

EMA/536538/2018

European Medicines Agency decision

P/0270/2018

of 16 August 2018

on the agreement of a paediatric investigation plan and on the granting of a deferral for entrectinib (EMEA-002096-PIP01-16) 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 entrectinib (EMA-002096-PIP01-16) 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 Roche Registration GmbH on 20 March 2017 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 27 July 2018, in accordance with Article 17 of Regulation (EC) No 1901/2006 and 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 entrectinib, capsule, hard, age-appropriate solid 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 entrectinib, capsule, hard, age-appropriate solid 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

This decision is addressed to Roche Registration GmbH, Emil-Barell-Strasse 1, 79639 - Grenzach-Wyhlen, Germany.

EMA/PDCO/299229/2018

London, 27 July 2018

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

EMA-002096-PIP01-16

Scope of the application

Active substance(s):

Entrectinib

Condition(s):

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

Pharmaceutical form(s):

Capsule, hard

Age-appropriate solid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Roche Registration GmbH

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Roche Registration GmbH submitted for agreement to the European Medicines Agency on 20 March 2017 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 25 April 2017.

Supplementary information was provided by the applicant on 7 May 2018. 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 17(1) of said Regulation;
- to grant a deferral 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, 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 extracranial solid tumours harbouring NTRK1/2/3 ALK gene fusions

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

Age-appropriate solid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	Study 1 Development of an age-appropriate solid dosage form (e.g. mini-tablets, granules or pellets) suitable for children unable to swallow the already available capsules.
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 extracranial 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 extracranial 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