

Clinical Policy: Larotrectinib (Vitrakvi)

Reference Number: CP.PHAR.414

Effective Date: 01.15.18

Last Review Date: 02.19

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Larotrectinib (Vitrakvi[®]) is a first-generation selective tropomyosin receptor kinase (TRK) tyrosine kinase inhibitor (TKI).

FDA Approved Indication(s)

Vitrakvi is indicated for the treatment of adult and pediatric patients with solid tumors that:

- Have a neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion without a known acquired resistance mutation,
- Are metastatic or where surgical resection is likely to result in severe morbidity, and
- Have no satisfactory alternative treatments or that have progressed following treatment

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Vitrakvi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria**A. NTRK Fusion-Positive Cancer** (must meet all):

1. Diagnosis of a solid tumor with both characteristics (a and b):
 - a. Tumor is positive for NTRK-gene fusion;
 - b. Disease is metastatic or surgical resection is likely to result in severe morbidity;
2. Disease has progressed following initial treatment or medical justification supports that there are no appropriate alternative treatments;
3. Documentation of no known acquired tropomyosin receptor kinase resistance mutation;
4. Prescribed by or in consultation with an oncologist;
5. Request meets one of the following (a or b):
 - a. Dose does not exceed 200 mg/day;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:

Medicaid/HIM – 6 months
Commercial – Length of Benefit

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. NTRK-Fusion Positive Cancer (must meet all):

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Vitrakvi for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
 - a. New dose does not exceed 200 mg/day;
 - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:

Medicaid/HIM – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
NTRK: neurotrophic receptor tyrosine kinase

TKI: tyrosine kinase inhibitor
TRK: tropomyosin receptor kinase

Appendix B: Therapeutic Alternatives

Vitakvi should be used following progression after initial therapy that is standard of care for the specific solid tumor type based on NCCN guidelines, unless there are no such alternative therapies available.

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- There exists a higher incidence (60 to 100%) of NTRK-fusion mutation in certain rare solid tumor types (e.g., secretory breast cancer, secretory salivary gland, infantile fibrosarcoma, mesoblastic nephroma), while there exists a much lower (about 1%) incidence of NTRK-fusion mutations in more common tumor types (e.g., colorectal cancer, lung cancer, melanoma).
- Currently, there are no FDA-approved tests available yet for the detection of NTRK gene fusion, but Loxo Oncology is partnering with Ventana Medical Systems to develop a pan-TRK fusion IHC test as a companion diagnostic for Vitakvi.
- Acceptable laboratory diagnostic tests for NTRK-mutation status include:
 - Fluorescent in situ hybridization (FISH)
 - Next generation sequencing (NGS)
 - Immunohistochemistry assay (IHC)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NTRK fusion-positive solid tumors	<ul style="list-style-type: none"> • Adult and pediatric patients with body surface area $\geq 1.0 \text{ m}^2$: 100 mg PO BID until disease progression or until unacceptable toxicity • Pediatric patients with body surface area $< 1.0 \text{ m}^2$: 100 mg/m² PO BID until disease progression or until unacceptable toxicity 	200 mg/day

VI. Product Availability

- Capsules: 25 mg, 100 mg
- Oral solution (100 mL bottle): 20 mg/mL

VII. References

1. Vitakvi Prescribing Information. Stamford, CT: Loxo Oncology, Inc.; November 2018. Available at: www.vitakvi.com. Accessed December 13, 2018.
2. Drilon A, Laetsch TW, Kummar S, et al. Efficacy of larotrectinib in TRK fusion-positive cancers in adults and children. *N Eng J Med* 2018;378:731-9. DOI:10.1056/NEJMoa1714448.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.15.18	02.19
No significant changes; finalized line of business to apply to HIM.	04.22.19	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.

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