RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title: **Larotrectinib (Vitrakvi)**
Policy Number: **RxA. 555**
Drug(s) Applied: **Larotrectinib (Vitravki®)**
Last Review Date: **01/2020**
Line of Business: **Commercial, HIM, Medicaid**

Background

Larotrectinib (Vitravki®) is a first-generation selective tropomyosin receptor kinase (TRK) tyrosine kinase inhibitor (TKI). It 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.

Indication	Dosing Regimen	Maximum Dose
NTRK fusion-positive solid tumors	• Adult and pediatric patients with body surface area ≥ 1.0 m^2: 100 mg PO BID until disease progression or until unacceptable toxicity • Pediatric patients with body surface area < 1.0 m^2: 100 mg/m^2 PO BID until disease progression or until unacceptable toxicity	200 mg/day

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

Clinical Policy

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

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):

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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

II. Continued Therapy

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

1. Currently receiving medication via RxAdvance 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

III. Appendices

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
Vitrakvi 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 panTRK fusion IHC test as a companion diagnostic for Vitrakvi.
- Acceptable laboratory diagnostic tests for NTRK-mutation status include:
  - Fluorescent in situ hybridization (FISH) o Next generation sequencing (NGS)
  - Immunohistochemistry assay (IHC)

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References

1. Vitrakvi Prescribing Information. Stamford, CT: Loxo Oncology, Inc.; November 2018. Available at: www.vitrakvi.com. Accessed December 13, 2018.
2. 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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established	01/2020	03/06/2020

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