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Paediatric Committee (PDCO)

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

05-07 December 2012

Opinions on paediatric investigation plans

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

- Apixaban, from Bristol-Myers Squibb / Pfizer EEIG, in the therapeutic area of cardiovascular diseases;
- Human dermal fibroblasts cultured on bioresorbable polyglactin mesh (ABH001), from TMC Pharma, in the therapeutic area of dermatology;
- Dobutamine (hydrochloride), from Proveca Limited, in the therapeutic area of neonatology – paediatric intensive care
- Everolimus, from Novartis Europharm Limited, in the therapeutic area of uro-nephrology / Neurology.

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:

- Amlodipine besilate / indapamide / perindopril erbumine, from Billev Pharma Aps, in the therapeutic area of cardiovascular diseases;

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- Atorvastatin calcium / Amlodipine besylate, from Billev Pharma ApS, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism / cardiovascular diseases.
- Oxycodone hydrochloride / morphine sulfate, from QRxPharma Inc, 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:

- Propranolol hydrochloride, from Pierre Fabre Dermatologie, in the therapeutic area of dermatology.
- Dapagliflozin, from Bristol Myers Squibb /AstraZeneca EEIG, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Empagliflozin, from Boehringer Ingelheim International GmbH, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Linagliptin, from Boehringer Ingelheim International GmbH, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Liraglutide, from Novo Nordisk A/S, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Sitagliptin, from Merck Sharp and Dohme (Europe), Inc., in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Catridecacog, from Novo Nordisk A/S, in the therapeutic area of haematology-hemostaseology;
- Eltrombopag, from GlaxoSmithKline Trading Services Limited, in the therapeutic area of haematology-hemostaseology;
- Ferumoxytol, from AMAG Pharmaceuticals Inc., in the therapeutic area of haematology-hemostaseology;
- Eculizumab, from Alexion Europe SAS, in the therapeutic area of immunology-rheumatology-transplantation;
- Ustekinumab, from Janssen-Cilag International NV, in the therapeutic area of immunology-rheumatology-transplantation;
- Atazanavir sulphate, from Bristol-Myers Squibb Pharma EEIG, in the therapeutic area of infectious diseases;
- Ceftaroline fosamil, from AstraZeneca AB, in the therapeutic area of infectious diseases;
- Fidaxomicin, from Astellas Pharma Europe B.V., in the therapeutic area of infectious diseases;
- Valganciclovir hydrochloride, from Roche Registration Limited, in the therapeutic area of infectious diseases;
- Laquinimod (sodium), from Teva Pharma GmbH, in the therapeutic area of neurology;

- Tigecycline, from Pfizer Limited, in the therapeutic area of other (anti-infectives).

Withdrawals

The PDCO noted that 8 applications were withdrawn during the late stages of the evaluation (30 days or less before opinion).

PDCO interactions

An expert from the Medical and Pharmaceutical Statistics Research Unit of the University of Lancaster, United Kingdom, presented an analysis of methods of dose-finding studies in agreed PIPs and discussed with the PDCO.

Informal meeting

On 22-23 November, the PDCO held an informal meeting in Rome, organised by the Ospedale Bambino Gesu' and the Italian Medicines Agency (AIFA), to review the work done and the processes put in place during its sixth year. On the first day, several presentations on the issues of paediatric clinical trials were given. On the second day, The PDCO discussed improvements in the functioning of the Committee, in particular: application summaries, model PIPs for asthma, interactions with the COMP (a joint session between the two Committees was also organised), and Paediatric Use Marketing Authorisations..

Other matters

European Commission

Mr Florian Schmidt, Legal Officer in the Medicinal Products-Authorisations Unit of the Directorate General for Health and Consumers (European Commission), attended the PDCO meeting to present an initial feedback on the number and type of responses received during the public consultation on the Paediatric Regulation.

Inventory of therapeutic needs

In the course of establishing an inventory of therapeutic needs according to article 43 of the Paediatric Regulation (Regulation (EC) No 1901/2006) the PDCO adopted the inventory for the therapeutic area of cardiovascular diseases. The inventory for the therapeutic area of infectious diseases was adopted for public consultation.

PDCO membership

The PDCO welcomed the new alternate for United Kingdom, Dr Angeliki Siapkara, who has been nominated by the Medicines and Healthcare products Regulatory Agency.

The next meeting of the PDCO will be held on 09-11 January 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 December 2012 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	178	1322[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	280	153	149	999 *(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[2])*	43	33	28	296* *(22%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	4	1	1	27 *(2%)*
PIPs and full waiver indications covered by these applications	403	220	218	1802

Number of Paediatric Committee (PDCO) opinions	2010	2011	2012	Cumulative total (2007 to present)
Positive on full waiver	52	45	47	268
Positive on PIP, including potential deferral	201	107	87	600
Negative opinions adopted	7	3	3	30
Positive opinions adopted on modification of a PIP	103	153	165	480
Negative opinions adopted on modification of a PIP	4	2	1	7
Positive opinions on compliance with a PIP	9	9	4	35
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 339 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	11
Uro-nephrology	2	4	5
Gastroenterology-hepatology	1	10	8
Pneumology-allergology	41	10	9
Infectious diseases	4	15	19
Cardiovascular diseases	8	21	34
Diagnostics	1	5	3
Endocrinology-gynaecology-fertility-metabolism	6	28	27
Neonatology-paediatric intensive care	0	0	2
Immunology-rheumatology-transplantation	5	13	15
Psychiatry	1	9	0
Pain	1	2	9
Haematology-haemostaseology	4	18	9
Otorhinolaryngology	3	2	1
Oncology	9	19	19
Dermatology	1	10	14
Vaccines	2	12	2
Ophthalmology	4	8	5
Anaesthesiology	2	1	2
Nutrition	0	0	0
Other		7	16

** One PIP can cover several therapeutic areas*