EMA/531413/2021 corr

European Medicines Agency decision

P/0398/2021

of 30 September 2021

on the acceptance of a modification of an agreed paediatric investigation plan for selpercatinib (Retsevmo), (EMEA-002544-PIP01-18-M01) 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 European Medicines Agency's decision P/0369/2019 issued on 8 November 2019,

Having regard to the application submitted by Eli Lilly and Company on 2 July 2021 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 10 September 2021, 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for selpercatinib (Retsevmo), capsule, hard, age-appropriate dosage form, 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 is addressed to Eli Lilly and Company, 8 Arlington Square West, Downshire Way, RG12 1PU – Bracknell, United Kingdom.

EMA/PDCO/403830/2021 corr
Amsterdam, 10 September 2021

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

EMEA-002544-PIP01-18-M01

Scope of the application

Active substance(s):

Selpercatinib

Invented name:

Retsevmo

Condition(s):

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

Authorised indication(s):

See Annex II

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

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Eli Lilly and Company submitted to the European Medicines Agency on 2 July 2021 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/0369/2019 issued on 8 November 2019.

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

The procedure started on 17 August 2021.

Scope of the modification

Some timelines 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 Norwegian Paediatric Committee member 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 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).

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

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

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

Authorised indications:

- As monotherapy for the treatment of adults with:
  - advanced RET fusion-positive non-small cell lung cancer (NSCLC) who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy;
  - advanced RET fusion-positive thyroid cancer who require systemic therapy following prior treatment with sorafenib and/or lenvatinib;
- As monotherapy for the treatment of adults and adolescents 12 years and older with advanced RET-mutant medullary thyroid cancer (MTC) who require systemic therapy following prior treatment with cabozantinib and/or vandetanib.

Authorised pharmaceutical form(s):

Capsule, hard

Authorised route(s) of administration:

Oral use