25 June 2015
EMA/411248/2015
Procedure Management and Committees Support Division

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

17-19 June 2015

Opinions on paediatric investigation plans

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

- Glucagon, from Locemia Solutions ULC, for the treatment of hypoglycaemia;
- Atrasentan (hydrochloride), from AbbVie, Ltd, for the treatment of nephropathy;
- Enalapril (maleate), from Ethicare GmbH, for the treatment of heart failure;
- Recombinant human nerve growth factor, from Dompé farmaceutici SpA, for the treatment of neurotrophic keratitis;
- Influenza virus surface antigens (haemagglutinin and neuraminidase) of the following strains: A/(H1N1), A/(H3N2), B/Yamagata lineage, B/Victoria lineage, from Abbott Biologicals B.V., for the Prevention of influenza infection.

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:

- Brentuximab vedotin, from Takeda Pharma A/S, for the treatment of Cutaneous T-Cell Lymphoma;

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

- Carvedilol / ivabradine (hydrochloride), from Les Laboratoires Servier, for the treatment of ischaemic coronary artery disorders and treatment of heart failure;
- (S)-1-{5-Phenyl-4-[(pyridin-2-ylmethyl)-amino]-thieno[2,3-d]pyrimidin-2-yl}-piperidine-3-carboxylic acid (2-hydroxy-ethyl)-amide, from Xention Limited, for the treatment of supraventricular arrhythmias;
- Rifamycin, from Dr. Falk Pharma GmbH, for the treatment of acute infectious diarrhoea;
- DNA, d(P-thio)([2'-0-(2-methoxyethyl)]m5rU-[2'-0-(2-methoxyethyl)]m5rC-[2'-0-(2-methoxyethyl)]m5rU-[2'-0-(2-methoxyethyl)]m5rU-[2'-0-(2-methoxyethyl)]rG-G-T-T-A-m5C-A-T-G-A-A-[2'-0-(2-methoxyethyl)]rA-[2'-0-(2-methoxyethyl)]m5rU-[2'-0-(2-methoxyethyl)]m5rC-[2'-0-(2-methoxyethy l)]m5rC-[2'-0-(2-methoxyethyl)]m5rC), sodium salt, from Isis Pharmaceuticals, Inc., for the treatment of transthyretin-related amyloidosis (ATTR amyloidosis).

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:

- Ipilimumab, from Bristol-Myers Squibb Pharma EEIG, for the treatment of melanoma;
- Etravirine, from Janssen-Cilag International NV, for the treatment of Human Immunodeficiency Virus Infection;
- Fluticasone furoate / vilanterol, from Glaxo Group Limited, for the treatment of asthma;
- Tadalafil, from Eli Lilly and Company Ltd, for the treatment of pulmonary arterial hypertension;
- Dapagliflozin, from Bristol Myers Squibb / AstraZeneca EEIG, for the treatment of type 2 diabetes mellitus;
- Apremilast, from Celgene Europe Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis);
- Apremilast, from Celgene Europe Limited, for the treatment of psoriasis;
- Neisseria meningitidis serogroup B recombinant lipoprotein (rLP2086; subfamily A; Escherichia coli) / Neisseria meningitidis serogroup B recombinant lipoprotein (rLP2086; subfamily B; Escherichia coli), from Pfizer Ltd, for the Prevention of invasive meningococcal disease caused by *N. meningitidis* serogroup B;
- L-Cysteinyl-L-prolyl-L-alanyl-L-valyl-L-lysyl-L-arginyl-L-aspartyl-L-valyl-L-aspartyl-L-leucyl-L-phenylalanyl-L-leucyl-L-threonine, hydrochloride salt / L-Glutamyl-L-glutaminyl-L-valyl-L-alanyl-L-glutaminyl-L-tyrosyl-L-lysyl-L-alanyl-L-leucyl-L-prolyl-L-valyl-L-valyl-L-leucyl-L-glutamyl-L-asparaginyl-L-alanine, acetate salt / L-Lysyl-L-alanyl-L-leucyl-L-prolyl-L-valyl-L-valyl-L-leucyl-L-glutamyl-L-asparaginyl-L-alanyl-L-arginyl-L-isoleucyl-L-leucyl-L-lysyl-L-asparaginyl-L-cysteinyl-L-valine, acetate salt / L-Arginyl-L-isoleucyl-L-leucyl-L-lysyl-L-asparaginyl-L-cysteinyl-L-valyl-L-

