EMA/288163/2020

European Medicines Agency decision

P/0210/2020

of 16 June 2020

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for lenvatinib (Lenvima, Kisplyx), (EMEA-001119-PIP03-19) 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 application submitted by Eisai GmbH on 7 August 2019 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 30 April 2020, in accordance with Article 17 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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

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

(4) It is therefore appropriate to adopt a decision granting 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

A paediatric investigation plan for lenvatinib (Lenvima, Kisplyx), capsule, hard, 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 deferral for lenvatinib (Lenvima, Kisplyx), capsule, hard, 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 granted.

Article 3

A waiver for lenvatinib (Lenvima, Kisplyx), capsule, hard, 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 granted.

Article 4

This decision covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0033/2020 issued on 29 January 2020, including subsequent modifications thereof.

Article 5

This decision is addressed to Eisai GmbH, Lyoner Straβe 36, 60528 - Frankfurt am Main, Germany.

EMA/PDCO/127029/2020
Amsterdam, 30 April 2020

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-001119-PIP03-19

Scope of the application

Active substance(s):

Lenvatinib

Invented name:

Lenvima, Kisplyx

Condition(s):

Treatment of all conditions included in the category of malignant neoplasms except haematopoietic and lymphoid tissue neoplasms, papillary thyroid cancer, follicular thyroid cancer and osteosarcoma

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Capsule, hard

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Eisai GmbH

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Eisai GmbH submitted for agreement to the European Medicines Agency on 7 August 2019 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 17 September 2019.

Supplementary information was provided by the applicant on 24 January 2020. The applicant proposed modifications to the paediatric investigation plan.

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 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and 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 Norwegian Paediatric Committee member agrees 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 European Medicines Agency, together with its annexes and appendix.

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 (PIP)

1. Waiver

1.1. Condition:

Treatment of all conditions included in the category of malignant neoplasms except haematopoietic and lymphoid tissue neoplasms, papillary thyroid cancer, follicular thyroid cancer and osteosarcoma

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- 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 all conditions included in the category of malignant neoplasms except haematopoietic and lymphoid tissue neoplasms, papillary thyroid cancer, follicular thyroid cancer and osteosarcoma

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from 2 years to less than 18 years old with a relapsed or refractory solid malignant tumour including Ewing sarcoma/peripheral primitive neuroectodermal tumour, rhabdomyosarcoma and high-grade glioma

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-related studies	1	**Study 1** Development of an oral suspension prepared from the hard capsule
Non-clinical studies	0	Not applicable.
Clinical studies	3	**Study 2** Open-label, multicentre, single arm two stages trial to evaluate the pharmacokinetics, the safety and the anti-tumour activity, of lenvatinib in children from 2 years to less than 18 years of age (and young adults) with a relapsed or refractory solid malignant tumour

		(including Ewing sarcoma/peripheral primitive neuroectodermal tumour, rhabdomyosarcoma and high-grade glioma) (E7080-G000-231) **Study 3** Open-label, multi-centre, single-arm trial including a dose-escalation phase (stage 1) and expansion phase (stage 2) to evaluate the pharmacokinetics, safety, tolerability and anti-tumour activity of lenvatinib used in in combination with everolimus in children from 2 years to less than 18 years of age (and young adults) with a relapsed or refractory paediatric solid malignant tumour (non-CNS and CNS tumours) (E7080-A001-216) **Study 4** Randomised open-label controlled trial to evaluate the efficacy and safety of lenvatinib as single-agent or used in combination with a rationally selected therapy, in children from 2 years to less than 18 years of age with a solid malignant tumour type selected based on the results of study 2 (E7080-G000-231) and as applicable of study 3 (E7080-A001-216)
Extrapolation, modelling and simulation studies	1	**Study 5** Modelling and simulation study to evaluate the use and support the dosing regimen of lenvatinib in children from 2 to less than 18 years of age with a refractory or relapsed solid malignant tumour (non-CNS tumours and CNS tumours) including Ewing sarcoma/peripheral primitive neuroectodermal tumour, rhabdomyosarcoma and high-grade glioma
Other studies	0	Not applicable.
Other measures	0	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By July 2030
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of all conditions included in the category of malignant neoplasms except haematopoietic and lymphoid tissue neoplasms, papillary thyroid cancer, follicular thyroid cancer and osteosarcoma

Authorised indication(s):

- Kisplyx is indicated in combination with everolimus for the treatment of adult patients with advanced renal cell carcinoma (RCC) following one prior vascular endothelial growth factor (VEGF)-targeted therapy.
- LENVIMA is indicated as monotherapy for the treatment of adult patients with advanced or unresectable hepatocellular carcinoma (HCC) who have received no prior systemic therapy.

2. Treatment of papillary thyroid cancer
3. Treatment of follicular thyroid cancer

Authorised indication(s):

- LENVIMA is indicated for the treatment of adult patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine (RAI).

Authorised pharmaceutical form(s):

Capsule, hard

Authorised route(s) of administration:

Oral use.