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Procedure Management and Committees Support Division

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

9 - 11 December 2015

Opinions on paediatric investigation plans

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

- Osilodrostat, from Novartis Europharm Limited, for the treatment of adrenal cortical hyperfunction;
- Abrilumab, from MedImmune Ltd, for the treatment of Crohn's disease and treatment of ulcerative colitis;
- 17 beta-estradiol / etonogestrel, from Merck Sharp & Dohme (Europe), Inc., for the prevention of pregnancy and treatment of dysmenorrhea;
- Eteplirsen, from Sarepta International C.V., for the treatment of Duchenne muscular dystrophy;
- Recombinant human antibody against the respiratory syncytial virus fusion protein (REGN2222), from Regeneron Ireland, for the prevention of lower respiratory tract disease caused by respiratory syncytial virus;
- Rilpivirine / Dolutegravir, from ViiV Healthcare Limited, for the treatment of human immunodeficiency virus 1 (HIV-1) infection.

The PDCO adopted an opinion on the **refusal** of a PIP, including a deferral, for 13C-Methacetin, from Humedics GmbH, for the diagnosis of liver disease.

For this medicine the PDCO granted a product-specific waiver on its own motion for all subsets of the paediatric population from birth to less than 18 years of age, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing diagnostic methods.

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

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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:

- Tiprelestat, from Proteo Biotech AG, for the treatment of oesophageal carcinoma;
- Processed nerve allograft (human), from AxoGen Corporation, for the treatment of nerve injuries;
- Revusiran, from Alnylam Pharmaceuticals, Inc., for the treatment of transthyretin-mediated amyloidosis (ATTR amyloidosis;
- Pexiganan acetate, from Dipexium Pharmaceuticals, Inc., for the treatment of diabetic foot ulcers;
- (3Z,5S)-5-(hydroxymethyl)-1-[(2'-methyl[1,1'-biphenyl]-4-yl)-carbonyl]-3-pyrrolidinone-O-methyloxime, from ObsEva Ireland Limited, for the treatment of female infertility.

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:

- Human heterologous liver cells, from Cytonet GmbH & Co. KG, for the treatment of urea cycle disorders;
- Mepolizumab, from GSK Trading Services Limited, for the treatment of Hypereosinophilic Syndrome;
- Cinacalcet hydrochloride, from Amgen Europe B.V., for the treatment of parathyroid carcinoma, treatment of primary hyperparathyroidism and treatment of secondary hyperparathyroidism in patients with end-stage renal disease;
- Ataluren, from PTC Therapeutics International Limited, for the treatment of dystrophinopathy;
- Retigabine, from Glaxo Group Limited, for the treatment of epilepsy with partial onset seizures and treatment of Lennox-Gastaut Syndrome;
- Peginterferon alfa-2a, from Roche Registration Limited, for the treatment of chronic hepatitis C and treatment of chronic hepatitis B;
- Ustekinumab, from Janssen-Cilag International NV, for the treatment of chronic plaque psoriasis;
- Rilpivirine (hydrochloride), from Janssen-Cilag International NV, for the treatment of human immunodeficiency virus (HIV-1) infection;

- Conestat alfa, from Pharming Group N.V., for the treatment of hereditary angioedema;
- Selepressin, from Ferring Pharmaceuticals A/S, for the treatment of septic shock;
- Blinatumomab, from Amgen Europe B.V., for the treatment of acute lymphoblastic leukaemia;
- Vedolizumab, from Takeda Pharma A/S, for the treatment of Crohn's disease and treatment of ulcerative colitis;
- Bosutinib, from Pfizer Limited, for the treatment of chronic myeloid leukaemia (CML);
- Dulaglutide, from Eli Lilly & Company, for the treatment of type 2 diabetes mellitus;
- Sonidegib, from Novartis Europharm Ltd., for the treatment of medulloblastoma;
- Canagliflozin, from Janssen-Cilag International NV, for the treatment of type 2 diabetes mellitus;
- Clostridium Botulinum neurotoxin type A (150 kD), free of complexing proteins, from Merz Pharmaceuticals GmbH, for the treatment of sialorrhoea;
- Sirukumab, from Janssen-Cilag International N.V., for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Nonacog alfa, from Baxalta Innovations GmbH, for the treatment of haemophilia B (congenital factor IX deficiency);
- Dabrafenib, from Novartis Europharm Limited, for the treatment of melanoma and treatment of solid malignant tumours (excluding melanoma);
- Albiglutide, from GlaxoSmithKline Trading Services Limited, for the treatment of type 2 diabetes mellitus;
- Trametinib, from Novartis Europharm Limited, for the treatment of melanoma and treatment of all conditions included in the category of malignant neoplasms (except melanoma, nervous system, haematopoietic and lymphoid tissue);
- Damoctocog alfa pegol, from Bayer Pharma AG, for the treatment of hereditary factor VIII deficiency;
- PEGylated recombinant factor VIII, from Baxalta Innovations GmbH, for the treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency);
- Vancomycin, from Fondazione PENTA Onlus, for the treatment of bacterial sepsis.

Opinion on compliance check

The PDCO adopted a positive opinion on (full) compliance check for Ipilimumab, from Bristol-Myers Squibb Pharma EEIG, for the treatment of all conditions included in the category of malignant neoplasms (except melanoma, nervous system, haematopoietic and lymphoid tissue).

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 6 applications were withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure).

Other matters

The PDCO welcomed the new member, Dimitar Russinov, who has been nominated to represent Bulgaria.

The PDCO thanked Violeta Iotova for her work following the end of her mandate as member.

The next meeting of the PDCO will be held on 27-29 January 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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