EMA/146941/2023

European Medicines Agency decision

P/0133/2023

of 13 April 2023

on the acceptance of a modification of an agreed paediatric investigation plan for selpercatinib (Retsevmo), (EMEA-002544-PIP01-18-M02) 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 Union procedures for the authorisation and supervision of medicinal products for human 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 and the decision P/0398/2021 issued on 30 September 2021,

Having regard to the application submitted by Eli Lilly and Company on 18 November 2022 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 24 February 2023, 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 and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for selpercatinib (Retsevmo), capsule, hard, tablet, oral use, including changes to the deferral, 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/925143/2022
Amsterdam, 24 February 2023

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

EMEA-002544-PIP01-18-M02

Scope of the application

Active substance(s):

Selpercatinib

Invented name and authorisation status:

See Annex II

Condition(s):

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

Pharmaceutical form(s):

Capsule, hard

Tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Eli Lilly and Company

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 18 November 2022 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 and the decision P/0398/2021 issued on 30 September 2021.

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

The procedure started on 3 January 2023.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. A pharmaceutical form was amended. The waiver ground has been amended.

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 and to the deferral and to the waiver in the scope set out in the Annex I of this opinion.

   The Paediatric Committee member of Norway 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(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 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, tablet, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

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

Tablet

2.1.4. Measures

Area	**Description**
Quality-related studies	**Study 1** Development of age-appropriate tablets

Non-clinical studies	**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	**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	**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	Not applicable
Other measures	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 December 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

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 indication(s):

- As monotherapy for the treatment of adults with:

  advanced RET fusion-positive non-small cell lung cancer (NSCLC) not previously treated with a RET inhibitor;

  advanced RET fusion-positive thyroid cancer who require systemic therapy following prior treatment with sorafenib and/or lenvatinib;

  - Invented name(s): Retsevmo
  - Authorised pharmaceutical form(s): Capsule, hard
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure
- As monotherapy for the treatment of adults and adolescents 12 years and older with advanced RET-mutant medullary thyroid cancer (MTC)
  - Invented name(s): Retsevmo
  - Authorised pharmaceutical form(s): Capsule, hard
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure