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Procedure Management and Committees Support Division

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

27-29 January 2016

Opinions on paediatric investigation plans

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

- Eculizumab, from Alexion Europe SAS, for the treatment of myasthenia gravis;
- Romosozumab, from Amgen Europe B.V., for the treatment of osteoporosis;
- Nivolumab, from Bristol-Myers Squibb Pharma EEIG, for the treatment of malignant neoplasms of lymphoid tissue and treatment of malignant neoplasms of the central nervous system;
- Binimetinib, from Pierre Fabre Médicament, for the treatment of melanoma;
- Guselkumab, from Janssen Cilag International NV, for the treatment of psoriasis;
- Encorafenib, from Pierre Fabre Médicament, for the treatment of melanoma;
- Gemtuzumab linked to ozogamicin, from Pfizer Limited, for the treatment of acute myeloid leukaemia;
- Arimoclomol (citrate), from Orphazyme ApS, for the treatment of Niemann-Pick disease, type C;
- Exenatide, from Les Laboratoires Servier, for the treatment of type 2 diabetes mellitus;
- (2R,3R,4R,5R)-5-(4-amino-2-oxopyrimidin-1(2H)-yl)-2-(chloromethyl)-4-fluoro-2-((isobutyryloxy)methyl)tetrahydrofuran-3-yl isobutyrate (ALS-008176), from Alios Biopharma, Inc, for the treatment of lower respiratory tract disease caused by human respiratory syncytial virus;
- Tetracaine (hydrochloride) / oxymetazoline (hydrochloride), from St. Renatus, LLC, for local anaesthesia;
- Rolapitant, from TESARO UK Ltd, for the prevention of nausea and vomiting;

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- Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with lentiviral vector that encodes for the human Wiskott Aldrich Syndrome (WAS) cDNA sequence, from GlaxoSmithKline Trading Services Limited, for the treatment of Wiskott Aldrich Syndrome;
- Human normal immunoglobulin, from Octapharma Pharmazeutika Produktionsges.m.b.H, for the treatment of primary immunodeficiency;
- Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted), from Novartis Vaccines Influenza S.r.l., for the prevention of influenza infection;
- Levamisole (hydrochloride), from ACE Pharmaceuticals BV, for the treatment of glomerulonephritis and nephrotic 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.

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:

- Biotin, from MEDDAY SAS, for the treatment of multiple sclerosis;
- Azithromycin / Miconazole / Sulfamethoxazole, from Lukács és Társa Gyógyszerkereskedelmi Bt., for the treatment of burns;
- Recombinant human monoclonal antibody against growth differentiation factor 8 (REGN1033), from Regeneron Pharmaceuticals, Inc, for the treatment of sporadic inclusion body myositis;
- Humanised IgG4 monoclonal antibody against extracellular tau (BMS-986168), from Bristol-Myers Squibb International Corporation, for the treatment of progressive supranuclear palsy;
- Ramipril / amlodipine, from Krka, d.d., Novo mesto, for the treatment of hypertension;
- Testosterone, from Allergan Pharmaceuticals Ireland, for the treatment of dry eye disease;
- Fluoroestradiol (^{18}F), from Florentin Artner, for the detection of increased expression of oestrogen receptors in tissues and organs for diagnostic purposes.

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:

- Dalbavancin, from Durata Therapeutics International B.V., for the treatment of acute bacterial skin and skin structure infections;
- Saxagliptin, from AstraZeneca AB, for the treatment of type 2 diabetes mellitus;
- Dabigatran etexilate, from Boehringer Ingelheim International GmbH, for the prevention of thromboembolic events and treatment of thromboembolic events;
- Denosumab, from Amgen Europe B.V., for the treatment of osteoporosis;
- Rituximab, from Roche Registration Limited, for the treatment of granulomatosis with polyangiitis (Wegener's) and treatment of microscopic polyangiitis;
- Tapentadol (hydrochloride), from Grünenthal GmbH, for the treatment of chronic pain;
- Pazopanib, from Glaxo Group Limited, for the treatment of rhabdomyosarcoma, treatment of non-rhabdomyosarcoma soft tissue sarcoma and treatment of Ewing sarcoma family of tumours;
- Trenonacog alfa, from Cangene Europe Limited, for the treatment of hereditary factor IX deficiency (Haemophilia B);
- Dapagliflozin, from AstraZeneca AB, for the treatment of type 1 Diabetes Mellitus;
- Rufinamide, from Eisai Limited, for the treatment of Lennox-Gastaut Syndrome;
- Midostaurin, from Novartis Europharm Ltd, for the treatment of acute myeloid leukaemia, treatment of malignant mastocytosis and treatment of mast cell leukaemia;
- Aztreonam, from Gilead Sciences International Limited, for the treatment of *Pseudomonas aeruginosa* pulmonary infection / colonisation in patients with cystic fibrosis;
- Meropenem, from NeoMero Consortium, for the treatment of bacterial sepsis and treatment of bacterial meningitis;
- Macitentan, from Actelion Registration Ltd., for the treatment of pulmonary arterial hypertension, treatment of systemic sclerosis and treatment of idiopathic pulmonary fibrosis;
- Loxapine, from Ferrer Internacional, S.A., for the treatment of schizophrenia and treatment of bipolar disorder;
- Human fibrinogen / human thrombin, from Omrix Biopharmaceuticals N.V., for the treatment of haemorrhage resulting from a surgical procedure and treatment of cerebrospinal fluid leakage resulting from a neurosurgical procedure;
- Recombinant dimer of 6 kD early secretory antigenic target / recombinant 10 kD culture filtrate protein, from Statens Serum Institut, for the diagnosis of tuberculosis;
- Ferric maltol, from Iron Therapeutics (UK) Ltd., for the treatment of iron deficiency anaemia (IDA);

