EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Procedure Management and Committees Support Division

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

20-22 May 2015

Opinions on paediatric investigation plans

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

- (4R,5R)-1-[[4-[[4-[3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenoxy]methyl]phenyl]methyl]-4-aza-1-azoniabicyclo[2.2.2]octane chloride (SHP625), from Lumena Pharmaceuticals Inc, for the treatment of Alagille syndrome;
- Sotagliflozin, from Lexicon Celtic Limited, for the treatment of type 1 diabetes mellitus;
- Selumetinib, from AstraZeneca AB, for the treatment of neurofibromatosis type 1, treatment of melanoma and treatment of thyroid cancer;
- Calcipotriol, from Polichem SA, for the treatment of psoriasis;
- Humanised anti-IL-6 receptor (IL-6R) monoclonal antibody, from Chugai Pharma Europe Ltd, for the treatment of neuromyelitis optica;
- Letermovir, from Merck Sharp & Dohme (Europe), Inc., for the prevention of cytomegalovirus infection;
- Cariprazine (hydrochloride), from Gedeon Richter Plc., for the treatment of schizophrenia;
- Momelotinib, from Gilead Sciences International Ltd, for the treatment of acute lymphoblastic leukaemia, including waivers granted for treatment of essential thrombocythaemia, treatment of post-essential thrombocythaemia myelofibrosis, treatment of polycythaemia vera and treatment of post-polycythaemia vera myelofibrosis.

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.

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Adoption of an opinion following re-examination

The PDCO adopted opinions for the following products:

- Following the re-examination of the opinion on the refusal of a modification of an agreed PIP and on the granting of a product-specific waiver adopted on 13 February 2015 for Sunitinib, from Pfizer Limited, for the treatment of gastro-intestinal stromal tumour, the PDCO adopted a revised positive opinion on the acceptance of a modification of an agreed PIP.
- Following the re-examination of the positive opinion on a modification of an agreed PIP adopted on 17 April 2015 for Recombinant single chain coagulation factor VIII, from CSL Behring GmbH, for the treatment of congenital factor VIII deficiency, the PDCO recommended to revise its opinion agreeing 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:

- Tocilizumab, from Roche Registration Limited, for the treatment of vasculitides;
- Atorvastatin / Perindopril / Acetylsalicylic acid, from Les Laboratoires Servier, for the treatment of ischemic coronary artery disorders and treatment of elevated cholesterol;
- Clonidine, from BioDelivery Sciences International, Inc., for the treatment of painful diabetic neuropathy.

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:

- Dalbavancin, from Durata Therapeutics International B.V., for the treatment of acute bacterial skin and skin structure infections;
- Mepolizumab, from GSK Trading Services Limited, for the treatment of asthma;
- Ataluren, from PTC Therapeutics International Limited, for the treatment of dystrophinopathy;

- Ataluren, from PTC Therapeutics International Limited, for the treatment of cystic fibrosis;
- Tocilizumab, from Roche Registration Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis);
- Adalimumab, from AbbVie Limited, for the treatment of ulcerative colitis;
- Secukinumab, from Novartis Europharm Ltd, for the treatment of psoriasis;
- Posaconazole, from Merck Sharp & Dohme (Europe), Inc., for the prevention of invasive fungal infections and treatment of invasive fungal infections;
- Teduglutide, from Nycomed Danmark ApS, for the treatment of short bowel syndrome;
- Ciclosporin, from Santen SAS, for the treatment of keratoconjunctivitis sicca and treatment of vernal keratoconjunctivitis;
- Drisapersen, from BioMarin International Limited, for the treatment of Duchenne muscular dystrophy;
- Human normal immunoglobulin, from Kedrion S.p.A., for the treatment of Idiopathic thrombocytopenic purpura (ITP) and treatment of Primary Immunodeficiency (PID);
- Dimethyl fumarate, from Biogen Idec Ltd., for the treatment of multiple sclerosis;
- Meropenem, from NeoMero Consortium, for the treatment of bacterial sepsis and treatment of bacterial meningitis;
- Loxapine, from Alexza UK, Limited, for the treatment of schizophrenia and treatment of bipolar disorder;
- Benralizumab, from MedImmune Ltd, for the treatment of asthma;
- Eribulin, from Eisai Europe Ltd, for the treatment of soft tissue sarcoma;
- Gabapentin, from PHARM SRL, for the treatment of chronic pain;
- Etrolizumab, from Roche Products Limited, for the treatment of ulcerative colitis and treatment of Crohn's disease;
- Dupilumab, from Sanofi-Aventis Recherche & Développement, for the treatment of asthma.

Opinion on compliance check

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

- Human coagulation Factor VIII / von Willebrand Factor, from CSL Behring GmbH, for the treatment of hereditary Factor VIII deficiency (Haemophilia A) and treatment of von Willebrand disease;
- Solifenacin (succinate), from Astellas Pharma Europe B.V., for the treatment of idiopathic overactive bladder;
- Eculizumab, from Alexion Europe SAS, for the treatment of Paroxysmal Nocturnal Haemoglobinuria and treatment of Atypical Haemolytic Uraemic Syndrome;

- Everolimus, from Novartis Europharm Limited, for the prevention of rejection of transplanted kidney, prevention of rejection of transplanted heart and prevention of rejection of transplanted liver.

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 2 applications were withdrawn during the late stages of the evaluation (30 days or less before completion of the procedure).

The PDCO also noted that the application leading to the opinion adopted during the March PDCO meeting for Tanezumab, from Pfizer Limited, for the treatment of chronic pain, was withdrawn before the decision was adopted by the Agency.

Other matters

The next meeting of the PDCO will be held on 17-19 June 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

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