European Medicines Agency

Doc. Ref. EMEA/551360/2009
P/175/2009

EUROPEAN MEDICINES AGENCY DECISION

of 7 September 2009

on the acceptance of a modification of an agreed Paediatric Investigation Plan for N-Acetyl-L-Cysteine (corresponds to L-Cysteine), L-Alanine, L-Alanyl-L-Glutamine (corresponds to to L-Alanine and L-Glutamine), L-Arginine, Glycine, Glycyl-L-Tyrosine (corresponds to Glycine and L-Tyrosine), L-Histidine, L-Isoleucine, L-Leucine, L-Lysine acetate (corresponds to L-Lysine), L-Methionine, L-Phenylalanine, L-Proline, L-Serine, Taurine, L-Threonine, L-Tryptophan, L-Valine (EMEA-000042-PIP01-07-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

DISCLAIMER: This Decision does not entitle to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006, as amended.

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THE EUROPEAN MEDICINES AGENCY,

Having regard to the Treaty establishing the European Community,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use as amended and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the decision P/24/2008 of the European Medicines Agency on 23 May 2008,

Having regard to the application submitted by Fresenius Kabi Deutschland GmbH on 14 May 2009 under Article 22 of Regulation (EC) No 1901/2006 as amended proposing changes to the agreed Paediatric Investigation Plan,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 24 July 2009, in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended,

Having regard to Article 25 of Regulation (EC) No 1901/2006 as amended,

WHEREAS:

(1) The Paediatric Committee of the European Medicines Agency has an opinion on the acceptance of changes to an agreed Paediatric Investigation Plan,

(2) It is therefore appropriate to adopt a Decision on the acceptance of changes to an agreed Paediatric Investigation Plan.

[1] OJ L 378, 27.12.2006, p.1
[2] OJ L 136, 30.4.2004, p. 1

HAS ADOPTED THIS DECISION:

Article 1

Changes to the agreed Paediatric Investigation Plan for N-Acetyl-L-Cysteine (corresponds to L-Cysteine), L-Alanine, L-Alanyl-L-Glutamine (corresponds to to L-Alanine and L-Glutamine), L-Arginine, Glycine, Glycyl-L-Tyrosine (corresponds to Glycine and L-Tyrosine), L-Histidine, L-Isoleucine, L-Leucine, L-Lysine acetate (corresponds to L-Lysine), L-Methionine, L-Phenylalanine, L-Proline, L-Serine, Taurine, L-Threonine, L-Tryptophan, L-Valine, solution for infusion, intravenous use, the details of which are set out in the Opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, are hereby accepted.

Article 2

This decision, that supersedes previous decision of the European Medicines Agency P/24/2008, is addressed to Fresenius Kabi Deutschland GmbH, Else-Kröner-Strasse 1, 61352 Bad Homburg, Germany.

Done at London, 7 September 2009

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

Doc. Ref. EMEA/PDCO/437118/2009
EMEA-000042-PIP01-07-M01

OPINION OF THE PAEDIATRIC COMMITTEE ON THE ACCEPTANCE OF A MODIFICATION OF AN AGREED PAEDIATRIC INVESTIGATION PLAN

Scope of the application

Active substance(s):
N-Acetyl-L-Cysteine (corresponds to L-Cysteine), L-Alanine, L-Alanyl-L-Glutamine (corresponds to to L-Alanine and L-Glutamine), L-Arginine, Glycine, Glycyl-L-Tyrosine (corresponds to Glycine and L-Tyrosine), L-Histidine, L-Isoleucine, L-Leucine, L-Lysine acetate (corresponds to L-Lysine), L-Methionine, L-Phenylalanine, L-Proline, L-Serine, Taurine, L-Threonine, L-Tryptophan, L-Valine

Condition(s):
Supplementation of amino-acids where parenteral nutrition is required.

Pharmaceutical form(s):
Solution for infusion

Route(s) of administration:
Intravenous use

Name/corporate name of the PIP applicant:
Fresenius Kabi Deutschland GmbH

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Fresenius Kabi Deutschland GmbH submitted to the EMEA on 14 May 2009 an application for modification of the agreed paediatric investigation plan and a waiver as set out in the EMEA decision P/24/2008 of 23 May 2008. The application for modification proposed changes to the agreed PIP.

The procedure started on 28 May 2009.

Scope of the modification

The changes mainly relate to the endpoints and the statistical plan of the clinical studies.

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Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

- to agree to the changes proposed by the applicant regarding the measures and the timelines of the paediatric investigation plan.

The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the Agency, together with its annex(es) and appendix.

London, 24 July 2009

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman

(Signature on file)

ANNEX I

THE MEASURES AND TIMELINES OF THE AGREED PAEDIATRIC INVESTIGATION PLAN AND THE SUBSET(S) OF THE PAEDIATRIC POPULATION AND CONDITION(S) COVERED BY THE WAIVER

A. CONDITION(S)

Supplementation of amino-acids where parenteral nutrition is required.

B. WAIVER

- **Condition**

Supplementation of amino-acids where parenteral nutrition is required.

The waiver applies to:

- Adolescents from 12 to less than 18 years, for the solution for infusion, intravenous use.

- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

C. PAEDIATRIC INVESTIGATION PLAN

- **Condition to be investigated**

Supplementation of amino-acids where parenteral nutrition is required.

- **Proposed PIP indication**

Supply of essential and non-essential amino acids as part of parenteral nutrition for pre-term and full-term neonates, infants and children, when oral or enteral nutrition is impossible, insufficient or contraindicated.

- **Subset(s) of the paediatric population concerned by the paediatric development**

Preterm newborn infants, term newborn infants (0 days to less than 28 days), infants and toddlers (from 28 days to less than 24 months), children (from 2 to less than 12 years).

- **Formulation(s)**

Solution for infusion, 10% (10g/100ml), intravenous use

- **Studies**

Area	Number of studies	Description
Quality		Not applicable
Non-clinical		Preclinical 13 weeks toxicity trial – completed October 2007
Clinical	4	• double-blind, 2:1 randomisation, multicentre, parallel group, active controlled trial in term newborn infants and infants and toddlers aged 0 to less than 24 months after surgical interventions. • double-blind, randomised, parallel group, multicentre, active controlled trial in preterm infants with a birth weight from 800 to less than 1500g. • double-blind, randomised, parallel group, multicentre active controlled trial in preterm infants with a birth weight less than

		1000g. • double-blind, randomised, parallel group, active controlled trial in children aged 1 month to less than 12 years

Measures to address long term follow-up of safety and efficacy in relation to paediatric use:	**Yes**
Date of completion of the paediatric investigation plan:	**By December 2011**
Deferral for some or all studies contained in the paediatric investigation plan:	**No**