aspartyl-L-alanyl-L-lysyl-L-methionyl-L-threonyl-L-glutamyl-L-glutamyl-L-aspartyl-L-lysyl-L-glutamic acid, acetate salt / L-Lysyl-L-glutamyl-L-asparaginyl-L-alanyl-L-leucyl-L-seryl-L-leucyl-L-leucyl-L-aspartyl-L-lysyl-L-isoleucyl-L-tyrosyl-L-threonyl-L-seryl-L-prolyl-L-leucine, acetate salt / L-Threonyl-L-alanyl-L-methionyl-L-lysyl-L-lysyl-L-isoleucyl-L-glutaminyl-L-aspartyl-L-cysteinyl-L-tyrosyl-L-valyl-L-glutamyl-L-asparaginyl-glycyl-L-leucyl-L-isoleucine, acetate salt / L-Seryl-L-arginyl-L-valyl-L-leucyl-L-aspartyl-glycyl-L-leucyl-L-valyl-L-methionyl-L-threonyl-L-threonyl-L-isoleucyl-L-seryl-L-seryl-L-seryl-L-lysine, acetate salt, from Circassia Limited, for the treatment of perennial allergic rhinitis;

- Human fibrinogen / human thrombin, from Omrix Biopharmaceuticals N.V., for the treatment of haemorrhage resulting from a surgical procedure and treatment of cerebrospinal fluid leakage resulting from a neurosurgical procedure;
- Clonidine (hydrochloride), from Therakind Limited, for sedation;
- Sebelipase alfa, from Synageva BioPharma Ltd., for the treatment of lysosomal acid lipase deficiency;
- Live, attenuated, chimeric dengue virus, serotype 1 / Live, attenuated, chimeric dengue virus, serotype 2 / Live, attenuated, chimeric dengue virus, serotype 3 / Live, attenuated, chimeric dengue virus, serotype 4, from Sanofi Pasteur SA, for the prevention of dengue;
- Lumacaftor / ivacaftor, from Vertex Pharmaceuticals (Europe) Ltd., for the treatment of cystic fibrosis.

Opinion on compliance check

The PDCO adopted a positive opinion on (full) compliance check for Canakinumab, from Novartis Europharm Limited, for the Cryopyrin Associated Periodic Syndromes (CAPS) including: Familial Cold Autoinflammatory Syndrome (FCAS) / Familial Cold Urticaria (FCU), Muckle-Wells Syndrome (MWS) and Neonatal-Onset Multisystem Inflammatory Disease (NOMID) / Chronic Infantile Neurological, Cutaneous, Articular Syndrome (CINCA);

The PDCO adopted a positive opinion on (full) compliance check for Sieved freeze-dried allergen extract of Dermatophagoides pteronyssinus / Sieved freeze-dried allergen extract of Dermatophagoides farinae, from Stallergenes, for the treatment of allergic rhinitis and treatment of asthma.

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.

Withdrawals

The PDCO noted that 1 application was withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure).

Strategic Review and Learning Meeting

On 28-29 May 2015, the PDCO held a joint Strategic Review and Learning Meeting with the Pharmacovigilance Risk Assessment Committee (PRAC) hosted by the Paul-Ehrlich-Institut (PEI) to discuss synergies between Paediatric and Pharmacovigilance EU Regulations and proposals to strengthen collaboration between PDCO and PRAC. In addition, the PDCO discussed the PDCO work plan 2016, requirements for paediatric signal detection, options for regular communication to stakeholders on PDCO activities and outcomes, improvements in the functioning of the PDCO.

The next meeting of the PDCO will be held on 15-17 July 2015.

– 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

Enquiries to: AskEMA
(http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/landing/ask_ema_landing_page.jsp&mid=)