13 October 2017
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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

10 – 13 October 2017

Opinions on paediatric investigation plans

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

- Ruxolitinib phosphate, EMEA-000901-PIP03-16, from Novartis Europharm Limited, for the treatment of acute Graft versus Host Disease (aGvHD);
- Emapalumab, EMEA-002031-PIP01-16, from Novimmune B.V, for the treatment of haemophagocytic lymphohistiocytosis;
- *Neisseria meningitidis* serogroup A polysaccharide conjugated to tetanus toxoid / *N. meningitidis* serogroup C polysaccharide conjugated to tetanus toxoid / *N. meningitidis* serogroup Y polysaccharide conjugated to tetanus toxoid / *N. meningitidis* serogroup W polysaccharide conjugated to tetanus toxoid (MenACYW), EMEA-001930-PIP01-16, from Sanofi Pasteur Inc., for the prevention of meningococcal disease;
- Omega-3-carboxylic acids, EMEA-001865-PIP02-16, from AstraZeneca AB, for the treatment of dyslipidemia;
- Synthetic double-stranded siRNA oligonucleotide directed against hydroxyacid oxidase 1 mRNA that is covalently linked to a ligand containing three N-acetylgalactosamine residues, EMEA-002079-PIP01-16, from Alnylam UK Limited, for the treatment of hyperoxaluria;
- Allopregnanolone, EMEA-002051-PIP02-16, from Sage Therapeutics Inc, for the treatment of postpartum depression;
- Recombinant humanised IgG4 monoclonal antibody against MSRV-Envelope protein (GNbAC1), EMEA-002127-PIP01-17, from GeNeuro SA, for the treatment of multiple sclerosis;
- β-ferric oxyhydroxide hydroxyethyl amylopectin glucoheptonic acid (polyglucoferron), EMEA-002094-PIP01-16, from iron4u, for the treatment of iron deficiency or iron deficiency anaemia;
- Pneumococcal polysaccharide serotype 1 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 3 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 4

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– diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 5 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 6A – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 6B – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 7F – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 9V – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 14 – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 18C – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 19A – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 19F – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 22F – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 23F – diphtheria CRM197 conjugate / pneumococcal polysaccharide serotype 33F – diphtheria CRM197 conjugate (15-valent pneumococcal polysaccharide conjugate vaccine [V114]), EMEA-002215-PIP01-17, from Merck Sharp & Dohme (Europe), Inc., for the prevention of disease caused by *Streptococcus pneumoniae;*

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:

- Vonapanitase, EMEA-002195-PIP01-17, from Proteon Therapeutics Limited, for the prevention of arteriovenous access dysfunction;
- Atorvastatin / ezetimibe, EMEA-002207-PIP01-17, from EGIS Pharmaceuticals PLC, for the treatment of hypercholesterolaemia;
- Tolonium chloride, EMEA-002170-PIP01-17, from Cumdente GmbH, for the dental and oral soft tissue infections;
- Opicinumab, EMEA-002194-PIP01-17, from Biogen Idec Limited, for the treatment of multiple sclerosis;
- Soluble human T cell receptor (TCR) directed against the glycoprotein 100 (gp100) melanoma antigen, linked to the single-chain variable fragment (ScFv) domain of the anti-cluster of differentiation 3 (CD3) antibody, EMEA-002197-PIP01-17, from Immunocore Ltd, for the treatment of ocular melanoma;
- Resminostat, EMEA-002211-PIP01-17, from 4SC AG, for Treatment of Cutaneous T-Cell Lymphoma;

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

- Human Neutrophil Elastase Inhibitor, EMEA-002196-PIP01-17, from Chiesi Farmaceutici S.p.A, for the treatment of bronchiectasis;

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:

- Sarilumab, EMEA-001045-PIP01-10-M01, from sanofi-aventis recherche et développement, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, spondylarthritis, psoriatic arthritis and juvenile idiopathic arthritis);
- Secukinumab, EMEA-000380-PIP01-08-M04, from Novartis Europharm Ltd, for the treatment of psoriasis;
- Tapentadol, EMEA-000018-PIP01-07-M14, from Grünenthal GmbH, for the treatment of acute pain;
- Fc- and CDR-modified humanised monoclonal antibody against C5, EMEA-002077-PIP01-16-M01, from Alexion Europe SAS, for the treatment of paroxysmal nocturnal haemoglobinuria;
- Eculizumab, EMEA-000876-PIP03-14-M01, from Alexion Europe SAS, for the neuromyelitis optica spectrum disorders;
- Ozanimod, EMEA-001710-PIP02-14-M02, from Celgene Europe Limited, for the treatment of multiple sclerosis;
- Naltrexone (hydrochloride) / Bupropion (hydrochloride), EMEA-001373-PIP01-12-M03, from Orexigen Therapeutics Ireland Limited, for the treatment of obesity;
- Upadacitinib, EMEA-001741-PIP01-14-M01, from AbbVie Ltd, for the treatment of chronic idiopathic arthritis (including rheumathoid arthritis, psoriatic arthritis, spondyloarthritis and juvenile idiopathic arthritis);
- Adalimumab, EMEA-000366-PIP02-09-M05, from AbbVie Limited, for the treatment of ulcerative colitis;
- Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H1N1) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A (H3N2) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Yamagata lineage) / Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain B (Victoria lineage) [QIVc], EMEA-002068-PIP01-16-M01, from Seqirus UK Limited, for the prevention of influenza;
- Teduglutide EMEA-000482-PIP01-08-M04, from Shire Pharmaceuticals Ireland Limited, for the treatment of short bowel syndrome;
- Avelumab, EMEA-001849-PIP02-15-M01, from Merck KGaA, for the treatment of all conditions included in the category of solid malignant neoplasms (except central nervous system tumours and lymphoma), treatment of malignant neoplasms of lymphoid tissue and treatment of malignant neoplasms of the central nervous system;
- Telavancin hydrochloride, EMEA-000239-PIP01-08-M03, from Theravance Biopharma Ireland Ltd., for the treatment of complicated skin and soft tissue infections (cSSTI) and treatment of nosocomial pneumonia;
- Lumicitabine, EMEA-001758-PIP01-15-M02, from Janssen-Cilag International NV, for the treatment

of lower respiratory tract disease caused by human respiratory syncytial virus;

- Lacosamide, EMEA-000402-PIP03-17-M01, from UCB Pharma S.A., for the treatment of generalised epilepsy and epileptic syndromes;
- Sotagliflozin, EMEA-001517-PIP02-14-M02, from sanofi-aventis R&D, for the treatment of type 1 diabetes mellitus;
- Palovarotene, EMEA-001662-PIP01-14-M01, from Clementia Pharmaceuticals Inc., for the treatment of fibrodysplasia ossificans progressiva;
- Bumetanide, EMEA-001303-PIP01-12-M02, from Les Laboratoires Servier, for the treatment of autistic spectrum disorder;
- Lubiprostone, EMEA-000245-PIP01-08-M04, from Sucampo AG, for the treatment of constipation;
- Thrombomodulin alfa, EMEA-001363-PIP01-12-M01, from Asahi Kasei Pharma America Corporation, for the treatment of sepsis;

The following product was granted a product-specific waiver in replacement of an agreed PIP:

- Tolvaptan, EMEA-001231-PIP02-13-M05, from Otsuka Pharmaceutical Europe Ltd., for the treatment of dilutional hyponatraemia and treatment of polycystic kidney disease;

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

- Mirabegron, EMEA-000597-PIP02-10-M06, from Astellas Pharma Europe B.V., for the treatment of idiopathic overactive bladder;

Withdrawals

The PDCO noted that 4 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 Slovakia, Mr Peter Sisovsky and the new alternate from Slovenia, Dr Janez Jazbec.

The next meeting of the PDCO will be held on 7 – 10 November 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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