- Tolvaptan, from Otsuka Pharmaceutical Europe Ltd., for the treatment of dilutional hyponatraemia and treatment of polycystic kidney disease;
- Evolocumab, from Amgen Europe B.V., for the treatment of elevated cholesterol and treatment of mixed dyslipidaemia;
- Naltrexone (hydrochloride) / bupropion (hydrochloride), from Orexigen Therapeutics Ireland Limited, for the treatment of obesity;
- Dupilumab, from Regeneron Pharmaceuticals, Inc, for the treatment of atopic dermatitis;
- Basmisanil, from Roche Registration Ltd, for the treatment of Down syndrome;
- Etelcalcetide, from Amgen Europe B.V., for the treatment of hyperparathyroidism;
- Cariprazine (hydrochloride), from Gedeon Richter Plc., for the treatment of schizophrenia;
- Naloxone (hydrochloride), from Develco Pharma GmbH, for treatment of opioid-induced constipation;
- Tasimelteon, from Vanda Pharmaceuticals Ltd., for the treatment of non-24-hour sleep-wake disorder in the totally blind.

The PDCO adopted 1 opinion on the **refusal** of modifications to an agreed PIP for:

- Zoledronic acid, from Novartis Europharm Limited, for the treatment of osteoporosis and treatment of Paget's disease of the bone.

Opinion on compliance check

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

- Everolimus, from Novartis Europharm Limited, for the treatment of subependymal giant cell astrocytoma;
- Velaglucerase alfa, from Shire Pharmaceuticals Ireland Limited, for the treatment of Gaucher Disease, Types 1 and 3 and treatment of Gaucher Disease, Type 2;
- Human normal immunoglobulin, from Bio Products Laboratory Limited, for the treatment of primary immunodeficiency as model for replacement therapy and treatment of idiopathic thrombocytopenic purpura as model for immunomodulation;
- Ozenoxacin, from Ferrer Internacional, S.A., for the treatment of impetigo.

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

Other matters

PDCO Work Plan 2016

The PDCO adopted its work plan 2016 outlining objectives to be achieved by the Committee in specific scientific and regulatory areas. The PDCO work plan 2016 is available here:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000124.jsp&mid=WC0b01ac0580028e9e.com

Increased transparency of ongoing applications for paediatric medicines

In line with its commitment for increased transparency, the European Medicines Agency has started publishing additional information on applications for paediatric procedures in the agendas of the Paediatric Committee (PDCO). The new level of transparency in the PDCO agenda relates to information on on-going applications for Paediatric Investigation Plans (PIPs), applications for a full or partial waiver and assessment of applications for deferrals and modifications of agreed PIPs (see Agenda of PDCO meeting of 27-29 January 2016). Once opinions on these paediatric procedures will be adopted, additional information will be made available in the PDCO minutes. The increased level of transparency is part of the Agency's continuing efforts to ensure EU regulatory processes are transparent and open. The PDCO has been publishing agendas and minutes of its meetings since July 2012. All seven of the Agency's scientific committees, including the CHMP, are publishing agendas and minutes systematically.

PDCO Membership

The PDCO welcomed Immanuel Barth in his new role as member and Sabine Scherer in her role as alternate, both nominated to represent Germany.

The PDCO thanked Birka Lehmann for her work at the end of her mandate as member for Germany.

The PDCO welcomed Adriana Andrić in her role as member and Suzana Mimica Matanovic in her new role as alternate, both nominated to represent Croatia.

The PDCO thanked Marina Dimov Di Giusti for her work at the end of her mandate as alternate for Croatia.

The next meeting of the PDCO will be held on 24-26 February 2016.

– 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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