

EMA/474725/2019

## European Medicines Agency decision

P/0318/2019

of 11 September 2019

on the acceptance of a modification of an agreed paediatric investigation plan for larotrectinib (EMA-001971-PIP02-16-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<sup>1</sup>,

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<sup>2</sup>,

Having regard to the European Medicines Agency's decision P/0179/2017 issued on 3 July 2017 and the decision P/0182/2018 issued on 15 June 2018,

Having regard to the application submitted by Bayer AG on 23 April 2019 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 26 July 2019, 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.

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<sup>1</sup> OJ L 378, 27.12.2006, p.1.

<sup>2</sup> OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

**Article 1**

Changes to the agreed paediatric investigation plan for larotrectinib, capsule, hard, oral solution, oral use, gastric 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 Bayer AG, Kaiser-Wilhelm-Allee 1, 51373 – Leverkusen, Germany.

EMA/PDCO/257703/2019  
Amsterdam, 26 July 2019

## Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA-001971-PIP02-16-M02

### 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

#### Route(s) of administration:

Oral use

Gastric use

#### Name/corporate name of the PIP applicant:

Bayer AG

### Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bayer AG submitted to the European Medicines Agency on 23 April 2019 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0179/2017 issued on 3 July 2017, and the decision P/0182/2018 issued on 15 June 2018.

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

The procedure started on 28 May 2019.

## Scope of the modification

Some measures and 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 and to the deferral 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 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

#### 2.1.4. Measures

| Area                    | Number of measures | Description                                                                                                                                                                                               |
|-------------------------|--------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Quality-related studies | 2                  | <b>Study 1</b><br>Development of an oral solution (not containing ORA-SWEET)<br><b>Study 2</b><br>Assessment of the administration of the oral solution (not containing ORA-SWEET) via nasal gastric tube |
| Non-clinical studies    | 2                  | <b>Study 3</b><br>Dose range finding toxicity study in juvenile Sprague Dawley rats<br><b>Study 4</b><br>Juvenile toxicity study in Sprague Dawley rats                                                   |

|                                                 |   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-------------------------------------------------|---|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Clinical studies                                | 1 | <b>Study 5</b><br><br>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 | <b>Study 6</b><br><br>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 April 2021 |
| Deferral for one or more measures contained in the paediatric investigation plan:     | Yes           |