6 January 2014
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Paediatric Committee (PDCO)

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

04-06 December 2013

Opinions on paediatric investigation plans

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

- Mesalazine / prednisolone metasulphobenzoate, from Disphar International B.V., for the treatment of ulcerative colitis;
- Cobimetinib, from Roche Registration Limited, for the treatment of a malignant solid tumour;
- Etrolizumab, from Roche Products Limited, for the treatment of ulcerative colitis;
- Raltegravir 300 mg / Lamivudine 150 mg, from Merck Sharp & Dohme (Europe), Inc., for the treatment of human immunodeficiency virus (HIV-1) infection;
- 9-cis-retinyl acetate, from QLT Ophthalmics (UK), Ltd., for the treatment of Retinitis Pigmentosa and treatment of Leber's Congenital Amaurosis;
- Elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide, from Gilead Sciences International Limited, for the treatment of human immunodeficiency virus (HIV-1) infection.

The PDCO adopted an opinion on the **refusal** of a PIP, including a deferral and waiver, for Azacitidine, from Celgene Europe Ltd, for the treatment of acute myeloid leukaemia and treatment of myelodysplastic 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 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:

- Caffeine / Ibuprofen, from Boehringer Ingelheim International GmbH, for the treatment of pain.
- Diclofenac / Levomenthol, from GlaxoSmithKline Consumer Trading Services Limited, for the treatment of local pain and inflammation.

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:

- Everolimus, from Novartis Europharm Ltd, for the treatment of subependymal giant cell astrocytoma and treatment of angiomyolipoma;
- Bevacizumab, from Roche Registration Ltd., for the treatment of rhabdomyosarcoma and treatment of non-rhabdomyosarcoma soft tissue sarcoma;
- Bevacizumab, from Roche Registration Ltd., for the treatment of high-grade glioma;
- Telbivudine, from Novartis Europharma Limited, for the treatment of chronic hepatitis B;
- Dabigatran etexilate, from Boehringer Ingelheim International GmbH, for the prevention of thromboembolic events and treatment of thromboembolic events;
- Aprepitant, from Merck Sharp & Dohme Ltd., for the prevention of nausea and vomiting;
- Clevidipine butyrate, from The Medicines Company UK Ltd., for the treatment of hypertensive disease;
- Rilpivirine (hydrochloride), from Janssen-Cilag International NV, for the treatment of Human Immunodeficiency Virus (HIV-1) infection;
- Adalimumab, from AbbVie Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis), treatment of Crohn's disease and treatment of psoriasis;
- Secukinumab, from Novartis Europharm Limited, for treatment of chronic idiopathic arthritis (including rheumatoid arthritis, spondyloarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Fosaprepitant, from Merck Sharp & Dohme Ltd., for the prevention of nausea and vomiting;
- Lisdexamfetamine (dimesylate), from Shire Pharmaceutical Contracts Ltd, for the treatment of attention deficit hyperactivity disorder (ADHD);

- Mirabegron, from Astellas Pharma Europe B.V., for the treatment of idiopathic overactive bladder and treatment of neurogenic detrusor overactivity;
- Simeprevir, from Janssen Infectious Diseases BVBA, for the treatment of chronic viral hepatitis C;
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extract from the pollen of Betula alba, from LETI Pharma GmbH, for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extract of birch, alder and hazel pollen, from LETI Pharma GmbH, for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Cysteamine hydrochloride, from Orphan Europe SARL, for the treatment of cystinosis;
- Siponimod (hemifumarate), from Novartis Europharm Limited, for the treatment of multiple sclerosis;
- Empagliflozin, from Boehringer Ingelheim International GmbH, for the treatment of type 2 diabetes mellitus;
- Human coagulation factor X, from Bio Products Laboratory, for the treatment of hereditary factor X deficiency;
- Lomitapide, from Aegerion Pharmaceuticals SAS, for the treatment of heterozygous and homozygous familial hypercholesterolaemia;
- Albiglutide, from GlaxoSmithKline LLC, for the treatment of type 2 diabetes mellitus;
- Benralizumab, from MedImmune Ltd, for the treatment of asthma;
- Anagrelide (hydrochloride), from Shire Pharmaceuticals Contracts Limited, for the treatment of essential thrombocythaemia.

Opinion on compliance check

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

- Prucalopride, from Shire Pharmaceuticals Ireland Limited, for the treatment of chronic constipation;
- Guanfacine (hydrochloride), from Shire Pharmaceuticals Contracts Ltd., for the treatment of attention deficit hyperactivity disorder (ADHD);
- Atomoxetine (hydrochloride), from Eli Lilly & Company, for the treatment of attention deficit hyperactivity disorder.

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.

Interaction with external experts

The PDCO has regular interactions with academic experts, with a view to obtain state-of-the-art knowledge in the PDCO scientific discussions. One expert was invited to the December meeting, with a clinical expertise in paediatric neuro-oncology, with whom the PDCO discussed therapeutic needs and treatment approaches in young children.

Informal meeting

On 25-26 November 2013, the PDCO and CAT held an informal meeting in Trieste, hosted by Italy and Slovenia, to review the work done. The PDCO discussed improvements, interactions with experts, learned societies and industry, and priorities in the implementation of the Paediatric Regulation.

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 update the PDCO on some on-going topics of shared interest (e.g. the public consultation on the EC guideline on the format and content of PIP applications, the call for new civil society representatives in the PDCO, and other issues of legal relevance).

PDCO Membership

The PDCO welcomed the new alternate from Bulgaria, Dr Vessela Boudinova.

The PDCO thanked Margarita Guizova for her work, following the end of her mandate.

The next meeting of the PDCO will be held on 15-17 January 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 December 2013 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	198*	1520*[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	153	149	176*	1175* *(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])*	33	28	22	318 *(21%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	1	1	0	27 *(2%)*
PIPs and full waiver indications covered by these applications	220	218	225*	2027*

Number of Paediatric Committee (PDCO) opinions	2011	2012	2013	Cumulative total (2007 to present)
Positive on full waiver	45	47	52	320
Positive on PIP, including potential deferral	107	87	97	697
Negative opinions adopted	3	3	4	34
Positive opinions adopted on modification of a PIP	153	165	186	666
Negative opinions adopted on modification of a PIP	2	1	3	9
Positive opinions on compliance with a PIP	9	4	16	51
Negative opinions on compliance check with a PIP	0	0	1	2
Opinions adopted under Art. 14.2	0	0	0	2

[1] Of which 398 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	2011 *(Number of areas covered)**	2012 *(Number of areas covered)**	2013 *(Number of areas covered)**
Neurology	11	11	13
Uro-nephrology	4	5	9
Gastroenterology-hepatology	10	8	17
Pneumology-allergology	10	9	10
Infectious diseases	15	19	20
Cardiovascular diseases	21	34	21
Diagnostics	5	3	3
Endocrinology-gynaecology-fertility-metabolism	28	27	32*
Neonatology-paediatric intensive care	0	2	3
Immunology-rheumatology-transplantation	13	15	11
Psychiatry	9	0	9
Pain	2	9	6
Haematology-haemostaseology	18	9	14
Otorhinolaryngology	2	1	3
Oncology	19	19	27
Dermatology	10	14	12
Vaccines	12	2	5
Ophthalmology	8	5	6
Anaesthesiology	1	2	0
Nutrition	0	0	0
Other	7	16	11

** One PIP can cover several therapeutic areas*