24 August 2016
EMA/PDCO/567509/2016
Procedure Management and Committees Support Division

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

17-19 August 2016

Opinions on paediatric investigation plans

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

- Guadecitabine, EMEA-001730-PIP02-15, from Otsuka Europe Development and Commercialisation Ltd., for the treatment of acute myeloid leukemia;
- Bivalent anti-human myostatin adnectin recombinant human IgG1-Fc fusion protein, EMEA-001793-PIP01-15, from Bristol-Myers Squibb International Corporation, for the treatment of Duchenne Muscular Dystrophy;
- copanlisib, EMEA-001757-PIP02-15, from Bayer Pharma AG, for the treatment of all conditions included in the category of malignant neoplasms (except hematopoietic and lymphoid tissue);;
- Recombinant, CHO cell expressed, fully human IgG1, kappa light chain, monoclonal antibody, EMEA-001864-PIP01-15, from Dyax Corp., for the prevention of hereditary angioedema;
- Ragweed pollen extract (Ambrosia artemisiifolia), EMEA-001881-PIP01-15, from ALK Abelló A/S, for the treatment of allergic rhinitis / rhino-conjunctivitis.

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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- lifitegrast, EMEA-001979-PIP01-16, from Shire Pharmaceuticals Ireland Limited, for the treatment of dry eye disease;
- Recombinant respiratory syncytial virus vaccine, EMEA-001966-PIP01-16, from MedImmune Limited, for the prevention of lower respiratory tract disease caused by respiratory syncytial virus;
- Gentamicin sulphate, EMEA-001982-PIP01-16, from Innocoll, for the treatment of infected diabetic foot ulcers;
- Ibuprofen / paracetamol, EMEA-002002-PIP01-16, from FARMALIDER, S.A, for the treatment of pain.

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

- 18F fluoromisonidazole, EMEA-001977-PIP02-16, from RadioMedic s.r.o., for the imaging of hypoxic tissue in non-small cell lung cancer for diagnostic purposes, imaging of hypoxic tissue in renal cell carcinoma for diagnostic purposes, imaging of hypoxic tissue in gliomas for diagnostic purposes and imaging of hypoxic tissue in head and neck squamous cell carcinoma 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:

- Reslizumab, EMEA-001202-PIP02-13-M01, from Teva Pharmaceuticals Europe, for the treatment of asthma;
- eftrenonacog alfa, EMEA-000914-PIP01-10-M03, from Biogen Idec Ltd, for the treatment of hereditary factor IX deficiency;
- Tedizolid (phosphate), EMEA-001379-PIP01-12-M02, from Merck Sharp & Dohme (Europe), Inc., for the treatment of acute bacterial skin and skin structure infections;
- Alogliptin benzoate (as alogliptin), EMEA-000496-PIP01-08-M05, from Takeda Development Centre Europe Ltd, for the treatment of type 2 diabetes melitus;
- Delamanid, EMEA-001113-PIP01-10-M05, from Otsuka Europe Development and Commercialisation Ltd., for the treatment of multi drug resistant tuberculosis;
- albiglutide, EMEA-001175-PIP01-11-M04, from Glaxo Group Limited, for the treatment of type 2 diabetes mellitus;
- Human recombinant IgG1 monoclonal antibody targeting fibroblast growth factor 23 (FGF23), EMEA-001659-PIP01-15-M01, from Ultragenyx Pharmaceutical Inc., for the treatment of X-linked hypophosphataemia;
- zuretinol (acetate), EMEA-001453-PIP01-13-M01, from QLT Ophthalmics (UK), Ltd., for the treatment of Leber congenital amaurosis and treatment of retinitis pigmentosa;
- Peanut flour, EMEA-001734-PIP01-14-M01, from Aimmune Therapeutics, for the treatment of peanut allergy;

- Sapropterin dihydrochloride, EMEA-001476-PIP01-13-M01, from BioMarin International Limited, for the treatment of hyperphenylalaninemia;
- nusinersen, EMEA-001448-PIP01-13-M02, from Biogen Idec Ltd, for the treatment of spinal muscular atrophy;
- Autologous CD34+ cells transduced with lentiviral vector containing the human Wiskott Aldrich Syndrom Protein gene., EMEA-000786-PIP01-09-M02, from Genethon, for the treatment of Wiskott-Aldrich syndrome;
- selepressin, EMEA-000506-PIP01-08-M02, from Ferring Pharmaceuticals A/S, for the treatment of septic shock;
- apixaban, EMEA-000183-PIP01-08-M04, from Bristol-Myers Squibb / Pfizer EEIG, for the prevention of arterial thromboembolism and prevention of venous thromboembolism;
- Elvitegravir, EMEA-000968-PIP02-11-M05, from Gilead Sciences International Ltd, for the treatment of human immunodeficiency virus (HIV-1) infection;
- vilanterol / fluticasone furoate, EMEA-000431-PIP01-08-M09, from Glaxo Group Limited, for the treatment of asthma;
- Cerliponase alfa, EMEA-001362-PIP01-12-M03, from BioMarin International Limited, for the treatment of Neuronal Ceroid Lipofuscinosis type 2.

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

- Human Fibrinogen / Human Thrombin, EMEA-001598-PIP01-13-M02, from Instituto Grifols, S.A., for the treatment of haemorrhage resulting from a surgical procedure.

Opinion on compliance check

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

- Icatibant (acetate), EMEA-C-000408-PIP01-08-M05, from Shire Orphan Therapies GmbH, for the treatment of hereditary angioedema (HAE);
- Pitavastatin (calcium), EMEA-C-000054-PIP01-07-M04, from Kowa Pharmaceutical Europe Co. Ltd., treatment of disorders of lipoprotein metabolism and other lipidaemias and treatment of homozygous familial hypercholesterolaemia;
- Pitavastatin (calcium), EMEA-C-000300-PIP01-08-M04, from Kowa Pharmaceutical Europe Co. Ltd., for the treatment of disorders of lipoprotein metabolism and other lipidaemias and treatment of homozygous familial hypercholesterolaemia;

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.

Adoption of an opinion following re-examination

The PDCO adopted opinions for the following products:

- Following the re-examination of the positive opinion on a modification of an agreed PIP, adopted on 27 May 2016 for Dulaglutide, EMEA-000783-PIP01-09-M04, from Eli Lilly & Company, for the treatment of type 2 diabetes mellitus, the PDCO adopted a revised positive opinion.
- Following the re-examination of the positive opinion on a modification of a PIP adopted on 24 June 2016 for Lumacaftor / ivacaftor, EMEA-001582-PIP01-13-M04, from Vertex Pharmaceuticals (Europe) Limited, for the treatment of cystic fibrosis, the PDCO adopted a revised positive 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 7 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 from Greece, Eleni Katsomiti.

The PDCO welcomed the new alternate from Greece, Anastasia Mountaki.

PDCO thanked Grigorios Melas for his work at the end of his mandate as member for Greece.

PDCO thanked Stefanos Mantagos for his work at the end of his mandate as alternate for Greece.

The next meeting of the PDCO will be held on 14-16 September 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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