

**MHRA**  
10 South Colonnade  
Canary Wharf  
London  
E14 4PU  
United Kingdom

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## **Decision Cover Letter**

### **Decision of the licensing authority to:**

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-100024-PIP01-21-M02

### **Scope of the Application**

#### **Active Substance(s)**

LAROTRECTINIB

#### **Condition(s)**

Malignant neoplasms (except CNS 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 plc

#### **Basis for the Decision**

Pursuant to the Human Medicines Regulations 2012, Bayer plc submitted to the licensing authority on 29/09/2021 00:41 BST an application for a Modification

The procedure started on 18/01/2022 14:11 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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## Final Decision Letter

MHRA-100024-PIP01-21-M02

Of 09/02/2022 20:15 GMT

On the adopted decision for LAROTRECTINIB (MHRA-100024-PIP01-21-M02) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for LAROTRECTINIB, Capsule, hard, Oral solution , Oral use, Gastric use .

This decision is addressed to Bayer plc, 400, South Oak Way, Reading, United Kingdom, RG2 6AD

## ANNEX I

### 1. Waiver

#### 1.1 Condition:

Not applicable

### 2. Paediatric Investigation Plan:

#### 2.1 Condition(s):

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

#### 2.2 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

### 2.3 Subset(s) of the paediatric population concerned by the paediatric development:

All subsets of the paediatric population from birth to less than 18 years of age

### 2.4 Pharmaceutical Form(s):

Capsule, hard; Oral solution

### 2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	Study 1 Development of an oral solution (not containing ORA-SWEET) Study 2 Assessment of the administration of the oral solution (not containing ORA-SWEET) via a nasogastric tube
Non-Clinical Studies	2	Study 3 Dose range finding juvenile toxicity study in Sprague Dawley Rats Study 4 Juvenile toxicity study in Sprague Dawley Rats
Clinical Studies	1	Study 5 Open-label trial to evaluate the pharmacokinetics 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, Modeling & 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 NTK fusion (LOXO-101-DMPK-052).

<b>Other Studies</b>	0	Not applicable
<b>Other Measures</b>	0	Not applicable

### 3. Follow-up, completion and deferral of a PIP:

<b>Concerns on potential long term safety and efficacy issues in relation to paediatric use:</b>	Yes
<b>Date of completion of the paediatric investigation plan:</b>	31/10/2022
<b>Deferral of one or more studies contained in the paediatric investigation plan:</b>	Yes