European Medicines Agency

Doc. Ref. EMEA/288303/2009
P/87/2009

EUROPEAN MEDICINES AGENCY DECISION

of 18 May 2009

on the agreement of a Paediatric Investigation Plan and on the granting of a deferral for rolofylline (EMEA-000275-PIP01-08) 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 application submitted by Merck Sharp & Dohme (Europe), Inc**.** on 21 July 2008 under Article 16(1) of Regulation (EC) No 1901/2006 as amended also requesting a deferral under Article 20 of said Regulation,

Having regard to the Opinion of the Paediatric Committee of the European Medicines Agency, issued on 3 April 2009, in accordance with Article 18 of Regulation (EC) No 1901/2006 as amended, and Article 21 of said Regulation**,**

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

WHEREAS:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the agreement of a Paediatric Investigation Plan and on the granting of a deferral,

(2) It is therefore appropriate to adopt a Decision granting a Paediatric Investigation Plan.

(3) It is therefore appropriate to adopt a Decision granting a deferral.

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

HAS ADOPTED THIS DECISION:

Article 1

A Paediatric Investigation Plan for rolofylline, emulsion for injection, 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, is hereby agreed.

Article 2

A deferral for rolofylline, emulsion for injection, 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, is hereby granted.

Article 3

This decision is addressed to Merck Sharp & Dohme (Europe), Inc., Lynx Binnenhof 5, 1200 Brussels, Belgium.

Done at London, 18 May 2009

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

European Medicines Agency

Doc. Ref. EMEA/200102/2009
EMEA-000275-PIP01-08

OPINION OF THE PAEDIATRIC COMMITTEE ON THE AGREEMENT OF A PAEDIATRIC INVESTIGATION PLAN AND A DEFERRAL

Scope of the application

Active substance(s):
Rolofylline

Condition(s):
Heart Failure

Pharmaceutical form(s):
Emulsion for injection

Route(s) of administration:
Intravenous use

Name/corporate name of the PIP applicant:
Merck Sharp & Dohme (Europe), Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Merck Sharp & Dohme (Europe), Inc. submitted for agreement to the EMEA on 21 July 2008 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 27 August 2008.

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Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

- to agree the paediatric investigation plan in accordance with Article 18 of said Regulation,

- to grant a deferral in accordance with Article 21 of said Regulation,

The Icelandic and the Norwegian Paediatric Committee members agree with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan and the subsets of the paediatric population 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, 3 April 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 SUBSETS OF THE PAEDIATRIC POPULATION

A. CONDITION

Heart Failure

B. WAIVER

Not applicable.

C. PAEDIATRIC INVESTIGATION PLAN

- **Condition to be investigated**

Heart Failure

- **Proposed PIP indication**

Treatment of post operative volume overload and acute heart failure syndrome in children from 0 to less than 18 years.

- **Subsets of the paediatric population concerned by the paediatric development**

From 0 years to less than 18 years.

- **Formulation**

Emulsion for injection

- **Studies**

Area	Number of studies	Description
Quality		Not applicable.
Non-clinical	2	Dose range finding study for the juvenile toxicity study in rats. Juvenile toxicity study to evaluate the potential toxicity of rolofylline on growth and behaviour in juvenile rats.
Clinical	4	Prospective, observational study among children hospitalized for acute heart failure syndrome presenting with dilated cardiomyopathy or experiencing post-operative volume overload as a consequence of coronary pulmonary bypass post surgical repair of a congenital heart defect. An open-label, sequential panel, single-dose IV study to evaluate the safety, tolerability, and pharmacokinetics of rolofylline in children from 0 to less than 18 years. Randomized, parallel-group, double-blind, placebo-controlled study of rolofylline in addition to IV loop diuretic therapy in acute heart failure syndrome (AHFS) children from 0 to less than 18 years hospitalized with volume overload. Randomized, parallel-group, double-blind, placebo-controlled study

		objective of the study of rolofylline in addition to IV loop diuretic therapy in children from 0 to less then 18 years presenting with postoperative volume overload (POVO) following surgical repair of a congenital heart defect.

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	**Yes**
Date of completion of the paediatric investigation plan:	**By December 2017**
Deferral for some or all studies contained in the paediatric investigation plan:	**Yes**