EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Human Medicines Development and Evaluation

Meeting report

Paediatric Committee (PDCO)

6-8 October 2010

Opinions on paediatric investigation plans

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

- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergic extract from the pollen of Betula alba, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergic extract of equal amounts of birch, alder and hazel pollen (1/3 each), from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergic extract of equal amounts of Phleum pratense, Dactylis glomerata, Festuca elatior, Lolium perenne and Poa pratensis pollen (Grasses-Mix) and Birch, Alder and Hazel pollen (Tree-Mix) (50/50) in non-buffered 0.5 % phenol saline solution, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergic extract of equal amounts of Phleum pratense, Dactylis glomerata, Festuca elatior, Lolium perenne and Poa pratensis pollen (Grasses-Mix) and Birch pollen (50/50) in non-buffered 0.5 % phenol saline solution, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergic extract of equal amounts of Phleum pratense, Dactylis glomerata, Festuca elatior, Lolium perenne and Poa pratensis pollen (Grasses-Mix) and Secale cereale (Cultivated Rye) pollen (75/25), from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergic extract of equal amounts of Phleum pratense, Dactylis glomerata, Festuca elatior, Lolium perenne and Poa

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pratensis pollen (Grasses-Mix) and Secale cereale (Cultivated Rye) pollen (50/50), from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.

- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergic extract of equal amounts of Phleum pratense pollen and Secale cereale (Cultivated Rye) pollen (50/50), from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergic extract of equal amounts of Phleum pratense, Dactylis glomerata, Festuca elatior, Lolium perenne and Poa pratensis pollen (Grasses-Mix) (1/5) each, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergic extract of Phleum pratense pollen, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extract of birch pollen, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extract of birch, alder and hazel pollen, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extract of Phleum pratense pollen, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extracts of Phleum pratense, Dactylis glomerata, Festuca elatior, Lolium perenne and Poa pratensis pollen (Grasses-Mix), from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Aluminium hydroxide adsorbed, depigmented glutaraldehyde polymerised, allergen extracts of Phleum pratense, Dactylis glomerata, Festuca elatior, Lolium perenne and Poa pratensis pollen (Grasses-Mix) and Secale cereale (Cultivated Rye) pollen (50/50), from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Mixture of Birch, Hazel and Alder allergen extracts, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Betula alba allergen extract, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Dermatophagoides pteronyssinus allergen extract, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Mixture of Dermatophagoides pteronyssinus and Dermatophagoides farinae allergen extracts, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Mixture of Phleum pratense, Dactylis glomerata, Festuca elatior, Lolium perenne and Poa pratensis allergen extracts, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Mixture of Phleum pratense, Dactylis glomerata, Festuca elatior, Lolium perenne and Poa pratensis (Grasses-Mix) and Secale cereale (50/50) allergen extracts, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.

- Mixture of Phleum pratense, Dactylis glomerata, Festuca elatior, Lolium perenne and Poa pratensis (Grasses-Mix) and Secale cereale (75/25) allergen extracts, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Mixture of Phleum pratense and Secale cereale allergen extracts, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Phleum pratense allergen extract, from LETI Pharma GmbH, in the therapeutic area of pneumology – allergology.
- Recombinant Bet v1 folding variant (rBet v1-FV), from Allergopharma Joachim Ganzer KG, in the therapeutic area of pneumology – allergology.
- Partially purified bromelain, from Teva Pharma GmbH, in the therapeutic area of dermatology.
- [(3S)-6-({2',6'-Dimethyl-4'-[3-(methylsulfonyl) propoxy] biphenyl-3-yl}methoxy)-2,3-dihydro-1-benzofuran-3-yl]acetic acid hydrate (TAK-875), from Takeda Global Research and Development Centre (Europe) Ltd., in the therapeutic area of endocrinology-gynaecology-fertility-metabolism.
- Teduglutide ([gly2] recombinant human glucagon-like peptide), from Nycomed Danmark ApS, in the therapeutic area of gastroenterology-hepatology.
- Anti-BAFF monoclonal antibody, from Eli Lilly & Company Limited, in the therapeutic area of immunology-rheumatology-transplantation / oncology / neurology.
- Atazanavir sulphate, from Bristol-Myers Squibb Pharma EEIG, in the therapeutic area of infectious diseases.
- Aztreonam, from Gilead Sciences International Limited, in the therapeutic area of infectious diseases.
- Recombinant human monoclonal antibody to human Interleukin (IL)-17A, from Novartis Europharm Limited, in the therapeutic area of ophthalmology.
- Pixantrone, from CTI Life Sciences Ltd, in the therapeutic area of oncology.
- Fentanyl citrate, from EPMC Pharma SPRL, in the therapeutic area of pain / neonatology - paediatric intensive care.

