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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

7 - 10 November 2017

Opinions on paediatric investigation plans

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

- Vosoritide, EMEA-002033-PIP01-16, from BioMarin International Limited, for the treatment of achondroplasia;
- Risankizumab, EMEA-001776-PIP02-17, from AbbVie Ltd, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, spondylarthritis and juvenile idiopathic arthritis);
- Brazikumab, EMEA-001929-PIP01-16, from Allergan Limited, for the treatment of Crohn's disease and for the treatment of ulcerative colitis;
- Trazodone (hydrochloride), EMEA-002142-PIP01-17, from Aziende Chimiche Riunite Angelini Francesco - A.C.R.A.F - S.p.A, for the treatment of insomnia;
- Susoctocog alfa, EMEA-000753-PIP02-16, from Baxalta Innovations GmbH, for the treatment of congenital haemophilia A with antibodies (inhibitors) to human factor VIII;
- Carotuximab, EMEA-002138-PIP01-17, from TRACON Pharma Limited, for the treatment of soft tissue sarcoma;
- Budesonide / glycopyrronium bromide / formoterol (fumarate), EMEA-002063-PIP01-16, from Pearl Therapeutics, Inc., for the treatment of asthma;
- Fremanezumab, EMEA-001877-PIP03-17, from Teva Pharma GmbH, for prevention of cluster headache
- Cemiplimab, EMEA-002007-PIP02-17, from Regeneron Ireland U.C., for the treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue)

A PIP sets out a programme for the development of a medicine in the paediatric population. The PIP

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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.

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 PIP with deferral and waiver adopted on 15 September 2017 for Crisaborole, EMEA-002065-PIP01-16, from Pfizer Ltd., for the treatment of atopic dermatitis, the PDCO recommended to maintain its opinion and:

1. to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
2. to grant a deferral in accordance with Article 21 of said Regulation;
3. to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of Regulation (EC) No 1901/2006 as amended, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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.

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:

- Synthetic double-stranded small interfering RNA (siRNA) oligonucleotide specific to the mRNA of the caspase 2 gene, EMEA-002224-PIP01-17, from Quark Pharmaceuticals, Inc., for the treatment of optic ischaemic neuropathy;
- Sirolimus, EMEA-002213-PIP01-17, from Vascular Therapies, Inc., for the prevention of arteriovenous access dysfunction;

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 coagulation factor X, EMEA-000971-PIP01-10-M03, from Bio Products Laboratory Limited, for the treatment of hereditary factor X deficiency;

- Human normal immunoglobulin, EMEA-001853-PIP01-15-M01, from Grifols Therapeutics Inc, for the treatment of primary immunodeficiency;
- Human fibrinogen / Human thrombin, EMEA-001149-PIP01-11-M04, from Omrix Biopharmaceuticals N.V., for the treatment of cerebrospinal fluid leakage resulting from a neurosurgical procedure and for the treatment of haemorrhage resulting from a surgical procedure;
- Blinatumomab, EMEA-000574-PIP02-12-M02, from Amgen Europe B.V., for the treatment of Acute Lymphoblastic Leukaemia;
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergic extract of equal amounts of Phleum pratense, Dactylis glomerata, Festuca elatior, Lolium perenne and Poa pratensis pollen (Grasses-Mix) and Secale cereale (Cultivated Rye) pollen (50/50), EMEA-000792-PIP01-09-M01, from LETI Pharma GmbH, for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergic extract of equal amounts of Phleum pratense, Dactylis glomerata, Festuca elatior, Lolium perenne and Poa pratensis pollen (Grasses-Mix) (1/5) each, EMEA-000794-PIP01-09-M01, from LETI Pharma GmbH, for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Eluxadoline, EMEA-001579-PIP01-13-M02, from Allergan Limited, for the treatment of diarrhoea-predominant irritable bowel syndrome;
- Lanadelumab, EMEA-001864-PIP01-15-M01, from Shire Pharmaceuticals Ireland Limited, for the prevention of hereditary angioedema attacks;
- Sildenafil, EMEA-000671-PIP01-09-M09, from Pfizer Limited, for the treatment of Pulmonary Arterial Hypertension;
- Ibrutinib, EMEA-001397-PIP03-14-M03, from Janssen-Cilag International N.V., for the treatment of mature B-cell neoplasm;
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergic extract of Phleum pratense pollen, EMEA-000795-PIP01-09-M01, from LETI Pharma GmbH, for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Ataluren, EMEA-000115-PIP01-07-M09, from PTC Therapeutics International, Limited, for the treatment of dystrophinopathy;
- Bezlotoxumab, EMEA-001645-PIP01-14-M02, from Merck Sharp & Dohme (Europe), Inc., for the treatment of *Clostridium difficile* infection;
- Avacopan, EMEA-002023-PIP01-16-M02, from ChemoCentryx, Ltd., for the treatment of anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis;
- Inotuzumab ozogamicin, EMEA-001429-PIP01-13-M02, from Pfizer Ltd., for the treatment of B cell acute lymphoblastic leukaemia

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

- Cannabidiol / Delta-9-tetrahydrocannabinol, EMEA-000181-PIP01-08-M04, from GW Pharma Ltd, for the treatment of spasticity;
- Recombinant human glutamic acid decarboxylase (rhGAD65), EMEA-000609-PIP01-09-M01, from Diamyd Medical AB, for the treatment of type I diabetes mellitus;

Opinion on compliance check

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

- Mepolizumab, EMEA-C-000069-PIP02-10-M08, from GlaxoSmithKline Trading Services, for the treatment of asthma;
- Recombinant human nerve growth factor, EMEA-C-001729-PIP01-14-M01, from Dompé farmaceutici SpA, for the treatment of neurotrophic keratitis;
- Japanese encephalitis vaccine (inactivated, absorbed), EMEA-C-000559-PIP01-09-M04, from Valneva Austria GmbH, for the prevention of Japanese encephalitis;
- Fingolimod (hydrochloride), EMEA-C-000087-PIP01-07-M05, from Novartis Europharm Limited, for the treatment of multiple sclerosis;

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 2 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 12 – 15 December 2017.

– 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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