EMA/630040/2022

European Medicines Agency decision

P/0289/2022

of 11 August 2022

on the acceptance of a modification of an agreed paediatric investigation plan for larotrectinib (Vitrakvi), (EMEA-001971-PIP03-18-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[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0401/2019 issued on 4 December 2019 and the decision P/0077/2021 issued on 17 March 2021,

Having regard to the application submitted by Bayer AG on 18 March 2022 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 24 June 2022, 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.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for larotrectinib (Vitrakvi), 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 covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0179/2017 issued on 3 July 2017, including subsequent modifications thereof.

Article 3

This decision is addressed to Bayer AG, 1 Kaiser-Wilhelm-Allee, 51373 – Leverkusen, Germany.

EMA/PDCO/193103/2022
Amsterdam, 24 June 2022

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

EMEA-001971-PIP03-18-M02

Scope of the application

Active substance(s):

Larotrectinib

Invented name:

Vitrakvi

Condition(s):

Treatment of malignant neoplasms of the central nervous system

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Capsule, hard

Oral solution

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

Bayer AG

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bayer AG submitted to the European Medicines Agency on 18 March 2022 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0401/2019 issued on 4 December 2019 and the decision P/0077/2021 issued on 17 March 2021.

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

The procedure started on 25 April 2022.

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 Paediatric Committee member of Norway 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 malignant neoplasms of the central nervous system

2.1.1. 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

2.1.2. 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	Description
Quality-related studies	**Study 1** Development of an oral solution (not containing ORA-SWEET) (same study as Study 1 in EMEA-001971-PIP02-16 and modifications thereof) **Study 2** Assessment of the administration of the oral solution (not containing ORA-SWEET) via nasal gastric tube (same study as Study 2 agreed in EMEA-001971-PIP02-16 and modifications thereof)
Non-clinical studies	Not applicable
Clinical studies	**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 EMEA-001971-PIP02-16 and modifications thereof))

Extrapolation, modelling and simulation studies	**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 EMEA-001971-PIP02-16 and modifications thereof)
Other studies	Not applicable
Other measures	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 August 2024
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 malignant neoplasms of the central nervous system

Authorised indication(s):

- Vitrakvi as monotherapy is indicated for the treatment of adult and paediatric patients with solid tumours that display 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 no satisfactory treatment options.

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

Authorised indication(s):

- Vitrakvi as monotherapy is indicated for the treatment of adult and paediatric patients with solid tumours that display 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 no satisfactory treatment options.

Authorised pharmaceutical form(s):

Capsule, hard

Oral solution

Authorised route(s) of administration:

Oral use