EMA/929776/2022

European Medicines Agency decision

P/0528/2022

of 30 December 2022

on the acceptance of a modification of an agreed paediatric investigation plan for lenvatinib (Lenvima, Kisplyx), (EMEA-001119-PIP03-19-M03) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0210/2020 issued on 16 June 2020, the decision P/0205/2021 issued on 10 May 2021 and the decision P/0154/2022 issued on 13 May 2022,

Having regard to the application submitted by Eisai GmbH on 28 July 2022 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 11 November 2022, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for Lenvatinib (Lenvima, Kisplyx), 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

This decision covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0125/2013 issued on 28 May 2013, including subsequent modifications thereof.

Article 3

This decision is addressed to Eisai GmbH, Edmund-Rumpler-Strasse 3, 60549 - Frankfurt am Main, Germany.

EMA/PDCO/691486/2022
Amsterdam, 11 November 2022

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

EMEA-001119-PIP03-19-M03

Scope of the application

Active substance(s):

Lenvatinib

Invented name and authorisation status:

See Annex II

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

Pharmaceutical form(s):

Capsule, hard

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Eisai GmbH

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Eisai GmbH submitted to the European Medicines Agency on 28 July 2022 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/0210/2020 issued on 16 June 2020, the decision P/0205/2021 issued on 10 May 2021 and the decision P/0154/2022 issued on 13 May 2022.

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

The procedure started on 12 September 2022.

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 Paediatric Committee member of Norway 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 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

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	Description
Quality-related studies	**Study 1** Development of an oral suspension prepared from the hard capsule
Non-clinical studies	Not applicable
Clinical studies	**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** deleted in procedure EMEA-001119-PIP03-19-M02
Extrapolation, modelling and simulation studies	**Study 5** deleted in procedure EMEA-001119-PIP03-19-M02
Other studies	Not applicable
Other measures	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 December 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

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 for the treatment of adults with advanced renal cell carcinoma (RCC):
    - in combination with pembrolizumab, as first-line treatment;
    - in combination with everolimus, following one prior vascular endothelial growth factor (VEGF)-targeted therapy;
    - Lenvima as monotherapy is indicated for the treatment of adult patients with advanced or unresectable hepatocellular carcinoma (HCC) who have received no prior systemic therapy;
    - Lenvima in combination with pembrolizumab is indicated for the treatment of adult patients with advanced or recurrent endometrial carcinoma (EC) who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and are not candidates for curative surgery or radiation.
    - Invented name(s): Kisplyx; Lenvima
    - Authorised pharmaceutical form(s): Capsule, hard
    - Authorised route(s) of administration: Oral use
    - Authorised via centralised procedure

2. Treatment papillary thyroid cancer

3. Treatment of follicular thyroid cancer

Authorised indication(s):

- Lenvima as monotherapy 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).
    - Invented name(s): Lenvima
    - Authorised pharmaceutical form(s): Capsule, hard
    - Authorised route(s) of administration: Oral use
    - Authorised via centralised procedure