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Procedure Management and Committees Support Division

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

7 – 9 October 2015

Opinions on paediatric investigation plans

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

- (3S,4R)-3-ethyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-N-(2,2,2-trifluoroethyl)pyrrolidine-1-carboxamide (2R,3R)-2,3-dihydroxybutanedioate (ABT-494), from AbbVie Ltd, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, spondyloarthritis and juvenile idiopathic arthritis);
- GS-9620, from Gilead Sciences International Ltd., for the treatment of chronic viral hepatitis B;
- Olaratumab, from Eli Lilly and Company Limited, for the treatment of soft tissue sarcoma and treatment of osteosarcoma.

The PDCO adopted opinions on the **refusal** of PIPs for the following medicines:

- Dimethyl fumarate, from Almirall S.A., for the treatment of psoriasis.

For this medicine the PDCO granted a product-specific waiver on its own motion for all subsets of the paediatric population in the specified condition, on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

- Recombinant human growth hormone fused to hybrid Fc composed of the hinge region and N-terminal of CH2 domain of IgD and C-terminal of CH2 and full CH3 domain of IgG4 (hGH-hyFc), from Genexine, Inc., for the treatment of growth hormone deficiency.

For this medicine the PDCO granted a product-specific waiver on its own motion for all subsets of the paediatric population in the specified condition, on the grounds that the specific medicinal product is likely to be unsafe and that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

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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:

- (R)-N-({5-[3-(2,5-Difluorophenyl)-2-(2,3-dihydro-1H-benzimidazol-2-ylidene)-3- oxopropanoyl]-2-fluorophenyl}sulfonyl)-2-hydroxypropanimidamide, from Astellas Pharma Europe B.V., for the treatment of endometriosis;
- Telmisartan / amlodipine (besilate), from Krka, d.d., Novo mesto, for the treatment of hypertension;
- Olmesartan medoxomil / amlodipine (besilate), from Krka, d.d., Novo mesto, for the treatment of hypertension.

The PDCO adopted 1 opinion on the **refusal** of a request for waiver for:

- *Yersinia pestis* recombinant F1V antigen (F1 capsular protein fused to V antigen), from DynPort Vaccine Company LLC, for the prevention of *Yersinia pestis* infections.

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:

- Tocilizumab, from Roche Registration Limited, for the treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis);
- Oseltamivir (phosphate), from Roche Registration Limited, for the treatment and prevention of influenza;
- Rivaroxaban, from Bayer Pharma AG, for the prevention of thromboembolic events and treatment of thromboembolic events;
- Mirabegron, from Astellas Pharma Europe B.V., for the treatment of neurogenic detrusor overactivity;

- Pneumococcal polysaccharide serotype 6B conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 1 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 18C conjugated to tetanus toxoid / Pneumococcal polysaccharide serotype 5 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 19F conjugated to diphtheria toxoid / Pneumococcal polysaccharide serotype 14 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 9V conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 4 conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 23F conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein / Pneumococcal polysaccharide serotype 7F conjugated to protein D (derived from non-typeable Haemophilus influenzae) carrier protein, from GlaxoSmithKline Biologicals S.A., for the prevention of diseases caused by streptococcus pneumoniae and prevention of acute otitis media caused by non-typeable Haemophilus influenzae;
- Vigabatrin, from Targeon SAS, for the treatment of epilepsy;
- Pollen from Dactylis glomerata, Lolium perenne, Phleum pratense, Festuca pratensis, Secale cereale, from ALK-Abelló A/S, for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Pollen from Betula verrucosa, from ALK-Abelló A/S, for the treatment of allergic rhinitis/rhino-conjunctivitis;
- Allergens from Dermatophagoides pteronyssinus and Dermatophagoides farinae, from ALK-Abelló A/S, for the Treatment of allergic rhinitis/rhino-conjunctivitis;
- Pollen from Phleum pratense, from ALK-Abelló A/S, for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Pollen from Alnus glutinosa, Betula verrucosa and Corylus avellana, from ALK-Abelló A/S, for the treatment of allergic rhinitis/rhino-conjunctivitis;
- Pollen from betula pendula (33%), corylus avellana (33%) and alnus glutinosa (33%), from ALK-Abelló A/S, for the treatment of allergic rhinitis/rhino-conjunctivitis;
- Pollen from Betula pendula, from ALK-Abelló A/S, for the treatment of allergic rhinitis/rhino-conjunctivitis;
- Pollen from Dactylis glomarata, Lolium perenne, Phleum pratense, Poa pratensis, Anthoxhantum odoratum and Secale cereale, from ALK-Abelló A/S, for the treatment of allergic rhinitis / rhino-conjunctivitis;
- Allergen extracts of dermatophagoides farinae and dermatophagoides pteronyssinus, from ALK-Abelló A/S, for the treatment of allergic rhinitis/rhino-conjunctivitis;
- Elvitegravir, from Gilead Sciences International Ltd, for the treatment of human immunodeficiency virus (HIV-1) infection;
- Lebrikizumab, from Roche Product Limited, for the treatment of asthma;
- Lomitapide, from Aegerion Pharmaceuticals Limited, for the treatment of (heterozygous or homozygous) familial hypercholesterolaemia;
- Benralizumab, from MedImmune Ltd, for the treatment of asthma;

- Dermatophagoides pteronyssinus / dermatophagoides farinae, from ALK-Abelló A/S, for the treatment of allergic rhinitis, prevention of asthma and treatment of asthma;
- Febuxostat, from Menarini International Operations Luxembourg S.A., for the treatment of hyperuricaemia and prevention of hyperuricaemia;
- Peanut allergen extract, from DBV Technologies S.A., for the treatment of peanut allergy.

The PDCO adopted 1 opinion on the **refusal** of modifications to an agreed PIP for:

- Rufinamide, from Eisai Limited, for the treatment of Lennox-Gastaut Syndrome.

Opinion on compliance check

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

- Canakinumab, from Novartis Europharm Limited, for the treatment of juvenile idiopathic arthritis, treatment of 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)).
- Artemether / lumefantrine, from Novartis Europharm Limited, for the treatment of *Plasmodium falciparum* malaria.

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

Committee interactions

The manager of the Scottish Clinical Research Network together with a young person from its young person advisory group and a representative from the European Cancer Patient Coalition, who is leading a young cancer patient group in Poland presented to the committee their work and proposals for how young people could contribute and provide their expertise to the activities of PDCO and EMA.

Other matters

The PDCO thanked Gylfi Oskarsson for his work at the end of his mandate as member representing Iceland.

The next meeting of the PDCO will be held on 11 - 13 November 2015.

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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