European Medicines Agency

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EUROPEAN MEDICINES AGENCY DECISION

of 23 June 2008

on the application for agreement of a Paediatric Investigation Plan for Nicotinic acid and laropiprant (EMEA-000063-PIP01-07) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

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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 and Dohme (Europe), Inc. on 19 October 2007 under Article 16(1) of Regulation (EC) No 1901/2006 as amended also requesting a waiver under Article 13 of said Regulation and a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 4 June 2008, in accordance with Article 18 of Regulation (EC) No 1901/2006 as amended and Article 13 of said Regulation 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 a positive opinion,

(2) It is therefore appropriate to adopt a Decision following the Paediatric Committee's opinion on the Paediatric Investigation Plan.

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

(4) 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 nicotinic acid and laropiprant, extended release tablet, oral 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 waiver for nicotinic acid and laropiprant, extended release tablet, oral use, the details of which are set out in the Opinion of the Paediatric Committee the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A deferral for nicotinic acid and laropiprant, extended release tablet, oral use, the details of which are set out in the Opinion of the Paediatric Committee the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

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

Done at London, 23 June 2008

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

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

EMEA/315476/2008
EMEA-000063-PIP01-07

POSITIVE OPINION OF THE PAEDIATRIC COMMITTEE ON A REQUEST FOR AGREEMENT OF A PAEDIATRIC INVESTIGATION PLAN FOR

Scope of the application

Active substance:
Nicotinic acid and laropiprant

Condition(s):
Homozygous Familial Hypercholesterolaemia
Heterozygous Familial Hypercholesterolaemia

Pharmaceutical form(s):
Extended release tablet

Route(s) of administration:
Oral use

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

Basis for opinion

Pursuant to Article 16.1 of Regulation (EC) No 1901/2006 as amended, Merck Sharp and Dohme (Europe), Inc. submitted for agreement to the EMEA on 19 October 2007 a paediatric investigation plan for the above mentioned medicinal product.

The procedure started on 22 November 2007.

Supplementary information was provided by the applicant on 28 March 2008.

A meeting with the Paediatric Committee took place on 2 June 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 Regulation (EC) No 1901/2006 as amended,
- to grant a deferral in accordance with Article 21 of Regulation (EC) No 1901/2006 as amended,
- to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of Regulation (EC) No 1901/2006 as amended and concluded in accordance with Article 11(1)(c) of Regulation (EC) No 1901/2006 as amended, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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

2. 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 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(ces).

London, 4 June 2008

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) / DISEASE(S)

Homozygous Familial Hypercholesterolaemia
Heterozygous Familial Hypercholesterolaemia

B. WAIVER

- **Condition**

Homozygous Familial Hypercholesterolaemia

  - **Subset(s) of the paediatric population, pharmaceutical form(s) and route(s) of administration covered**

The waiver applies to:

- All paediatric subsets for extended release tablet for oral use.

- **Condition**

Heterozygous Familial Hypercholesterolaemia

  - **Subset(s) of the paediatric population, pharmaceutical form(s) and route(s) of administration covered**

The waiver applies to:

- Preterm newborn infants, term newborn infants, infants and toddlers and children less than 7 years old for extended release tablets for oral use.

C. PAEDIATRIC INVESTIGATION PLAN

C.1. Condition to be investigated

Heterozygous Familial Hypercholesterolaemia

- **Subset(s) covered**

Children from 7 years old until puberty as defined below
Post-pubertal children younger than 18 years old
The cutoff between the above two groups is defined by the stage of sexual maturity, i.e. post Tanner stage II for boys and post-menarche for girls.

- **Formulation(s)**

Extended release tablet for oral use
A new paediatric formulation shall be developed before initiating studies in the pre-pubertal subgroup. This is deferred until September 2018.

- **Studies/Measures**

Area	Subarea	Description
Clinical	Clinical Pharmacology	1. Clinical pharmacology study to evaluate the safety, tolerability and pharmacokinetics of extended release niacin/laropiprant in post-pubertal children. 2. Clinical pharmacology study to evaluate the safety, tolerability and pharmacokinetics of extended release niacin/laropiprant in pre-pubertal children.
Clinical	Efficacy and Safety	1. Multi-center, randomised, double-blind, placebo-controlled study with an open-label extension phase to evaluate the safety and efficacy of extended release niacin/laropiprant when added to ongoing lipid-modifying therapy in post-pubertal children with heterozygous familial hypercholesterolemia. 2. Randomised, double-blind, placebo-controlled study to

		evaluate the safety and efficacy of extended release niacin/laropiprant when added to ongoing lipid-modifying therapy in pre-pubertal children with heterozygous familial hypercholesterolemia.

Need for paediatric measures in a EU-Risk Management Plan: Yes
Date of completion of the paediatric investigation plan: March 2019
A deferral has been granted: Yes