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.

Adoption of opinions following re-examination

The PDCO adopted one opinion after re-examination, on a request for modification of an agreed PIP.

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 one positive opinion on a product-specific waiver, 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 medicine:

- Ocriplasmin, from ThromboGenics, in the therapeutic area of ophthalmology.

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

- 4-hydroxy-n-(2-hydroxyethyl)-butyramide, from Dr. Franz Köhler Chemie GmbH, in the therapeutic area of anaesthesiology / neurology.

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.

Withdrawals

The PDCO noted that five applications, one of which was a modification to an agreed PIP, 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. One expert was invited to the October meeting with a clinical expertise in paediatric anaesthesiology/intensive care and the PDCO discussed the potential needs of a specific active ingredient for pain management in infants.

PDCO interactions

A hearing of a delegation of the EAACI and EFA took place during the October meeting, in order to exchange views with the PDCO on the standard PIP for specific immunotherapy (SIT) for allergic rhinitis.

A CHMP co-rapporteur participated in the PDCO discussion on an opinion for a request for modification of an agreed paediatric investigation plan in the therapeutic area of cardiovascular diseases adopted by the PDCO.

Informal meetings

On 30 September and 1 October 2010, the PDCO held an informal meeting in Antwerp (Belgium) to review the work done and the processes put in place during its fourth year. The PDCO discussed improvements in the functioning of the PDCO (in particular timelines, presentations during plenary meetings, summary reports, interactions with experts, learned societies and industry), extrapolation,

interactions with other committees of the European Medicines Agency (in particular with SAWG and CHMP), and priorities in the implementation of the Paediatric Regulation.

Other issues

The PDCO welcomed the new alternate from Romania, Ms Nela Vilceanu, who has been nominated by the Committee for Medicinal Products for Human Use.

The PDCO thanked Dr Sophie Fornairon for her outstanding work and very active participation during her mandate, as she has resigned from the Committee.

The next meeting of the PDCO will be held on 10-12 November 2010.

Notes

1. PDCO opinions on PIPs and waivers are transformed into Agency 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 decision on a waiver or on a deferral.
3. See Paediatric medicine on the Agency's website for more information about the PDCO and the Paediatric Regulation.
4. This meeting report, together with other information on the work of the Agency, can be found on the Agency's website: www.ema.europa.eu

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Annex of the October 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	297	927[1]
Applications submitted for a product not yet authorised *(Article 7[2])*	186	191	258	674 *(70%)*
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	38	230 *(28%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30[2])*	10	10	2	23 *(2%)*
PIPs and full waiver indications covered by these applications	395	395	345	1,306

Number of Paediatric Committee (PDCO) opinions	2008	2009	2010	Cumulative total
Positive on full waiver	48	67	45	169
Positive on PIP, including potential deferral	81	122	113	318
Negative opinions adopted	4	13	6	23
Positive opinions adopted on modification of a PIP	8	51	88	147
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

[1] Of which 205 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	1
Gastroenterology-hepatology	3	2	1
Pneumology-allergology	6	6	42
Infectious diseases	8	9	4
Cardiovascular diseases	14	9	8
Diagnostics	1	1	1
Endocrinology-gynaecology-fertility-metabolism	15	16	6
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	3
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