	11	6
Uro-nephrology	2	4	2
Gastroenterology-hepatology	1	10	2
Pneumology-allergology	41	10	5
Infectious diseases	4	15	13
Cardiovascular diseases	8	21	21
Diagnostics	1	5	2
Endocrinology-gynaecology-fertility-metabolism	6	28	12
Neonatology-paediatric intensive care	0	0	1
Immunology-rheumatology-transplantation	5	13	8
Psychiatry	1	9	0
Pain	1	2	6
Haematology-haemostaseology	4	18	7
Otorhinolaryngology	3	2	1
Oncology	9	19	14
Dermatology	1	10	7
Vaccines	2	12	2
Ophthalmology	4	8	3
Anaesthesiology	2	1	1
Nutrition	0	0	0
Other		7	6

** One PIP can cover several therapeutic areas*