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 and to the deferral

MHRA-100148-PIP01-21-M01

Scope of the Application

Active Substance(s)

LENVATINIB MESILATE

Condition(s)

Treatment of all conditions included in the category of malignant neoplasms

Pharmaceutical Form(s)

Capsule, hard, Oral suspension

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Eisai GmbH

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Eisai GmbH submitted to the licensing authority on 21/07/2021 15:25 BST an application for a Modification

The procedure started on 17/11/2021 08:48 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-100148-PIP01-21-M01

Of 24/11/2021 17:39 GMT

On the adopted decision for LENVATINIB MESILATE (MHRA-100148-PIP01-21-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 Modification for LENVATINIB MESILATE, Capsule, hard, Oral suspension , Oral use .

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

ANNEX I

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 / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Capsule, hard; Oral suspension 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):

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

2.2 Indication(s) targeted by the PIP:

Treatment of paediatric patients from 2 years to less than 18 years with a relapsed or refractory solid malignant tumour including rhabdomyosarcoma and high-grade glioma

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

The paediatric population from 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Capsule, hard; Oral suspension

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an oral suspension prepared from the hard capsule.
Non-Clinical Studies	0	Not applicable
Clinical Studies	3	Study 2: (E7080-G000-231) 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 [EWS], rhabdomyosarcoma [RMS] and high-grade glioma [HGG]); Study 3 (E7080-A001-216) 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 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); Study 4 Randomised open-label controlled trials 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, Modeling & Simulation Studies	1	Study 5: Modelling and simulation study to evaluate the use and support the dosing regimen of lenvatinib in children from 2 years to less than 18 years of age with a relapsed or refractory solid malignant tumour (non-CNS and CNS tumours), including Ewing sarcoma/ peripheral primitive neuroectodermal tumour [EWS], rhabdomyosarcoma [RMS] and high-grade glioma [HGG].
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:	31/07/2030
Deferral of one or more studies contained in the paediatric investigation plan:	Yes