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SCIENCE MEDICINES HEALTH

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Human Medicines Division

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

22-25 February 2022

Opinions on paediatric investigation plans

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

- Abelaclimab, EMEA-003017-PIP01-21, from Anthos Therapeutics, Inc., for the prevention of thromboembolic events and treatment of thromboembolic events;
- Dupilumab, EMEA-001501-PIP09-21, from Sanofi-Aventis Groupe, for the treatment of chronic inducible cold urticaria;
- Rozanolixizumab, EMEA-002681-PIP02-21, from UCB Pharma S.A, for the treatment of immune thrombocytopenia;
- Benzylamine derivative of benzofuran (BCX9930), EMEA-002974-PIP01-21, from BioCryst Ireland Limited, for the treatment of paroxysmal nocturnal haemoglobinuria;
- Invimestrocel, EMEA-002317-PIP02-21, from ReGenesys BVBA (Athersys), for the treatment of ischaemic stroke;
- Censavudine, EMEA-003075-PIP01-21, from Transposon Therapeutics, Inc., for the treatment of Aicardi-Goutières Syndrome;
- Catequentinib, EMEA-002486-PIP04-21, from Advenchen Laboratories, LLC, for the treatment of Ewing sarcoma and treatment of soft tissue sarcomas;
- Pamrevlumab, EMEA-002979-PIP01-21, from FibroGen, Inc., for the treatment of Duchenne muscular dystrophy;
- Autologous CD34+ hematopoietic stem and progenitor cells (HSPCs) genetically modified with the lentiviral vector IDUA LLV, encoding for the human α -L-iduronidase (IDUA) gene (OTL-203), EMEA-003001-PIP01-21, from Orchard Therapeutics (Netherlands) B.V., for the treatment of Mucopolysaccharidosis type I, Hurler syndrome;
- Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A/H5N1, EMEA-

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002869-PIP01-21, from Seqirus Netherlands B.V., for the influenza due to identified zoonotic or pandemic influenza virus;

- Influenza virus A/turkey/turkey/1/2005 (H5N1) NIBRG-23 strain, HA surface antigen, EMEA-002869-PIP03-21, from Seqirus Netherlands B.V., for the influenza due to identified zoonotic or pandemic influenza virus;

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.

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 adopted on 31 January 2022 for L-carnitine/glucose/calcium chloride dihydrate/magnesium chloride hexahydrate/sodium lactate/sodium chloride EMEA-003049-PIP01-21, from Iperboreal Pharma Srl, for the treatment of renal failure with carnitine deficiency, to maintain its opinion and
 - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
 - to grant a deferral in accordance with Article 21 of said Regulation, as per Annex I.

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:

- Acetylsalicylic acid / ticagrelor, EMEA-003146-PIP01-21, from PharOS Pharmaceutical Oriented Services Single Member Ltd, for the prevention of atherothrombotic events;
- Telmisartan / indapamide, EMEA-003151-PIP01-21, from KRKA, d.d., Novo mesto, for the treatment of hypertension;
- Secukinumab, EMEA-000380-PIP09-21, from Novartis Europharm Limited, for the treatment of lichen planus (including mucosal lichen planus);
- Adalimumab conjugated with (4S)-4-[2-(2-bromoacetamido)acetamido]-5-{3-[(4-{(4aR,4bS,5S,6aS,6bS,8R,9aR,10aS,10bS)-5-hydroxy-4a,6a-dimethyl-2-oxo-6b-[(phosphonoxy)acetyl]-4a,4b,5,6,6a,6b,9a,10,10a,10b,11,12-dodecahydro-2H,8H-naphtho[2',1':4,5]indeno[1,2-d][1,3]dioxol-8-yl}phenyl)methyl] anilino}-5-oxopentanoic acid; ABBV-154, EMEA-002927-PIP02-21, from AbbVie Ltd, for the treatment of polymyalgia rheumatica;

- Retifanlimab, EMEA-002798-PIP02-21, from Incyte Biosciences Distribution B.V., for the treatment of endometrial carcinoma;
- Sintilimab, EMEA-002919-PIP02-21, from Eli Lilly and Company Limited, for the treatment of oesophageal cancer;
- Cevostamab, EMEA-003145-PIP01-21, from Roche Registration GmbH, for the treatment of multiple myeloma;
- Human IgG4 monoclonal antibody against BCMA and CD3, EMEA-003147-PIP01-21, from AbbVie Ltd, for the treatment of multiple myeloma;

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:

