MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan

MHRA-100609-PIP01-22-M01

Scope of the Application

Active Substance(s)

LENVATINIB MESILATE

Condition(s)

Treatment of papillary thyroid cancer and 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 Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Eisai Europe Limited submitted to the licensing authority on 20/07/2022 16:48 BST an application for a

The procedure started on 13/01/2023 13:26 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100609-PIP01-22-M01

Of 13/02/2023 15:58 GMT

On the adopted decision for LENVATINIB MESILATE (MHRA-100609-PIP01-22-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a for LENVATINIB MESILATE, Capsule, hard , ORAL USE .

This decision is addressed to Eisai Europe Limited, European Knowledge Centre, Mosquito Way, Hatfield, UNITED KINGDOM, AL10 9SN

ANNEX I

1. Waiver

1.1 Condition:

Condition 1: Treatment of papillary thyroid cancer Condition 2: Treatment of follicular thyroid cancer Condition 3: Treatment of osteosarcoma For all 3 conditions, the waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Capsule, hard Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Condition 1: Treatment of papillary thyroid cancer Condition 2: Treatment of follicular thyroid cancer Condition 3: Treatment of osteosarcoma.

2.2 Indication(s) targeted by the PIP:

Conditions 1 and 2: Treatment of paediatric patients with 131I-refractory follicular or papillary thyroid cancer Condition 3: Treatment of paediatric patients with refractory or relapsed osteosarcoma

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

For all 3 conditions- the paediatric population from 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

For all 3 conditions- Capsule, hard

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	(Same study for all 3 conditions) Study 1 Development of an oral suspension prepared from the hard capsule.
Non-Clinical Studies	3	(Same studies for all 3 conditions) Study 2 Toxicity study in juvenile rats. Study 3 Toxicity study in juvenile rats. (Study for Condition 3 only) Study 4 Pharmacology study of lenvatinib in combination with ifosfamide and etoposide in paediatric tumour models.
Clinical Studies	2	(Same study for all 3 conditions) Study 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 ifosfamide and etoposide. (Study for Condition 3 only) Study 6 Deleted in procedure EMEA-001119-PIP02-12-M05 Study 8 (Added in procedure EMEA-001119-PIP02-12-M05) Multi-centre, randomised, controlled trial to evaluate the efficacy and

		safety of lenvatinib as add-on to ifosfamide and etoposide in children from 2 years to less than 18 years (and adults) with refractory or relapsed osteosarcoma.
Extrapolation, Modeling & Simulation Studies	1	(Study for Conditions 1 and 2) Study 7 (CPMS-E7080-014P-v1) (Added in procedure EMEA-001119-PIP02-12-M04) Population PK analysis to establish the dose-response relationship of lenvatinib in paediatric patients with differentiated thyroid cancer (DTC) and to support extrapolation of efficacy from adult patients to paediatric patients with DTC.
Other Studies	0	Not applicable.
Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	31/12/2022
Deferral of one or more studies contained in the paediatric investigation plan:	Yes