



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/797044/2013

European Medicines Agency decision

P/0040/2014

of 5 March 2014

on the acceptance of a modification of an agreed paediatric investigation plan for lenvatinib (EMA-001119-PIP02-12-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.



European Medicines Agency decision

P/0040/2014

of 5 March 2014

on the acceptance of a modification of an agreed paediatric investigation plan for lenvatinib (EMA-001119-PIP02-12-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 726/2004¹,

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 Agency²,

Having regard to the European Medicines Agency's decision P/0125/2013 issued on 28 May 2013,

Having regard to the application submitted by Eisai Europe Ltd on 24 October 2013 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and proposing a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 17 January 2013, in accordance with Article 22 of Regulation (EC) No 1901/2006, 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 on the granting of a waiver.
- (2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.
- (3) It is therefore appropriate to adopt a decision on the granting of a 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 lenvatinib, capsule, hard, 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

A waiver for lenvatinib, capsule, hard, 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

This decision is addressed to Eisai Europe Ltd, European Knowledge Centre, Mosquito Way, AL10 9SN - Hatfield, Herts, United Kingdom.

Done at London, 5 March 2014

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

EMA/PDCO/667002/2013

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

EMA-001119-PIP02-12-M01

Scope of the application

Active substance(s):

Lenvatinib

Condition(s):

Treatment of papillary thyroid cancer

Treatment of follicular thyroid cancer

Treatment of osteosarcoma

Pharmaceutical form(s):

Capsule, hard

Route(s) of administration:

Oral use

Name / corporate name of the PIP applicant:

Eisai Europe Ltd

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Eisai Europe Ltd submitted to the European Medicines Agency on 24 October 2013 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0125/2013 issued on 28 May 2013.

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

The procedure started on 19 November 2013.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified and a waiver for a paediatric subset has been added.

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;
 - to grant a waiver for one or more subsets of the paediatric population concluded in accordance with Article 11(1)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

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 and appendix.

London, 17 January 2013

On behalf of the Paediatric Committee
Dr Dirk Mentzer, 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. Conditions: treatment of follicular thyroid carcinoma, treatment of papillary thyroid carcinoma and treatment of osteosarcoma

The waiver applies to:

- the paediatric population from birth to less than 2 years;
- for capsule, hard, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition: treatment of follicular thyroid carcinoma and treatment of papillary thyroid carcinoma

2.1.1. Indication(s) targeted by the PIP

Treatment of children with ¹³¹I-refractory follicular or papillary thyroid carcinoma

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

From 2 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Capsule, hard

2.1.4. Measures

Area	Number of measures	Description
Quality	1	Measure 1: Development of an oral suspension prepared from the hard capsule
Non-clinical	2	Measure 2: Toxicity study in juvenile rats Measure 3: Toxicity study in juvenile rats
Clinical	1	Measure 5: Open-label, multi-centre, non-controlled trial to evaluate pharmacokinetics, pharmacodynamics, tolerability and safety of lenvatinib in children from 2 years to less than 18 years of age with a relapsed or refractory solid malignant tumour and, in patients with osteosarcoma, an extension phase to evaluate lenvatinib in combination with cyclophosphamide and etoposide

2.2. Condition: treatment of osteosarcoma

2.2.1. Indication(s) targeted by the PIP

Treatment of children with a first relapse of osteosarcoma

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

From 2 years to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Capsule, hard

2.2.4. Measures

Area	Number of measures	Description
Quality	1	Measure 1: As for conditions treatment of follicular thyroid carcinoma and treatment of papillary thyroid carcinoma
Non-clinical	3	Measure 2: As for conditions treatment of follicular thyroid carcinoma and treatment of papillary thyroid carcinoma Measure 3: As for conditions treatment of follicular thyroid carcinoma and treatment of papillary thyroid carcinoma Measure 4: Pharmacology study of lenvatinib in combination with cyclophosphamide and etoposide in paediatric tumour models
Clinical	2	Measure 5: As for conditions treatment of follicular thyroid carcinoma and treatment of papillary thyroid carcinoma Measure 6: Multi-centre, randomized, controlled trial to evaluate the efficacy and safety of lenvatinib as add-on to cyclophosphamide combined with etoposide in children from 5 years to less than 18 years (and adults) with relapsed osteosarcoma

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 December 2022
Deferral for one or more measures contained in the paediatric investigation plan:	Yes