Clinical Policy: Larotrectinib (Vitrakvi)

Reference Number: ERX.SPA.319
Effective Date: 03.01.19
Last Review Date: 02.21
Line of Business: Commercial, 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

Select patients for therapy based on an FDA-approved test. 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 *(see Appendix D for examples)*:
2. Prescribed by or in consultation with an oncologist;
3. For Vitrakvi request, medical justification supports inability to use larotrectinib, if available (e.g., contraindications to excipients);
4. Tumor is positive for an NTRK-gene fusion (e.g., ETV6-NTRK3, TPM3-NTRK1);
5. Confirmation of no known acquired tropomyosin receptor kinase resistance mutation;
6. Disease is recurrent, advanced, metastatic, unresectable, or resectable with adverse functional outcomes;
7. Member has not received prior NTRK targeted therapy (e.g., Rozlytrek®);
8. Request meets one of the following (a, b, or c):*
   a. Adults and pediatric members with body surface area ≥ 1 m^2: Dose does not exceed 200 mg per day;
   b. Pediatric members with body surface area < 1 m^2: Dose does not exceed 200 mg/m^2 per day;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Commercial – Length of Benefit

Medicaid – 6 months

B. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. NTRK Fusion-Positive Cancer (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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. For Vitrakvi request, medical justification supports inability to use larotrectinib, if available (e.g., contraindications to excipients);
4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. Adults and pediatric members with body surface area ≥ 1 m^2: New dose does not exceed 200 mg per day;
   b. Pediatric members with body surface area < 1 m^2: New dose does not exceed 200 mg/m^2 per day;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents;

B. Known acquired tropomyosin receptor kinase resistance mutation.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
NTRK: neurotrophic receptor tyrosine kinase
TKI: tyrosine kinase inhibitor
TRK: tropomyosin receptor kinase

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: Examples of Solid Tumors
(Examples are drawn from the Vitrakvi pivotal trials, as described in the FDA prescribing information, as well as the National Comprehensive Center Network (NCCN) Vitrakvi compendium.)
- Breast cancer

- Cancer of the appendix
- Cervical cancer
- Cholangiocarcinoma
- Colorectal cancer
- Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
- Lung cancer
- Melanoma
- Pancreatic cancer
- Salivary gland tumor
- Small bowel adenocarcinoma
- Soft tissue sarcoma (e.g., extremity/body wall, head/neck, retroperitoneal/intraabdominal, solitary fibrous tumor, infantile fibrosarcoma, gastrointestinal stromal tumor)
- Thyroid carcinoma (papillary, Hurthle cell, anaplastic, or follicular histology)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NTRK fusion-positive solid tumors	• Adult and pediatric patients with body surface area ≥ 1 m^2: 100 mg PO BID until disease progression or until unacceptable toxicity • Pediatric patients with body surface area < 1 m^2: 100 mg/m^2 PO BID until disease progression or until unacceptable toxicity	BSA ≥ 1 m^2: 200 mg/day BSA < 1 m^2: 200 mg/ m^2/day

VI. Product Availability

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

VII. References

1. Vitrakvi Prescribing Information. Stamford, CT: Loxo Oncology, Inc.; March 2021. Available at: www.vitrakvi.com. Accessed April 8, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 6, 2019.
3. Drilon A, Laetsch TW, Kummar S, et al. Efficay 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	01.15.19	02.19
1Q 2020 annual review: criteria adjusted to accommodate NCCN recommended uses; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	11.19.19	02.20
1Q 2021 annual review: oral oncology generic redirection language added; tumor subtype and subsequent therapy restrictions removed per NCCN; kinase resistance mutation confirmation added/if known, exclusion added (Section III); references reviewed and updated.	11.14.20	02.21
RT4: updated FDA indication to include additional language for use of a FDA-approved test.	04.08.21	

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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