- Saxagliptin, EMEA-000200-PIP01-08-M09, from AstraZeneca AB, for the treatment of type 2 diabetes;
- Migalastat hydrochloride, EMEA-001194-PIP01-11-M05, from Amicus Therapeutics Europe Limited, for the treatment of Fabry disease;
- Eluxadoline, EMEA-001579-PIP01-13-M05, from Allergan Pharmaceuticals International Limited, for the treatment of diarrhoea-predominant irritable bowel syndrome;
- Ozanimod, EMEA-001710-PIP04-17-M03, from Celgene Europe B.V., for the treatment of Crohn's disease;
- Rilpivirine (hydrochloride), EMEA-000317-PIP01-08-M13, from Janssen-Cilag International NV, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Cabotegravir, EMEA-001418-PIP02-15-M03, from ViiV Healthcare UK Limited, for the prevention of human immunodeficiency virus (HIV-1) infection;
- Bezlotoxumab, EMEA-001645-PIP01-14-M04, from Merck Sharp & Dohme (Europe), Inc., for the prevention of recurrence of *Clostridioides difficile* infection;
- Cannabidiol / delta-9-tetrahydrocannabinol, EMEA-000181-PIP01-08-M06, from GW Pharma (International) B.V, for the treatment of spasticity;
- Siponimod (hemifumarate), EMEA-000716-PIP01-09-M04, from Novartis Europharm Ltd, for the treatment of multiple sclerosis;
- Galcanezumab, EMEA-001860-PIP03-16-M07, from Eli Lilly and Company Limited, for the prevention of migraine headaches;
- Leriglitzazone, EMEA-002106-PIP01-16-M02, from Minoryx Therapeutics S.L., for the treatment of adrenoleukodystrophy;

- Ofatumumab, EMEA-002397-PIP01-18-M02, from Novartis Ireland Limited, for the treatment of multiple sclerosis;
- Ponatinib, EMEA-001186-PIP01-11-M03, from Incyte Biosciences Distribution B.V., for the treatment of Philadelphia chromosome positive acute lymphoblastic leukaemia and treatment of chronic myeloid leukaemia;
- Palbociclib, EMEA-002146-PIP01-17-M04, from Pfizer Europe MA EEIG, for the treatment of Ewing sarcoma;
- Bempegaldesleukin, EMEA-002492-PIP01-18-M02, from Nektar Therapeutics, for the treatment of all conditions included in the category of malignant neoplasms (except nervous system, haematopoietic, and lymphoid tissue neoplasms);
- (4S,7aR,9aR,10S,11E,14S,15R)-6'-chloro-10-methoxy-14,15-dimethyl-3',4',7a,8,9,9a,10,13,14,15-decahydro-2'H,7H-spiro[1,19-ethenocyclobuta[i][1,4]oxazepino[3,4f][1,2,7]thiadiazacyclohexadecine-4,1'-naphthalen]-18(17H)-one 16,16-dioxide (AMG 176), EMEA-002631-PIP01-19-M01, from Amgen Europe BV, for the treatment of acute myeloid leukaemia;
- Inotuzumab ozogamicin, EMEA-001429-PIP01-13-M05, from Pfizer Europe MA EEIG, for the treatment of B cell acute lymphoblastic leukaemia;
- Fosdenopterin, EMEA-001491-PIP01-13-M02, from Comharsa Life Sciences Limited, for the treatment of molybdenum cofactor deficiency type A;
- Amikacin sulfate, EMEA-000525-PIP01-08-M08, from Insmed Netherlands B.V., for the treatment of Pseudomonas aeruginosa lung infection/colonisation in cystic fibrosis patients and treatment of nontuberculous mycobacterial (NTM) lung infection;
- Benralizumab, EMEA-001214-PIP01-11-M11, from AstraZeneca AB, for the treatment of asthma;
- Lisdexamfetamine dimesylate, EMEA-000553-PIP01-09-M05, from Shire Pharmaceuticals Contract Limited, for the treatment of attention deficit hyperactivity disorder;
- Esketamine (hydrochloride), EMEA-001428-PIP03-15-M02, from Janssen-Cilag International NV, for the treatment of major depressive disorder;
- Daridorexant, EMEA-002121-PIP03-19-M01, from Idorsia Pharmaceuticals Deutschland GmbH, for the treatment of insomnia;
- Etelcalcetide, EMEA-001554-PIP01-13-M03, from Amgen Europe B.V., for the treatment of hyperparathyroidism;
- Ferumoxytol, EMEA-000373-PIP02-09-M05, from Covis Pharma Europe B.V., for the treatment of iron deficiency anaemia;
- Recombinant influenza hemagglutinin-strain B (Yamagata lineage) / Recombinant influenza hemagglutinin-strain B (Victoria lineage) / Recombinant influenza hemagglutinin-strain A (H3N2 subtype) / Recombinant influenza hemagglutinin-strain A (H1N1 subtype), EMEA-002418-PIP01-18-M02, from Sanofi Pasteur for the prevention of influenza infection;
- Axicabtagene ciloleucel, EMEA-002010-PIP01-16-M03, from Kite Pharma EU B.V., for the treatment of mature B-cell neoplasms;

Opinion on compliance check

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

- Dupilumab, EMEA-C-001501-PIP01-13-M07, from Regeneron Pharmaceuticals, Inc., for the treatment of atopic dermatitis;
- Ibrutinib, EMEA-C-001397-PIP03-14-M06, from Janssen-Cilag International NV, for the treatment of mature B cell neoplasm;
- Eribulin, EMEA-C-001261-PIP01-11-M07, from Eisai GmbH, for the treatment of soft tissue sarcoma;

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.

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. Opinions of the Paediatric Committee (PDCO) on PIPs and waivers lead to 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:
https://www.ema.europa.eu/en/medicines/ema_group_types/ema_pip

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