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 changes to the agreed paediatric investigation plan and to the deferral

MHRA-100025-PIP01-21-M01

Scope of the Application

Active Substance(s)

LAROTRECTINIB

Condition(s)

Treatment of malignant neoplasms of the central nervous system

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 02/03/2021 10:53 GMT an application for a Modification

The procedure started on 17/08/2021 15:08 BST

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 changes 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-100025-PIP01-21-M01

Of 17/09/2021 07:53 BST

On the adopted decision for LAROTRECTINIB (MHRA-100025-PIP01-21-M01) 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 , Reading, United Kingdom, RG2 6AD

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of malignant neoplasms of the central nervous system

2.2 Indication(s) targeted by the PIP:

Treatment of paediatric patients from birth to less than 18 years of age with a primary CNS tumour 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):

Oral solution; Capsule, hard

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	Study 1 Development of an oral solution (not containing ORA-SWEET). (same study as Study 1 agreed in MHRA-100024-PIP01-21-M01) Study 2 Assessment of the administration of the oral solution (not containing ORA-SWEET) via a nasogastric tube. (same study as Study 2 agreed in MHRA-100024-PIP01-21-M01)
Non-Clinical Studies	0	Not applicable
Clinical Studies	1	Study 3 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) (same study as Study 5 agreed in MHRA-100024-PIP01-21-M01)
Extrapolation, Modeling & Simulation Studies	1	Study 4 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) (same study as Study 6 agreed in MHRA-100024-PIP01-21-M01)
Other Studies	0	Not applicable
Other Measures	0	Not applicable

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

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	31/08/2023
Deferral of one or more studies contained in the paediatric investigation plan:	Yes