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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

29 May-01 June 2018

Opinions on paediatric investigation plans

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

- Itacitinib, EMEA-002178-PIP01-17, from Incyte Biosciences UK Ltd., for the treatment of acute graft versus host disease;
- Bimekizumab, EMEA-002189-PIP01-17, from UCB Biopharma SPRL, for the treatment of psoriasis;
- Ustekinumab, EMEA-000311-PIP05-17, from Janssen-Cilag International NV, for the treatment of Ulcerative Colitis;
- Palbociclib, EMEA-002146-PIP01-17, from Pfizer Limited, for the treatment of Ewing sarcoma;
- Purified inactivated rabies virus (WISTAR PM/WI 38-1503-3M strain), EMEA-002234-PIP01-17, from Sanofi Pasteur S.A., for the prevention of rabies viral infection;
- (R)-2-amino-3-phenylpropylcarbamate hydrochloride (solriamfetol), EMEA-002184-PIP01-17, from Jazz Pharmaceuticals UK Ltd, for the treatment of narcolepsy and treatment of obstructive sleep apnoea;
- Dasiglucagon, EMEA-002233-PIP01-17, from Zealand Pharma A/S, for the treatment of hypoglycaemia;
- Recombinant IgG degrading enzyme of Streptococcus pyogenes , EMEA-002183-PIP01-17, from Hansa Medical AB, for the prevention of graft rejection following solid organ transplantation;

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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Adoption of an opinion following re-examination

None

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:

- Dapagliflozin, EMEA-000694-PIP03-17, from AstraZeneca AB, for the prevention of cardiovascular events in patients with chronic heart failure;
- Patidegib, EMEA-002322-PIP01-17, from Blue-Reg Europe on behalf of Pellepharm Inc, for the treatment of naevoid basal-cell carcinoma syndrome (Gorlin syndrome);
- Upadacitinib, EMEA-001741-PIP05-17, from AbbVie Ltd, for the treatment of vasculitides;
- Fostamatinib, EMEA-001196-PIP02-17, from Rigel Pharmaceuticals Ltd, for the treatment of immune thrombocytopenia (idiopathic thrombocytopenic purpura);
- Abatacept, EMEA-000118-PIP04-17, from Bristol-Myers Squibb Pharma EEIG, for the treatment of Sjögren's Syndrome;
- Bilastine, EMEA-000347-PIP03-18, from FAES FARMA S.A., for the treatment of allergic rhinoconjunctivitis and treatment of urticaria;
- Nitrous oxide, EMEA-002340-PIP01-18, from Società Italiana Carburo Ossigeno Spa SICO, for anaesthesia, analgesia and sedation

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

- Liposomal ciclosporin A (L-CsA), EMEA-002344-PIP01-18, from Breath Therapeutics GmbH, for the treatment of bronchiolitis obliterans syndrome;
- Moxonidine, EMEA-002275-PIP01-17, from Abbott Laboratories, for the treatment of hypertension;
- Trandolapril, EMEA-002274-PIP01-17, from Abbott Laboratories, for the treatment of hypertension;

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:

- Fibrinogen / thrombin/ aprotinin / calcium chloride, EMEA-001079-PIP01-10-M04, from Kedrion S.p.A., for the prevention of haemorrhage resulting from a surgical procedure and treatment of haemorrhage resulting from a surgical procedure;
- Citric acid (as citric acid anhydrous) / sodium chloride / simeticone / macrogol 4000 / sodium citrate

/ sodium sulfate (as sodium sulfate anhydrous) / potassium chloride, EMEA-001356-PIP02-12-M02, from Alfasigma S.p.A., for the bowel cleansing prior to clinical procedures;

