EMA/418758/2021

European Medicines Agency decision

P/0351/2021

of 8 September 2021

on the acceptance of a modification of an agreed paediatric investigation plan for entrectinib (Rozlytrek), (EMEA-002096-PIP01-16-M03) 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/0270/2018 issued on 16 August 2018, the decision P/0010/2019 issued on 4 January 2019 and the decision P/0092/2020 issued on 18 March 2020,

Having regard to the application submitted by Roche Registration GmbH on 15 April 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 23 July 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 entrectinib (Rozlytrek), capsule, hard, coated granules, oral use, gastric 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 Roche Registration GmbH, Emil-Barell-Strasse 1, 79639 - Grenzach-Wyhlen, Germany.

EMA/PDCO/253028/2021
Amsterdam, 23 July 2021

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

EMEA-002096-PIP01-16-M03

Scope of the application

Active substance(s):

Entrectinib

Invented name:

Rozlytrek

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

Coated granules

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

Roche Registration GmbH

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Roche Registration GmbH submitted to the European Medicines Agency on 15 April 2021 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0270/2018 issued on 16 August 2018, the decision P/0010/2019 issued on 4 January 2019, and the decision P/0092/2020 issued on 18 March 2020.

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

The procedure started on 25 May 2021.

Scope of the modification

Some measures 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 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

Not applicable

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 NTRK fusion-positive locally advanced or metastatic solid tumours in paediatric patients from birth to less than 18 years of age who have either progressed following prior therapies or who have no acceptable standard therapies.

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

Coated granules

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of an age-appropriate solid dosage form (coated granules) suitable for children unable to swallow the already available capsules. **Study 6** (added in procedure EMEA-002096-PIP01-16-M02) Assessment of the administration of the content of the hard capsules and of the coated granules via naso-gastric and gastric tube.
Non-clinical studies	2	**Study 2** Dose range-finding juvenile toxicity study **Study 3** Definitive juvenile toxicity study

Clinical studies	1	**Study 4** Open-label trial to evaluate the pharmacokinetic, safety and anti-tumour activity of entrectinib in paediatric patients with relapsed or refractory extracranial solid tumours from 2 to less than 18 years of age (dose escalation part) and to evaluate the anti-cancer activity of entrectinib in an expansion cohort of paediatric patients from birth to less than 18 years of age with solid tumours harbouring NTRK1/2/3 fusions who have either progressed following prior therapies or who have no acceptable standard therapy (expansion part) ((STARTRK-NG (NCT02650401)).
Extrapolation, modelling and simulation studies	1	**Study 5** Modelling and simulation and partial extrapolation study to evaluate the use and support dosing regimen of entrectinib in paediatric patients from birth to less than 18 years of age with solid tumours harbouring NTRK1/2/3 fusions.
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 2022
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 indication(s):

- Rozlytrek as monotherapy is indicated for the treatment of adult and paediatric patients 12 years of age and older with solid tumours expressing a neurotrophic tyrosine receptor kinase (NTRK) gene fusion;
  - who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity; and
  - who have not received a prior NTRK inhibitor;
  - who have no satisfactory treatment option;
- Rozlytrek as monotherapy is indicated for the treatment of adult patients with ROS1-positive, advanced non-small cell lung cancer (NSCLC) not previously treated with ROS1 inhibitors.

Authorised pharmaceutical form(s):

Capsule, hard

Authorised route(s) of administration:

Oral use