

EMA/382606/2017

European Medicines Agency decision

P/0179/2017

of 3 July 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral for larotrectinib (EMEA-001971-PIP02-16) 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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on the agreement of a paediatric investigation plan and on the granting of a deferral for larotrectinib (EMA-001971-PIP02-16) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 726/2004¹,

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 Agency²,

Having regard to the application submitted by Loxo Oncology, Inc. on 14 October 2016 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 19 May 2017, in accordance with Article 18 of Regulation (EC) No 1901/2006 and of its own motion in accordance with Article 21 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.
- (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.

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 larotrectinib, capsule, hard, oral solution, oral use, gastric 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 larotrectinib, capsule, hard, oral solution, oral use, gastric 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

This decision is addressed to Loxo Oncology, Inc., 400 Oyster Point Blvd, Suite 520, 94080 - South San Francisco, CA, United States.



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/183049/2017

London, 19 May 2017

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

EMA-001971-PIP02-16

Scope of the application

Active substance(s):

Larotrectinib

Condition(s):

Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms)

Pharmaceutical form(s):

Capsule, hard

Oral solution

Age-appropriate solid dosage form

Route(s) of administration:

Oral use

Gastric use

Name / corporate name of the PIP applicant:

Loxo Oncology, Inc.



Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Loxo Oncology, Inc. submitted for agreement to the European Medicines Agency on 14 October 2016 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 29 November 2016.

Supplementary information was provided by the applicant on 27 February 2017. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a waiver.

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 18 of said Regulation;
- to grant a deferral on its own motion in accordance with Article 21 of said Regulation.

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 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

Not applicable.

2. Paediatric investigation plan

2.1. Condition:

Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms).

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from birth to less than 18 years of age with advanced solid tumours harbouring an NTRK fusion.

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

From birth to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Capsule, hard

Oral solution

Age-appropriate solid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	Study 1 Development of an age-appropriate solid dosage form Study 2 Assessment of the administration of the age-appropriate solid dosage form via nasal gastric tube
Non-clinical studies	2	Study 3 Dose range finding toxicity study in juvenile Sprague Dawley rats Study 4 Juvenile toxicity study in Sprague Dawley rats
Clinical studies	1	Study 5 Open-label trial to evaluate the pharmacokinetic and safety of larotrectinib in paediatric patients with advanced solid or primary

		central nervous system tumours from birth to less than 18 years of age (and young adults of less than 22 years of age) (part 1-dose escalation) and to evaluate the anti-cancer activity of larotrectinib in an expansion cohort of paediatric patients from birth to less than 18 years of age (and young adults of less than 22 years of age) with tumours harbouring NTRK fusions (part 2) (LOXO-TRK-15003)
Extrapolation, modelling and simulation studies	1	Study 6 Modelling and simulation study to evaluate the use and support dosing regimen of larotrectinib in paediatric patients from birth to less than 18 years of age with tumours harbouring an NTRK fusion (LOXO-101-DMPK-052).
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 December 2019
Deferral for one or more measures contained in the paediatric investigation plan:	Yes