Clinical Policy: Larotrectinib (Vitrakvi)

Reference Number: PA.CP.PHAR.414
Effective Date: 4.17.19
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Revision Log

Description
Larotrectinib (Vitravki®) 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 PA Health & Wellness® 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: 6 months

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): PA.CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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: 12 months

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   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): PA.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 policy – PA.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

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 pan-TRK fusion IHC test as a companion diagnostic for Vitrakvi.
- 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	• 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

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.; 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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