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Inspections, Human Medicines Pharmacovigilance and Committees Division

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

15 – 18 August 2017

Opinions on paediatric investigation plans

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

- Pyridopyrimidione SMN2 Splicing Modifier, EMEA-002070-PIP01-16, from Roche Registration Limited, for the treatment of spinal muscular atrophy;
- Filgotinib, EMEA-001619-PIP04-17, from Gilead Sciences International Ltd., for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylarthritis, psoriatic arthritis, and juvenile idiopathic arthritis);
- Enasidenib, EMEA-001798-PIP02-16, from Celgene Europe Ltd, for the treatment of acute myeloid leukaemia;
- Influenza virus surface antigens (haemagglutinin) of strain A (H1N1) / influenza virus surface antigens (haemagglutinin) of strain A (H3N2) / influenza virus surface antigens (haemagglutinin) of strain B (Victoria lineage) / influenza virus surface antigens (haemagglutinin) of strain B (Yamagata lineage), EMEA-002027-PIP02-17, from Adimmune Corporation, for prevention of influenza infection;
- Entospletinib, EMEA-002058-PIP01-16, from Gilead Sciences International Ltd, for the treatment of acute myeloid leukaemia;
- Recombinant human monoclonal antibody to GM-CSF, EMEA-001882-PIP02-16, from GlaxoSmithKline Trading Services Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylarthritis and juvenile idiopathic arthritis);
- Angiotensin II, EMEA-001912-PIP02-16, from La Jolla Pharmaceutical Company, for the treatment of catecholamine-resistant hypotension associated with distributive shock;
- Autologous CD4+ and CD8+ T cells Expressing a CD19-Specific Chimeric Antigen Receptor (JCAR017), EMEA-001995-PIP01-16, from Celgene Europe Limited, for the treatment of B-lymphoblastic leukemia/lymphoma and treatment of mature B-cell neoplasms;
- Phenyl- and piperidin-containing derivative of amiloride, EMEA-002082-PIP01-16, from Boehringer

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Ingelheim International GmbH, for the treatment of cystic fibrosis;

- Tazobactam / ceftolozane, EMEA-001142-PIP02-16, from Merck Sharp & Dohme (Europe), Inc., for the treatment of pneumonia;
- 5-(4-Fluoro-1-benzothiophen-2-yl)-8-methyl-1,9-dihydro-2H-[1,3]oxazolo[4,5-H][2,3]benzodiazepin-2-one, EMEA-002057-PIP01-16, from Les Laboratoires Servier, for the treatment of ischemic stroke to improve recovery;
- (Z)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-4-(2-(sulfamoylamino)ethylamino)-1,2,5-oxadiazole-3-carboximidamide, EMEA-002072-PIP01-16, from Incyte Corporation, for the treatment of all conditions included in the category of malignant neoplasms including Hodgkin lymphoma (except nervous system, haematopoietic and lymphoid tissue other than Hodgkin lymphoma).

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 / Perindopril arginine / Bisoprolol fumarate, EMEA-002173-PIP01-17, from Les Laboratoires Servier, for the treatment of hypertension and treatment of ischaemic coronary artery disorders;
- Ramucirumab, EMEA-002074-PIP01-16, from Eli Lilly and Company Limited, for the treatment of gastric cancer and gastro-oesophageal junction adenocarcinoma, treatment of intestinal malignant neoplasm, treatment of lung malignant neoplasm, treatment of liver cancer, treatment of urinary tract malignant neoplasm;
- Benralizumab, EMEA-001214-PIP02-17, from AstraZeneca AB, for the treatment of nasal polyposis;
- Amlodipine besylate / hydrochlorothiazide / candesartan cilexetil, EMEA-002174-PIP01-17, from Zentiva, k.s., for the treatment of hypertension;
- Latanoprost / Netarsudil, EMEA-002175-PIP01-17, from Aerie Pharmaceuticals Ireland Ltd, for the treatment of Glaucoma;
- Lenalidomide, EMEA-000371-PIP04-16, from Celgene Europe Limited, for the treatment of mature b-cell neoplasms.

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:

- Alirocumab, EMEA-001169-PIP01-11-M03, from Sanofi-aventis Recherche & Developpement, for the treatment of elevated cholesterol;

- Japanese encephalitis vaccine (inactivated, adsorbed), EMEA-000559-PIP01-09-M04, from Valneva Austria GmbH, for the prevention of Japanese encephalitis;
- L-asparaginase encapsulated in erythrocytes, EMEA-000341-PIP02-09-M04, from ERYTECH pharma S.A., for the treatment of acute lymphoblastic leukaemia;
- Roxadustat, EMEA-001557-PIP01-13-M01, from Astellas Pharma Europe B.V., for the treatment of anaemia due to chronic disorders;
- Avacopan, EMEA-002023-PIP01-16-M01, from ChemoCentryx, Ltd., for the treatment of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis;
- Eltrombopag (eltrombopag olamine), EMEA-000170-PIP03-13-M03, from Novartis Europharm Limited, for the treatment of aplastic anaemia;
- Naloxegol (as naloxegol oxalate), EMEA-001146-PIP01-11-M03, from Kyowa Kirin Pharmaceutical Development Limited, for the treatment of opioid-induced constipation;
- Human fibrinogen / Human thrombin , EMEA-001340-PIP01-12-M03, from Mallinckrodt Pharmaceuticals Ireland Ltd, for the treatment of haemorrhage resulting from a surgical procedure;
- Tenofovir alafenamide (as fumarate), EMEA-001584-PIP01-13-M02, from Gilead Sciences International Ltd., for the treatment of chronic hepatitis B.

Opinion on compliance check

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

- Asenapine (maleate), EMEA-C-000228-PIP01-08-M04, from N.V. Organon, for the treatment of bipolar I disorder;
- Damoctocog alfa pegol, EMEA-C-001229-PIP01-11-M03, from Bayer AG, for the treatment of hereditary Factor VIII deficiency.

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.

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 PDCO welcomed the new members Dimitrios Athanasiou, Francesca Rocchi and Fernando Cabanas who have been nominated by healthcare/patient organisation. The PDCO also welcomed the new alternate members Viviana Giannuzzi and Catherine Cornu who have been nominated by

healthcare/patient organisation.

The next meeting of the PDCO will be held on 12 – 15 September 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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