EMA/182693/2012

European Medicines Agency decision

P/0061/2012

of 28 March 2012

on the acceptance of a modification of an agreed paediatric investigation plan for Ezetimibe (Ezetrol and associated names), (EMEA-000007-PIP01-07-M02) 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/59/2008 issued on 20 July 2008, and the decision P/15/2011 issued on 21 January 2011,

Having regard to the application submitted by MSD-SP Limited on 17 November 2011 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 10 February 2012, in accordance with Article 22 of Regulation (EC) No 1901/2006,

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.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the 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 Ezetimibe (Ezetrol and associated names), tablet, oral use, 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 MSD-SP Limited, Hertford Road, Hertfordshire, EN11 9BU - Hoddesdon, United Kingdom.

Done at London, 28 March 2012

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

EMA/PDCO/29438/2012

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

EMEA-000007-PIP01-07-M02

Scope of the application

Active substance(s):

Ezetimibe

Invented name:

Ezetrol and associated names

Condition(s):

Treatment of hypercholesterolaemia

Treatment of sitosterolaemia

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

MSD-SP Limited

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, MSD-SP Limited submitted to the European Medicines Agency on 17 November 2011 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/59/2008 issued on 20 July 2008, the decision P/15/2011 issued on 21 January 2011.

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

The procedure started on 14 December 2011.

Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified.

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 in the scope set out in the Annex I of this opinion.

   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 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, 10 February 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: Treatment of hypercholesterolaemia

The waiver applies to:

- the paediatric population from birth to less than 6 years;
- for the tablet for oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

1.2. Condition: Treatment of sitosterolaemia

The waiver applies to:

- the paediatric population from birth to less than 18 years;
- for the tablet for oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as the needs are already covered.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of hypercholesterolaemia

2.1.1. Indication(s) targeted by the PIP

Treatment of primary (heterozygous familial and non-familial) hypercholesterolaemia

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

Paediatric population from 6 years to less than 18 years.

2.1.3. Pharmaceutical form(s)

Tablet for oral use.

2.1.4. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	2	Study 1: Phase 3 study of ezetimibe in coadministration with simvastatin for the treatment of children (10 to 17 years of age) with heterozygous familial hypercholesterolemia. Study 2: Phase 3 study of ezetimibe monotherapy in children (6 to 10 years of age) with heterozygous familial and non-familial

Area	Number of studies	Description
		hypercholesterolaemia.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety issues in relation to paediatric use:	Yes.
Date of completion of the paediatric investigation plan:	By April 2012.
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. Hypercholesterolaemia

   Authorised indications:

   Primary Hypercholesterolaemia:

   - Ezetrol co-administered with an HMG-CoA reductase inhibitor (statin) is indicated as adjunctive therapy to diet for use in patients with primary (heterozygous familial and non-familial) hypercholesterolaemia who are not appropriately controlled with a statin alone.
   - Ezetrol monotherapy is indicated as adjunctive therapy to diet for use in patients with primary (heterozygous familial and non-familial) hypercholesterolaemia in whom a statin is considered inappropriate or is not tolerated.

   Homozygous Familial Hypercholesterolaemia (HoFH):

   - Ezetrol co-administered with a statin, is indicated as adjunctive therapy to diet for use in patients with HoFH. Patients may also receive adjunctive treatments (e.g., LDL apheresis).

   Homozygous Sitosterolaemia (Phytosterolaemia):

   - Ezetrol is indicated as adjunctive therapy to diet for use in patients with homozygous familial sitosterolaemia.

   A beneficial effect of Ezetrol on cardiovascular morbidity and mortality has not yet been demonstrated.

Invented name	**Strength**	**Pharmaceutical form**	**Route of administration**
Ezetrol and associated names	10 mg	Tablet	Oral use