14 November 2013
EMA/PDCO/687508/2013
Paediatric Committee (PDCO)

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

06-08 November 2013

Opinions on paediatric investigation plans

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

- Sodium N-{6-[3-tert-Butyl-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2-methoxyphenyl]naphthalen-2-yl} methanesulfonamide hydrate (ABT-333), from AbbVie Ltd, for the treatment of chronic hepatitis C;
- 2R,6S,12Z,13aS,14aR,16aS)-N-(cyclopropylsulfonyl)-6-{[(5-methylpyrazin-2-yl)carbonyl]amino}-5,16-dioxo-2-(phenanthridin-6-yloxy)-1,2,3,6,7,8,9,10,11,13a,14,15,16,16a-tetradecahydrocyclopropa[e]pyrrolo[1,2-a][1,4]diazacyclopentadecine-14a(5H)-carboxamide hydrate (ABT-450) /Dimethyl ([(2S,5S)-1-(4-tert-butylphenyl) pyrrolidine-2,5-diyl]bis{benzene-4,1-diylcarbamoyl(2S)pyrrolidine-2,1-diyl[(2S)-3-methyl-1-oxobutane-1,2-diyl]})biscarbamate hydrate) (ABT-267) / ritonavir, from AbbVie Ltd, for the Treatment of chronic hepatitis C;
- Heterologous Human Adult Liver-derived Progenitor Cells (HHALPC), from Promethera Biosciences, for the treatment of urea cycle disorders and treatment of Crigler-Najjar syndrome;
- Estetrol / Levonorgestrel, from Estetra S.A., for the prevention of pregnancy.

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:

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- Amlodipine (besilate) / olmesartan (medoxomil), from Zentiva k.s., for the treatment of essential hypertension;
- Acetylsalicylic acid / omeprazole, from Pozen UK Limited, for the prevention of ischaemic coronary artery disorders and prevention of cerebrovascular embolism and thrombosis;
- Solifenacin (succinate) / mirabegron, from Astellas Pharma Europe B.V., for the treatment of myoneurogenic bladder disorders;
- Alpha-1 antitrypsin, from Triskel EU Services, Ltd., for the treatment of emphysema secondary to congenital deficiency of alpha-1 antitrypsin.

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:

- Gadobutrol, from Bayer Pharma AG, for the Diagnostic evaluation of tissue pathologies with contrast-enhanced magnetic resonance imaging (MRI);
- Treprostinil, from United Therapeutics Europe, Ltd., for the treatment of pulmonary arterial hypertension;
- Brivaracetam, from UCB Pharma SA, for the treatment of paediatric epilepsy syndromes, treatment of neonatal seizures and treatment of epilepsy with partial onset seizures;
- Perampanel, from Eisai Europe Limited, for the treatment of treatment-resistant epilepsies (localisation-related or generalised epilepsies and age-related epilepsy syndromes);
- Golimumab, from Janssen Biologics B.V., for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, spondyloarthritis, psoriatic arthritis, and juvenile idiopathic arthritis);
- Asfotase alfa, from Alexion Europe SAS, for the treatment of hypophosphatasia;
- Elvitegravir, from Gilead Sciences International Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Aciclovir, from BioAlliance PHARMA, for the treatment of herpes simplex labialis.

Opinion on compliance check

The PDCO adopted a positive opinion on (full) compliance check for Ulipristal acetate, from Laboratoire HRA Pharma, for the prevention of pregnancy.

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.

Class waivers

The PDCO adopted an opinion on the confirmation of the current list of class waivers for conditions that do not affect children, or for classes of medicinal products to be used in specific conditions, and for which the requirement to submit a PIP can therefore be waived. The list of class waivers is updated at least once a year by the PDCO.

Withdrawals

The PDCO noted that 2 applications were withdrawn during the late stages of the evaluation (30 days or less before opinion).

Committee interactions

Three members of the Advanced Therapies Committee (CAT) attended the November meeting of the PDCO bringing state-of-the-art knowledge to the PDCO scientific discussions as part of the collaboration between Committees.

Election of new Vice-chair

The European Medicines Agency's Paediatric Committee (PDCO) elected Koenraad Norga as its new Vice-chair. Prof Koenraad Norga is currently Head of Clinic, Paediatric Oncology, at the Antwerp University as well as an Academic Faculty Member at the Faculty of Medicine and Health Sciences in Antwerp, Belgium.

Other matters

Involvement of young people in clinical research

The involvement of young people in clinical research was discussed between the PDCO and 3 invited members of the UK Medicines for Children Research Network (MCRN) Young People Advisory Group (YPAG), respectively the MCRN Consumer Liaison Manager and 2 adolescents.

PDCO membership

The PDCO welcomed the new member for Bulgaria, Professor Violeta Iotova.

The next meeting of the PDCO will be held on 04-06 December 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 November 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	186	1508[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	153	149	165	1164 *(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	21	317 *(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	212	2014

Number of Paediatric Committee (PDCO) opinions	2011	2012	2013	Cumulative total (2007 to present)
Positive on full waiver	45	47	50	318
Positive on PIP, including potential deferral	107	87	91	691
Negative opinions adopted	3	3	3	33
Positive opinions adopted on modification of a PIP	153	165	162	642
Negative opinions adopted on modification of a PIP	2	1	3	9
Positive opinions on compliance with a PIP	9	4	13	48
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	10
Uro-nephrology	4	5	8
Gastroenterology-hepatology	10	8	15
Pneumology-allergology	10	9	9
Infectious diseases	15	19	18
Cardiovascular diseases	21	34	21
Diagnostics	5	3	3
Endocrinology-gynaecology-fertility-metabolism	28	27	31
Neonatology-paediatric intensive care	0	2	2
Immunology-rheumatology-transplantation	13	15	11
Psychiatry	9	0	8
Pain	2	9	6
Haematology-haemostaseology	18	9	10
Otorhinolaryngology	2	1	3
Oncology	19	19	26
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*