EMA/607430/2019

European Medicines Agency decision

P/0401/2019

of 4 December 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral for larotrectinib (VITRAKVI), (EMEA-001971-PIP03-18) 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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Bayer AG on 29 October 2018 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 18 October 2019, 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 larotrectinib (VITRAKVI), capsule, hard, oral solution, oral use, nasogastric 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 larotrectinib (VITRAKVI), capsule, hard, oral solution, oral use, nasogastric 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 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 4

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

EMA/PDCO/470/2019 Corr
Amsterdam, 18 October 2019

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

EMEA-001971-PIP03-18

Scope of the application

Active substance(s):

Larotrectinib

Invented name:

VITRAKVI

Condition(s):

Treatment of malignant neoplasms of the central nervous system

Pharmaceutical form(s):

Capsule, hard

Oral solution

Route(s) of administration:

Oral use

Nasogastric 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 16(1) of Regulation (EC) No 1901/2006 as amended, Bayer AG submitted for agreement to the European Medicines Agency on 29 October 2018 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 4 December 2018.

Supplementary information was provided by the applicant on 15 July 2019. The applicant proposed modifications to the paediatric investigation plan.

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 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	Number of measures	Description
Quality-related studies	2	**Study 1** Development of an oral solution (not containing ORA-SWEET) (same study as Study 1 in EMEA-001971-PIP02-16-M02) **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-M02)
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 EMEA-001971-PIP02-16-M02)
Extrapolation, modelling and 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 EMEA-001971-PIP02-16-M02)
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

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of malignant neoplasms of the central nervous system
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):

Hard capsule

Oral solution

Authorised route(s) of administration:

Oral use