MHRA
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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-100327-PIP01-21-M01

Scope of the Application

Active Substance(s)

SELPERCATINIB

Condition(s)

Treatment of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms).

Pharmaceutical Form(s)

Capsule, hard; Age-appropriate dosage form

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Eli Lilly Nederland B.V

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Eli Lilly Nederland B.V submitted to the licensing authority on 21/10/2021 15:44 BST an application for a Modification

The procedure started on 23/02/2022 15:20 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-100327-PIP01-21-M01

Of 08/03/2022 09:18 GMT

On the adopted decision for SELPERCATINIB (MHRA-100327-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 SELPERCATINIB, Capsule, hard; Age-appropriate dosage form , Oral use .

This decision is addressed to Eli Lilly Nederland B.V, Papendorpseweg 83, Utrecht, Netherlands, 352

ANNEX I

1. Waiver

1.1 Condition:

Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms) The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 6 months of age Pharmaceutical form(s): Capsule, hard; Age-appropriate dosage form Route(s) of administration: Oral use Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible

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)

2.2 Indication(s) targeted by the PIP:

Treatment of paediatric patients with RET-altered, locally advanced or metastatic, solid tumours or primary central nervous system (CNS) tumours. Treatment of adolescents with RET-mutant medullary thyroid cancer (MTC) who require systemic therapy, have progressed following prior treatment and have no acceptable alternative treatment options.

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

The paediatric population from 6 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

Capsule, hard; Age-appropriate dosage form

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age-appropriate suspension formulation.
Non-Clinical Studies	4	Study 2 (LOXO-292-TOX-017) Dose range finding study to determine the toxicity and toxicokinetic profile of selpercatinib as a single oral dose in juvenile rats. Study 3 (LOXO-292-TOX-019) Dose range finding study to evaluate the toxicity and toxicokinetic profile of selpercatinib in juvenile rats and to determine the dose levels to be evaluated in a definitive juvenile toxicity study. Study 4 (LOXO-292-TOX-022) Dose range finding study to evaluate the toxicity and toxicokinetic profile of selpercatinib in juvenile rats and to determine the dose levels to be evaluated in a definitive juvenile toxicity study. Study 5 Definitive study to evaluate the toxicity and toxicokinetic profile of selpercatinib in juvenile rats.
Clinical Studies	2	Study 6 (LOXO-RET-17001) Open-label, single arm, two phase trial to evaluate the maximum tolerated dose (MTD)/ recommended phase 2 dose (RP2D), pharmacokinetics, safety and activity of selpercatinib in adolescents from 12 years to less than 18 years of age (and adults) with relapsed/refractory solid tumours,

		including RET fusion-positive solid, medullary thyroid cancer, and other tumours with RET activation. Study 7 (LOXO-RET-18036) Open-label, single arm, two phase trial to evaluate dose-limiting toxicities, the maximum tolerated dose (MTD), pharmacokinetics, safety and activity of selpercatinib in children from 6 months to less than 18 years of age (and adults) with an activating RET alteration relapsed/ refractory solid or primary CNS tumour.
Extrapolation, Modeling & Simulation Studies	2	Study 8 (LOXO-292-DMPK-050) Use of Population-based-pharmacokinetic (PK)/ pharmacodynamic (PD) model to simulate PK in paediatric subjects, to be used as a basis for extrapolation and choice of paediatric posology in adolescents aged 12 years to less than 18 years with RET-mutant medullary thyroid cancer (MTC) who require systemic therapy, have progressed following prior treatment and have no acceptable alternative treatment options. Study 9 Use of Population-based/ pharmacokinetic (PK)- pharmacodynamic (PD) model to simulate PK in paediatric subjects, to be used as a basis for extrapolation and choice of paediatric posology in children aged 6 months to less than 18 years with RET-altered, locally advanced or metastatic, solid tumours or primary central nervous system (CNS) tumours.
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:	30/06/2023
Deferral of one or more studies contained in the paediatric investigation plan:	Yes