15 September 2017
EMEA/PDCO/644202/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

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

12-15 September 2017

Opinions on paediatric investigation plans

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

- Maribavir, EMEA-000353-PIP02-16, from Shire Pharmaceuticals Ireland Limited, for the treatment of cytomegalovirus (CMV) infection;
- (2S)-2-{[(2R)-2-[({[3,3-dibutyl-7-(methylthio)-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepin-8-l]oxy}acetyl)amino]-2-(4-hydroxyphenyl)acetyl]amino}butanoic acid, EMEA-002054-PIP01-16, from Albireo AB, for the treatment of Progressive Familial Intrahepatic Cholestasis;
- Crisaborole, EMEA-002065-PIP01-16, from Pfizer Ltd, for the treatment of atopic dermatitis;
- Lactobacillus reuteri, EMEA-001895-PIP01-15, from Infant Bacterial Therapeutics AB, for the prevention of necrotising enterocolitis;
- Acalabrutinib, EMEA-001796-PIP03-16, from ACERTA PHARMA, BV, for the treatment of mature B cell neoplasms;
- Ligelizumab, EMEA-001811-PIP02-15, from Novartis Europharm Ltd., for the treatment of chronic spontaneous urticaria;

The PDCO adopted an opinion(s) on the **refusal** of a PIP, including *waiver* and deferral for:

- 1H-Isoindol-1-one,2-[[1-[2-(4-fluorophenyl)-2-oxoethyl]-4-piperidinyl]methyl]-2,3-dihydro-, hydrochloride, hydrate (1:1:2) (MIN-101), EMEA-002222-PIP01-17, from Minerva Neurosciences, Inc., for the treatment of schizophrenia.

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

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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 modification to an agreed PIP adopted on 21 July 2017 for Autologous T-cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 (CTL019), EMEA-001654-PIP01-14-M02, from Novartis Europharm Limited, for the treatment of B cell acute lymphoblastic leukaemia / lymphoblastic lymphoma, the PDCO adopted a revised positive opinion and agreed to the changes regarding the measures of the paediatric investigation plan in the scope set out in the Annex I of the 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.

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:

- Amlodipine / irbesartan / hydrochlorothiazide, EMEA-002167-PIP01-17, from WIN MEDICA S.A., for the treatment of hypertension;
- Ibrutinib, EMEA-001397-PIP05-17, from Janssen-Cilag International N.V., for treatment of mantle cell lymphoma
- Ibrutinib, EMEA-001397-PIP06-17, from Janssen-Cilag International N.V., for treatment of lymphoplasmacytic lymphoma
- Rosuvastatin / ezetimibe, EMEA-002202-PIP01-17, from Krka, d.d., Novo mesto, for the treatment of hypercholesterolaemia;
- Capmatinib, EMEA-002203-PIP01-17, from Novartis Europharm Ltd, for the treatment of lung malignant neoplams;
- Veliparib, EMEA-000499-PIP03-17, from AbbVie Ltd, for the treatment of breast cancer;
- Pilocarpine (hydrochloride) / Oxymetazoline (hydrochloride), EMEA-002181-PIP01-17, from Allergan Pharmaceuticals International Limited, for the treatment of presbyopia;
- Bempedoic acid / ezetimibe, EMEA-002200-PIP01-17, from Esperion Therapeutics, Inc., for the treatment of elevated cholesterol;
- Meldonium (dihydrate), EMEA-002212-PIP01-17, from ELC GROUP s.r.o., for the treatment of angina pectoris;

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:

