EMA/646946/2012

European Medicines Agency decision

P/0262/2012

of 20 November 2012

on the acceptance of a modification of an agreed paediatric investigation plan for nicotinic acid / laropiprant (Tredaptive), (EMEA-000063-PIP01-07-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This Decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

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 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 European Medicines Agency's decision P/44/2008 issued on 23 June 2008,

Having regard to the application submitted by Merck Sharp & Dohme Ltd. on 10 August 2012 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 5 October 2012, in accordance with Article 22 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation and Article 13 of said Regulation,

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

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan and to the waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the waiver.

[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 nicotinic acid / laropiprant (Tredaptive), modified-release tablet, age-appropriate dosage form, oral use, including changes to the waiver, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Merck Sharp & Dohme Ltd., Hertford Road, Hoddesdon, Hertfordshire, EN11 9BU – Hoddesdon, United Kingdom.

Done at London, 20 November 2012

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/558711/2012

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-000063-PIP01-07-M01

Scope of the application

Active substance(s):

Nicotinic acid / laropiprant

Invented name:

Tredaptive

Condition(s):

Prevention of major vascular and major coronary events

Treatment of dyslipidaemia

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Modified-release tablet

Age-appropriate dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Merck Sharp & Dohme Ltd.

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Merck Sharp & Dohme Ltd. submitted to the European Medicines Agency on 10 August 2012 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/44/2008 issued on 23 June 2008.

The application for modification proposed changes to the agreed paediatric investigation plan and to the waiver.

The procedure started on 12 September 2012.

Scope of the modification

Amendment of the scope of the Paediatric Investigation Plan to revise the existing condition and to include another condition.

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 changes to the paediatric investigation plan and to the waiver in the scope set out in the Annex I of this opinion.

   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 European Medicines Agency, together with its annex(es) and appendix.

London, 5 October 2012

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman
(Signature on file)

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed Paediatric Investigation Plan

1. Waiver

1.1. Condition: Prevention of major vascular and major coronary events

The waiver applies to:

- All subsets of the paediatric population from birth to less than 18 years of age;
- for modified-release tablet and for age-appropriate dosage form for oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

1.2. Condition: Treatment of dyslipidaemia

The waiver applies to:

- All subsets of the paediatric population from birth to less than 7 years of age;
- for modified-release tablet and for age-appropriate dosage form for oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of dyslipidaemia

2.1.1. Indication(s) targeted by the PIP

Heterozygous familial hypercholesterolaemia.

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 7 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Modified-release tablet and age-appropriate dosage form for oral use.

2.1.4. Studies

Area	Number of studies	Description
Quality	1	**Study 1:** Development of a new, age-appropriate paediatric formulation.
Non-clinical	0	Not applicable.

Area	Number of studies	Description
Clinical	4	**Study 2:** Clinical pharmacology study to evaluate the safety, tolerability and pharmacokinetics of modified-release niacin/laropiprant in post-pubertal children. **Study 3:** Multi-center, randomised, double-blind, placebo-controlled study with an open-label extension phase to evaluate the safety and efficacy of modified-release niacin/laropiprant when added to ongoing lipid-modifying therapy in post-pubertal children with heterozygous familial hypercholesterolemia. **Study 4:** Clinical pharmacology study to evaluate the safety, tolerability and pharmacokinetics of modified-release niacin/laropiprant in pre-pubertal children. **Study 5:** Randomised, double-blind, placebo-controlled study to evaluate the safety and efficacy of modified-release niacin/laropiprant when added to ongoing lipid-modifying therapy in pre-pubertal children with heterozygous familial hypercholesterolemia.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By March 2019
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of dyslipidaemia

   Authorised indications:

   (The text of the indication is identical for the trade names Tredaptive, Trevaclyn and Pelzont)

   Tredaptive is indicated for the treatment of dyslipidaemia, particularly in patients with combined mixed dyslipidaemia (characterised by elevated levels of LDL-cholesterol and triglycerides and low HDL-cholesterol) and in patients with primary hypercholesterolaemia (heterozygous familial and non-familial).

   Tredaptive should be used in patients in combination with HMG-CoA reductase inhibitors (statins), when the cholesterol lowering effect of HMG-CoA reductase inhibitor monotherapy is inadequate. It can be used as monotherapy only in patients in whom HMG-CoA reductase inhibitors are considered inappropriate or not tolerated. Diet and other non-pharmacological treatments (e.g. exercise, weight reduction) should be continued during therapy with Tredaptive.

EU Number	**Invented name**	**Strength**	**Pharmaceutical form**	**Route of administration**	**Packaging**	**Package size**
EU/1/08/459/001	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (Aclar/PVC)	14 tablets
EU/1/08/459/002	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (Aclar/PVC)	28 tablets
EU/1/08/459/003	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (Aclar/PVC)	56 tablets
EU/1/08/459/004	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (Aclar/PVC)	84 tablets
EU/1/08/459/005	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (Aclar/PVC)	98 tablets
EU/1/08/459/006	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (Aclar/PVC)	168 tablets
EU/1/08/459/007	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (Aclar/PVC)	196 tablets
EU/1/08/459/008	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (Aclar/PVC)	49 x 1 tablets (unit dose)
EU/1/08/459/009	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (alu/alu)	14 tablets

EU/1/08/459/010	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (alu/alu)	28 tablets
EU/1/08/459/011	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (alu/alu)	56 tablets
EU/1/08/459/012	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (Aclar/PVC)	196 (2 x 98) tablets
EU/1/08/459/013	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (alu/alu)	168 tablets
EU/1/08/459/014	Tredaptive	1000 mg / 20 mg	Modified-release tablet	Oral use	blister (alu/alu)	32 x 1 tablets (unit dose)