- Potassium citrate monohydrated / potassium hydrogen carbonate, EMEA-001535-PIP01-13-M01, from Advicenne, for the treatment of cystinuria
- Eculizumab, EMEA-000876-PIP05-15-M03, from Alexion Europe SAS, for the treatment of myasthenia gravis;
- Tasimelteon, EMEA-001531-PIP01-13-M04, from Vanda Pharmaceuticals, for the treatment of non-24-hour sleep-wake disorder in the totally blind;
- Recombinant varicella zoster virus (VZV) glycoprotein E, EMEA-001426-PIP01-13-M02, from GlaxoSmithKline Biologicals SA, for the prevention of varicella zoster virus (VZV) reactivation;
- Empagliflozin, EMEA-000828-PIP01-09-M07, from Boehringer Ingelheim International GmbH, for the treatment of type 2 diabetes mellitus;
- Cobimetinib, EMEA-001425-PIP01-13-M03, from Roche Registration Limited, for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue) with Ras, Raf or MEK pathway activation;
- Gabapentin, EMEA-001310-PIP01-12-M03, from PHARM Srl, for the treatment of chronic pain;
- Expanded donor-derived allogenic T cells transduced with the retroviral vector expressing the transgenes for inducible caspase9 and the truncated CD19 selectable marker, EMEA-001869-PIP01-15-M01, from Bellicum Pharma Ltd, for the adjunctive treatment in haematopoietic stem cell transplantation;
- Pitolisant, EMEA-001176-PIP01-11-M03, from BIOPROJET PHARMA, for the treatment of narcolepsy;
- Mexiletine (hydrochloride), EMEA-002012-PIP01-16-M01, from Lupin (Europe) Ltd., for the treatment of myotonic disorders;
- Bempedoic acid, EMEA-001872-PIP01-15-M01, from Esperion Therapeutics, Inc., for the treatment of elevated cholesterol;
- Tocilizumab, EMEA-000309-PIP04-17-M01, from Roche Registration Ltd., for the treatment of systemic sclerosis and treatment of cytokine release syndrome associated with chimeric antigen receptor (CAR) T cell therapy;
- Ticagrelor, EMEA-000480-PIP01-08-M11, from AstraZeneca AB, for the prevention of thromboembolic events;
- Vonicog alfa, EMEA-001164-PIP01-11-M02, from Baxalta Innovations GmbH, for the treatment of Von Willebrand Disease;
- Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with lentiviral vector that encodes for the human ARSA cDNA sequence, EMEA-001765-PIP02-15-M02, from GlaxoSMithKline Trading Services Limited, for the treatment of metachromatic leukodystrophy;
- Ligelizumab, EMEA-001811-PIP02-15-M02, from Novartis Europharm Ltd., for the treatment of chronic spontaneous urticaria;
- Tofacitinib, EMEA-000576-PIP01-09-M09, from Pfizer Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis);

- Sucroferric oxyhydroxide (mixture of iron (III)-oxyhydroxide, sucrose, starch), EMEA-001061-PIP01-10-M03, from Vifor Fresenius Medical Care Renal Pharma France, for the treatment of hyperphosphataemia;
- 2-hydroxypropyl-ß-cyclodextrin (HP-ß-CD), EMEA-001866-PIP01-15-M02, from Mallinckrodt Pharmaceuticals Ireland Ltd, for the treatment of Niemann-Pick disease, type C;
- Rimiducid, EMEA-001870-PIP01-15-M01, from Bellicum Pharma Ltd., for the treatment of graft versus host disease;
- Brodalumab, EMEA-001089-PIP02-13-M01, from LEO Pharma A/S, for the treatment of psoriasis;
- Linagliptin, EMEA-000498-PIP01-08-M08, from Boehringer Ingelheim International GmbH, for the treatment of type 2 diabetes mellitus;
- Larotrectinib, EMEA-001971-PIP02-16-M01, from Bayer AG, for the treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms).;
- Influenza virus surface antigens (haemagglutinin and neuraminidase) of the following strains: A/(H1N1), A/(H3N2), B/Yamagata lineage, B/Victoria lineage, EMEA-001782-PIP01-15-M03, from Abbott Biologicals B.V., for the prevention of Influenza infection;
- Arimoclomol (citrate), EMEA-001748-PIP01-15-M01, from Orphazyme A/S, for the treatment of Niemann-Pick disease, type C;
- Glycerol phenylbutyrate, EMEA-000297-PIP02-12-M02, from Horizon Pharma Ireland Limited, for the treatment of urea cycle disorders;
- Sirolimus, EMEA-001416-PIP01-12-M02, from Santen Incorporated, for the treatment of chronic non-infectious uveitis;

The PDCO adopted opinions on the **refusal** of modifications to an agreed PIP for the following applications:

- Regadenoson, EMEA-000410-PIP01-08-M03, from GE Healthcare AS, for the diagnosis of myocardial perfusion disturbances;

Opinion on compliance check

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

- Everolimus, EMEA-C-000019-PIP08-12-M03, from Novartis Europharm Limited, for the treatment of tuberous sclerosis complex;

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/measures 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 next meeting of the PDCO will be held on 26–29 June 2018.

– 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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