EMA/593887/2019

European Medicines Agency decision

P/0369/2019

of 8 November 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for selpercatinib (EMEA-002544-PIP01-18) 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 Eli Lilly and Company Limited on 25 February 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 18 October 2019, 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 selpercatinib, capsule, hard, age-appropriate dosage form, 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 selpercatinib, capsule, hard, age-appropriate dosage form, 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 selpercatinib, capsule, hard, age-appropriate dosage form, 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 is addressed to Eli Lilly and Company Limited, Erl Wood Manor, Sunninghill Road, GU20 6PH Windlesham, United Kingdom.

EMA/PDCO/410630/2019
Amsterdam, 18 October 2019

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

EMEA-002544-PIP01-18

Scope of the application

Active substance(s):

Selpercatinib

Condition(s):

Treatment of all conditions included in the category 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 and Company Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Eli Lilly and Company Limited submitted for agreement to the European Medicines Agency on 25 February 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 1 April 2019.

Supplementary information was provided by the applicant on 15 July 2019. The applicant proposed modifications to the paediatric investigation plan and to the deferral.

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)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   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 annex 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).

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- capsule, hard, age-appropriate dosage form, oral use;
- 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:

Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms).

2.1.1. Indication(s) targeted by the PIP

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.

Treatment of paediatric patients with *RET*-altered, locally advanced or metastatic, solid tumours or primary central nervous system (CNS) tumours.

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 6 months to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Capsule, hard

Age-appropriate dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	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 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, modelling and 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 age 12 to less than 18 years of age 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 age 6 months to less than 18 years of age 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 PIP

Concerns on potential long-term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By June 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes