EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 November 2010
EMA/PDCO/690063/2010 – Corr. 1
Human Medicines Development and Evaluation

Paediatric Committee (PDCO) – monthly report

10-12 November 2010

Opinions on paediatric investigation plans

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

- Tazarotene, from Orfagen, in the therapeutic area of dermatology;
- Insulin detemir, from Novo Nordisk A/S, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- Dulaglutide, from Eli Lilly & Company, in the therapeutic area of endocrinology-gynaecology-fertility-metabolism;
- 40K Pegylated recombinant blood coagulation factor IX (N9-GP), from Novo Nordisk A/S, in the therapeutic area of haematology-hemostaseology;
- Recombinant human hyaluronidase, Human normal immunoglobulin, from Baxter Innovations GmbH, in the therapeutic area of immunology-rheumatology-transplantation;
- Pralatrexate, from Allos Therapeutics Limited, in the therapeutic area of oncology;
- Pazopanib, from Glaxo Group Limited, in the therapeutic area of oncology;
- Midostaurin, from Novartis Europharm Ltd, in the therapeutic area of oncology;
- Lanthanum carbonate hydrate, from Shire Pharmaceutical Contracts Ltd, in the therapeutic area of uro-nephrology;
- Dermatophagoides farinae extracts 100 %, from Allergopharma Joachim Ganzer KG, in the therapeutic area of pneumology - allergology;
- Dermatophagoides pteronyssinus extracts 100 %, from Allergopharma Joachim Ganzer KG, in the therapeutic area of pneumology - allergology;
- Dermatophagoides pteronyssinus 50 % and Dermatophagoides farinae extracts 50 %, from Allergopharma Joachim Ganzer KG, in the therapeutic area of pneumology - allergology;

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)2 7418 8613
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

- Preparation containing allergens of Birch pollen (Betula alba/pendula/verrucosa), from Allergopharma Joachim Ganzer KG, in the therapeutic area of pneumology - allergology;
- Pollen from Dactylis glomerata, Lolium perenne, Phleum pratense, Festuca pratensis, Secale cereale, from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Phleum pratense, from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Betula verrucosa, from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Alnus glutinosa, Betula verrucosa and Corylus avellana, from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Betula pendula, Corylus avellana and Alnus glutinosa (33 % each), from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Betula pendula, from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Dactylis glomarata, Lolium perenne, Phleum pratense, Poa pratensis and Anthoxhantum odoratum(20 % each), from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Dactylis glomarata (16%), Lolium perenne (16%), Phleum pratense (16%), Poa pratensis (16%), Anthoxhantum odoratum (16 %) and Secale cereale (20%), from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Dactylis glomarata (8%), Lolium perenne (8%), Phleum pratense (8%), Poa pratensis (8%), Anthoxhantum odoratum (8%), Secale cereale (10%), Betula pendula (16,7%), Corylus avellana (16,6%) and Alnus glutinosa (16,6%), from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Dactylis glomerata, Festuca pratensis, Lolium perenne, Phleum pratense, Poa pratensis, Secale cereale, Betula verrucosa, Corylus avellana and Alnus glutinosa, from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Dactylis glomerata, Festuca pratensis, Lolium perenne, Phleum pratense, Poa pratensis, Secale cereale and Artemisia vulgaris, from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Allergens from Dermatophagoides pteronyssinus and Dermatophagoides farinae, from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Allergen extracts of Dermatophagoides farinae and Dermatophagoides pteronyssinus (each 50%), from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Allergen extracts of Dermatophagoides pteronyssinus and Dermatophagoides farinae (each 50%), from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Alnus glutinosa (33%), Betula verrucosa (33%) and Corylus avellana (33%), from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Betula verrucosa, from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;

- Pollen from Phleum pratense, from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Dactylis glomarata (16%), Festuca pratensis (16%), Lolium perenne (16%), Phleum pratense (16%), Poa pratensis (16%), Secale cereale (20%), from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Pollen from Dactylis glomerata, Festuca pratensis, Lolium perenne, Phleum pratense, Secale cereale(20% each), from ALK-Abelló A/S, in the therapeutic area of pneumology - allergology;
- Adsorbed modified allergen extract of a mixture of 50% Dermatophagoides pteronyssinus and 50% Dermatophagoides farinae (subcutaneous use), from HAL Allergy BV, in the therapeutic area of pneumology - allergology;
- Adsorbed modified allergen extract of a mixture of 50% Dermatophagoides pteronyssinus and 50% Dermatophagoides farinae (sublingual use), from HAL Allergy BV, in the therapeutic area of pneumology - allergology;
- Allergen extract of a mixture of 50% Dermatophagoides pteronyssinus and 50% Dermatophagoides farinae, from HAL Allergy BV, in the therapeutic area of pneumology - allergology;
- Allergen extract of Alnus glutinosa pollen, from HAL Allergy BV, in the therapeutic area of pneumology - allergology;
- Allergen extract of Corylus avellana pollen, from HAL Allergy BV, in the therapeutic area of pneumology - allergology;
- Allergen extract of equal parts of Betula verrucosa, Corylus avellana and Alnus glutinosa pollen, from HAL Allergy BV, in the therapeutic area of pneumology - allergology;
- Allergen extract of equal parts of Lolium perenne, Phleum pratense and Poa pratensis pollen, from HAL Allergy BV, in the therapeutic area of pneumology - allergology;
- Allergen extract of 50% grass (equal parts of Lolium perenne pollen, Phleum pratense and Poa pratensis) and 50% Secale cereale pollen, from HAL Allergy BV, in the therapeutic area of pneumology - allergology;
- Allergen extract of Phleum pratense pollen, from HAL Allergy BV, in the therapeutic area of pneumology - allergology;
- Allergen extract of Secale cereale pollen, from HAL Allergy BV, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of birch, alder and hazel pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of birch and hazel pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of birch pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of hazel pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of Dermatophagoides farinae, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;

- Modified allergen extract of Dermatophagoides pteronyssinus and Dermatophagoides farinae, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of Dermatophagoides pteronyssinus, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of grass and birch pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of grass and cereal pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of grass and rye pollen (60/40), from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of grass and rye pollen (50/50), from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of grass pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of pollen from Phleum pratense, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of rye pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of birch, alder and hazel pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of birch and hazel pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of birch pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of hazel pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of Dermatophagoides farinae, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of Dermatophagoides pteronyssinus and Dermatophagoides farinae, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of Dermatophagoides pteronyssinus, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of grass and mugwort pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of grass and birch pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of grass and cereal pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of grass and rye pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;

- Modified allergen extract of grass pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of pollen from Phleum pratense, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Modified allergen extract of rye pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Aqueous allergen extract of birch, alder and hazel pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Aqueous allergen extract of birch pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Aqueous allergen extract of Dermatophagoides pteronyssinus, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Aqueous allergen extract of Dermatophagoides pteronyssinus and Dermatophagoides farinae, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Aqueous allergen extract of grass pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Aqueous allergen extract of grass and cereal pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Aqueous allergen extract of grass and rye pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Aqueous allergen extract of pollen from Phleum pratense, from ROXALL Medizin GmbH, in the therapeutic area of pneumology - allergology;
- Aqueous allergen extract of grass and birch pollen, from ROXALL Medizin GmbH, in the therapeutic area of pneumology – allergology.

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:

- Interferon alpha 2b, from Helix BioPharma Corp, in the therapeutic area of infectious diseases / oncology;
- Nalmefene HCl, from H. Lundbeck A/S, in the therapeutic area of psychiatry;
- Ranibizumab, from Novartis Europharm Limited, in the therapeutic area of ophthalmology.

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.

Opinions on the review of a granted waiver under Article 14(2)

According to Article 14(2) of Regulation (EC) No 1901/2006 as amended, the Paediatric Committee may, at any time, adopt an opinion advocating the review of a granted waiver. The following PDCO opinions including product-specific waivers have been reviewed by the PDCO during the November meeting:

- PDCO opinion EMEA-000420-PIO01-08, EMA decision P/21/2010, on the refusal of a Paediatric Investigation Plan and on the refusal of a deferral and on the granting of a waiver for duloxetine hydrochlorid.
- PDCO opinion EMEA-000249-PIP01-08, EMA decision P/101/2008, on the granting of a product specific waiver for influenza virus type A, H3N2, influenza virus type A, H1N1, influenza virus type B.

Withdrawals

The PDCO noted that 2 applications were withdrawn during the late stages of the evaluation (30 days or less before opinion).

Interaction with external experts

The PDCO has regular interactions with academic experts, with a view to bringing state-of-the-art knowledge to the PDCO scientific discussions. Two experts were invited to the November meeting with clinical expertise in paediatric endocrinology and bone metabolism. The PDCO discussed a rare metabolic bone disease.

PDCO interactions

Dr Ruxandra Draghia-Akli, Director of the Health Directorate of the European Commission Directorate-General for Research, and Dr Fergal Donnelly participated in the PDCO meeting and provided an update on the Seventh Framework Programme (FP7). They announced that it was probable that there would be no funding for research into off-patent medicines for children in 2011 and 2012. This programme was set up and included in Framework Programs based on art. 40 of the Paediatric Regulation. The Committee regretted to hear that the very successful support for such research will be discontinued in the next FP7 calls. The three calls so far financed had a high success rate for applications, with 12 projects financed for a total of 56 million €, and the first results should be available in the near future. The discontinuation of funding might affect the groups and consortia which were recently established with a view to the development of medicines for children that are devoid of commercial interest, whilst there is no other source of funding for such medicines.

New meeting dates adopted

PDCO meeting dates for 2014 were adopted during the November meeting. These dates are important for applicants in planning the submission of applications for PIPs, requests for waivers, requests for modification of an agreed PIP, and requests for compliance checks. The dates will be published on the Agency's website at: http://www.ema.europa.eu/htms/human/paediatrics/pdco.htm

Other issues

The PDCO was updated on the setting up of the Paediatric Medicines Regulatory Network (PmRN) with representatives from national medicines regulatory authorities from all regions. This network is coordinated by the World Health Organisation, as part of the WHO's Better Medicines for Children initiative (http://www.who.int/childmedicines/paediatric_regulators/en/).

The PDCO thanked Robert Ancuceanu for his exceptional work as he has resigned from the Committee.

The next meeting of the PDCO will be held on 08-10 December 2010.

– END –

Notes:

1. 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 European Medicines Agency's website has a searchable database of opinions and decisions on PIPs.
2. 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.
3. More information about the PDCO and the Paediatric Regulation is available in the 'Medicines for children' section of the Agency's website.
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 only to: paediatrics@ema.europa.eu

Annex of the November 2010 PDCO meeting report

	2008 (January to December)	2009 (January to December)	2010 (January to current month)	Cumulative total (2007 to 2010)
Total number of validated PIP/waiver applications	271	273	311	941[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	186	191	269	685 *(73%)*
Applications submitted for a product already authorised and still under patent, in view of a submission of a variation/extension for a new indication, pharmaceutical form or route of administration *(Article 8[2])*	75	72	40	232 *(25%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	10	10	3	24 *(2%)*
PIPs and full waiver indications covered by these applications	395	395	373	1334

Number of Paediatric Committee (PDCO) opinions	2008	2009	2010	Cumulative total
Positive on full waiver	48	67	49	173
Positive on PIP, including potential deferral	81	122	191	396
Negative opinions adopted	4	13	6	23
Positive opinions adopted on modification of a PIP	8	51	96	155
Negative opinions adopted on modification of a PIP	0	0	4	4
Positive opinions on compliance with a PIP	5	8	7	20
Negative opinions on compliance check with a PIP	0	1	0	1
Opinions adopted under Art 14.2	0	0	2	2

[1] Of which 209 have been requests for a full waiver.
[2] Applications submitted in accordance with the referenced article of Regulation (EC) No 1901/2006, as amended.

Areas covered by PIPs/waiver applications	2008 (%)	2009 (%)	2010 (%)
Neurology	6	4	4
Uro-nephrology	3	5	2
Gastroenterology-hepatology	3	2	1
Pneumology-allergology	6	6	41
Infectious diseases	8	9	4
Cardiovascular diseases	14	9	8
Diagnostics	1	1	1
Endocrinology-gynaecology-fertility-metabolism	15	16	5
Neonatology-paediatric intensive care	1	2	0
Immunology-rheumatology-transplantation	6	6	5
Psychiatry	3	3	2
Pain	3	6	1
Haematology-haemostaseology	5	6	4
Otorhinolaryngology	1	1	3
Oncology	12	11	8
Dermatology	3	6	3
Vaccines	6	4	2
Ophthalmology	2	2	4
Anaesthesiology	1	1	2
Nutrition	1	0	0