10 October 2012
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Paediatric Committee (PDCO)

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

03-05 October 2012

Opinions on paediatric investigation plans

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

- (2R,3S,5R)-2-(2,5-Difluorophenyl)-5-[2,6-dihydro-2-(methylsulfonyl)pyrrolo[3,4-c]pyrazol-5(4H)-yl]tetrahydro-2H-pyran-3-amine (MK-3102), from Merck Sharp & Dohme (Europe), Inc., in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Tofacitinib (citrate), from Pfizer Limited, in the therapeutic area of immunology-rheumatology-transplantation / dermatology;
- Tazobactam / ceftolozane, from Cubist Pharmaceuticals, Inc., in the therapeutic area of infectious diseases;
- Dolutegravir / abacavir / lamivudine, from ViiV Healthcare UK Limited., in the therapeutic area of infectious diseases;
- Ponesimod, from Actelion Registration Limited, in the therapeutic area of neurology;
- Natalizumab, from Elan Pharma International Limited, in the therapeutic area of neurology;
- Regorafenib, from Bayer Pharma AG, in the therapeutic area of oncology
- Travoprost, from Alcon Laboratories (UK) Ltd., in the therapeutic area of ophthalmology;
- Levofloxacin (hemihydrate), from Mpex London 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.

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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 (besylate) / valsartan, from Zentiva, k.s., in the therapeutic area of cardiovascular diseases;
- Perindopril / indapamide / amlodipine, from Krka, d.d., Novo mesto, in the therapeutic area of cardiovascular diseases;
- Brimonidine tartrate, from Galderma International, in the therapeutic area of dermatology;
- Ezetimibe / rosuvastatin, from Zentiva, k.s., in the therapeutic area of endocrinology-gynaecology-fertility-metabolism / cardiovascular diseases;
- Lopinavir / ritonavir / lamivudine, from Abbott Laboratories Limited, in the therapeutic area of infectious diseases;
- N-tert-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino]benzenesulfonamide dihydrochloride monohydrate (SAR302503), from Sanofi-aventis R&D, in the therapeutic area of oncology-haematology;
- Icatibant, from Shire Orphan Therapies GmbH, in the therapeutic area of other;
- Alpha1-proteinase inhibitor, from CSL Behring GmbH, in the therapeutic areas of pneumology – allergology and gastroenterology.

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:

- Azilsartan medoxomil, from Takeda Global Research and Development Centre (Europe) Ltd, in the therapeutic area of cardiovascular diseases;
- Bosentan, from Actelion Registration Ltd, in the therapeutic area of cardiovascular diseases / pneumology - allergology;
- Nicotinic acid / laropiprant, from Merck Sharp & Dohme Ltd., in the therapeutic area of cardiovascular diseases;
- Riociguat, from Bayer Schering Pharma AG in the therapeutic area of cardiovascular diseases;
- Methoxy polyethylene glycol- epoetin beta, from Roche Registration Limited, in the therapeutic area of haematology-hemostaseology;
- Human normal immunoglobulin, from Kedrion S.p.A., in the therapeutic area of haematology-haemostaseology / immunology-rheumatology-transplantation;

- Adalimumab, from Abbott Laboratories Ltd, in the therapeutic area of immunology-rheumatology-transplantation / dermatology / gastroenterology-hepatology;
- Simeprevir, from Janssen Infectious Diseases BVBA, in the therapeutic area of infectious diseases;
- Artemether / lumefantrine, from Novartis Europharm Limited, in the therapeutic area of infectious diseases;
- Eslicarbazepine (acetate), from Bial - Portela & Ca, SA, in the therapeutic area of neurology;
- Fingolimod (hydrochloride), from Novartis Europharm Limited, in the therapeutic area of neurology;
- Nilotinib, from Novartis Europharm Ltd, in the therapeutic area of oncology;
- Brentuximab vedotin, from Takeda Global Research and Development Centre (Europe) Ltd, in the therapeutic area of oncology;
- Methoxyflurane, from Orion Clinical Services, in the therapeutic area of pain;
- Lebrikizumab, from Roche Products Ltd, in the therapeutic area of pneumology - allergology;
- Aripiprazole, from Otsuka Pharmaceutical Europe Ltd, in the therapeutic area of psychiatry;
- 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 area of vaccines.

Opinion on compliance check

The PDCO adopted the following positive opinions on (full) compliance check for:

- Human normal immunoglobulin, from LFB Biotechnologies, in the therapeutic area of immunology-rheumatology-transplantation.
- Misoprostol, from Ferring Pharmaceuticals A/S, in the therapeutic area of other / endocrinology-gynaecology-fertility-metabolism;

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 one application was withdrawn during the late stages of the evaluation (30 days or less before opinion).

Other matters

The next meeting of the PDCO will be held on 07-09 November 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

Enquiries only to: paediatrics@ema.europa.eu

Annex of the October 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	147	1291[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	280	153	123	973 *(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	24	292 *(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	176	1760

Number of Paediatric Committee (PDCO) opinions	2010	2011	2012	Cumulative total (2007 to present)
Positive on full waiver	52	45	39	260
Positive on PIP, including potential deferral	201	107	75	588
Negative opinions adopted	7	3	3	30
Positive opinions adopted on modification of a PIP	103	153	142	457
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 323 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	9
Uro-nephrology	2	4	4
Gastroenterology-hepatology	1	10	6
Pneumology-allergology	41	10	7
Infectious diseases	4	15	18
Cardiovascular diseases	8	21	27
Diagnostics	1	5	2
Endocrinology-gynaecology-fertility-metabolism	6	28	22
Neonatology-paediatric intensive care	0	0	2
Immunology-rheumatology-transplantation	5	13	11
Psychiatry	1	9	0
Pain	1	2	9
Haematology-haemostaseology	4	18	9
Otorhinolaryngology	3	2	1
Oncology	9	19	16
Dermatology	1	10	12
Vaccines	2	12	2
Ophthalmology	4	8	4
Anaesthesiology	2	1	2
Nutrition	0	0	0
Other		7	10

** One PIP can cover several therapeutic areas*