- Autologous CD34+ haematopoietic stem cells transduced *ex vivo* with EFS lentiviral vector encoding for the human adenosine deaminase gene, EMEA-001974-PIP01-16-M01, from Pr Bobby Gaspar, for the treatment of severe combined immunodeficiency due to adenosine deaminase deficiency;
- 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-M01, from Abbott Biologicals B.V., for prevention of influenza infection
- Ceftazidime / avibactam, EMEA-001313-PIP01-12-M06, from Pfizer Limited, for treatment of intra-abdominal infections, treatment of urinary tract infections, treatment of pneumonia and treatment of Gram-negative bacterial infections
- Recombinant human A disintegrin and metalloprotease with thrombospondin type-1 motifs 13, EMEA-001160-PIP01-11-M01, from Baxalta Innovations GmbH, for treatment of thrombotic thrombocytopenic purpura (TTP);
- Everolimus, EMEA-000019-PIP08-12-M03, from Novartis Europharm Limited, for the treatment of Tuberous Sclerosis Complex;
- Dabigatran etexilate mesilate, EMEA-000081-PIP01-07-M10, from Boehringer Ingelheim International GmbH, for the prevention of thomboembolic events and treatment of thromboembolic events;
- Andexanet alfa, EMEA-001902-PIP01-15-M01, from Portola Pharma UK Limited, for the prevention of factor Xa inhibitor associated haemorrhage and treatment of factor Xa inhibitor associated haemorrhage;
- Beclometasone dipropionate / formoterol (fumarate dihydrate), EMEA-000548-PIP01-09-M07, from Chiesi Farmaceutici S.p.A., for the treatment of asthma;
- Cabotegravir, EMEA-001418-PIP01-13-M01, from ViiV Healthcare UK Limited, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Tapentadol (hydrochloride), EMEA-000325-PIP01-08-M08, from Grünenthal GmbH, for the treatment of chronic pain;
- Recombinant parathyroid hormone, EMEA-001526-PIP01-13-M02, from Shire Pharmaceuticals Ireland Limited, for the treatment of hypoparathyroidism;
- Entolimod, EMEA-002020-PIP01-16-M01, from Cleveland Biolabs, Inc, for the treatment of acute radiation syndrome;
- Fremanezumab, EMEA-001877-PIP01-15-M01, from Teva GmbH, for the prevention of migraine headaches;
- Dapagliflozin, EMEA-000694-PIP02-14-M02, from AstraZeneca AB, for the treatment of type 1 diabetes mellitus;

- Edoxaban (tosylate), EMEA-000788-PIP02-11-M06, from Daiichi Sankyo Europe GmbH, for the prevention of arterial thromboembolism, prevention of venous thromboembolism and treatment of venous thromboembolism;
- Tralokinumab, EMEA-000782-PIP01-09-M04, from MedImmune Ltd, for the treatment of asthma;
- Gemtuzumab Ozogamicin, EMEA-001733-PIP02-15-M01, from Pfizer Limited, for the treatment of acute myeloid leukaemia;
- Febuxostat, EMEA-001417-PIP01-12-M03, from Menarini International Operations Luxembourg S.A., for the prevention / treatment of hyperuricemia;
- Tofacitinib, EMEA-000576-PIP01-09-M07, from Pfizer Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis);
- 1-(2,2-difluoro-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluoro-2-(1-hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl}cyclopropanecarboxamide / ivacaftor, EMEA-001640-PIP01-14-M03, from Vertex Pharmaceuticals (Europe) Ltd., for the treatment of cystic fibrosis;
- Erenumab, EMEA-001664-PIP02-15-M01, from Novartis Europharm Limited, for the prevention of migraine headaches;
- Guselkumab, EMEA-001523-PIP02-14-M01, from Janssen Cilag International NV, for the treatment of psoriasis;
- Liposomal combination of cytarabine and daunorubicin, EMEA-001858-PIP02-16-M01, from JAZZ PHARMACEUTICALS IRELAND LIMITED, for the treatment of acute myeloid leukaemia;
- Eculizumab, EMEA-000876-PIP05-15-M02, from Alexion Europe SAS, for the treatment of myasthenia gravis;
- Domagrozumab, EMEA-001763-PIP01-15-M01, from Pfizer Limited, for the treatment of Duchenne Muscular Dystrophy;
- Methoxy polyethylene glycol- epoetin beta, EMEA-000172-PIP01-07-M03, from Roche Registration Limited, for the treatment of symptomatic anaemia associated with chronic kidney disease;

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 10 – 13 October 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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