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Procedure Management and Committees Support Division

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

15-17 April 2015

Opinions on paediatric investigation plans

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

- Mirabegron, from Astellas Pharma Europe B.V., for the treatment of neurogenic detrusor overactivity;
- Peanut allergen extract, from DBV Technologies S.A., for the treatment of peanut allergy;
- Misoprostol, from Azanta Danmark A/S, for the induction of labour;
- Norovirus GI.1 virus-like particle antigen / Norovirus GII.4 virus-like particle antigen, from Takeda Vaccines, Inc., for the prevention of acute norovirus gastroenteritis;
- Humanised monoclonal antibody IgG2 recognising the interleukin-31 receptor A (CIM331), from Chugai Pharma Europe Ltd., for the treatment of atopic dermatitis;
- Vericiguat, from Bayer Pharma AG, for the treatment of left ventricular failure;
- Palovarotene, from Clementia Pharmaceuticals Inc., for the treatment of fibrodysplasia ossificans progressiva;
- Emtricitabine / rilpivirine / tenofovir alafenamide, from Gilead Sciences International Ltd, for the treatment of human immunodeficiency virus (HIV-1) infection.

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 medicine:

- Ranolazine / Dronedarone, from Gilead Sciences International Ltd, for the treatment of supraventricular arrhythmias.
- Telavancin (hydrochloride), from Clinigen Healthcare Ltd, for the treatment of complicated skin and soft tissue infections (cSSTI);

The PDCO adopted 1 opinion on the **refusal** of a request for waiver for:

- Levomilnacipran, from Pierre Fabre Medicament, for the treatment of stroke.

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:

- Apixaban, from Bristol-Myers Squibb / Pfizer EEIG, for the prevention of venous thromboembolism and prevention of arterial thromboembolism;
- Telavancin (hydrochloride), from Clinigen Healthcare Ltd, for the treatment of nosocomial pneumonia;
- Ivacaftor, from Vertex Pharmaceuticals Incorporated, for the treatment of cystic fibrosis;
- Human normal immunoglobulin, from Kedrion S.p.A., for the treatment of Primary Immunodeficiency (PID);
- Alogliptin benzoate (as alogliptin), from Takeda Development Centre Europe Ltd, for the treatment of type 2 diabetes mellitus;
- Solifenacin (succinate), from Astellas Pharma Europe B.V., for the treatment of neurogenic detrusor overactivity;
- Mirabegron, from Astellas Pharma Europe B.V., for the treatment of idiopathic overactive bladder;
- Artemether / lumefantrine, from Novartis Europharm Limited, for the treatment of *Plasmodium falciparum* malaria;
- Human fibrinogen, from Octapharma Pharmazeutika Produktionsges.m.b.H, for the treatment of congenital fibrinogen deficiency;
- Recombinant single chain coagulation factor VIII, from CSL Behring GmbH, for the treatment of congenital factor VIII deficiency;
- Epratuzumab, from UCB Pharma S.A., for the treatment of systemic lupus erythematosus;
- Dupilumab, from Regeneron Pharmaceuticals, Inc, for the treatment of atopic dermatitis;

- Tasimelteon, from Vanda Pharmaceuticals Ltd., for the treatment of non-24-hour sleep-wake disorder in the totally blind.

Adoption of an opinion following re-examination

The PDCO adopted opinions for the following product:

- Following the re-examination of the positive opinion on a modification to an agreed PIP adopted on 13 February 2015 for Dulaglutide, from Eli Lilly & Company, for the treatment of type 2 diabetes mellitus, the PDCO recommended to revise its opinion and to agree to the changes regarding the measures of the paediatric investigation plan in the scope set out in the Annex I of the 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.

Withdrawals

The PDCO noted that 1 application was withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure).

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. The PDCO discussed, via teleconference, with an expert in paediatric PET imaging, the strategy for calculation of paediatric estimates of organ doses and paediatric effective dose.

Other matters

The next meeting of the PDCO will be held on 20-22 May 2015.

– 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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