PHARMACY COVERAGE GUIDELINE

VITRAKVI® (larotrectinib) oral capsule & solution
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Vitrakvi (Larotrectinib) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual is 28 days of age or older

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Solid tumors that:
        i. Have a neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion without a known acquired resistance mutation
        ii. Are metastatic or where surgical resection is likely to result in severe morbidity

iii. Have no satisfactory alternative treatments or that have progressed following treatment

b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. *NTRK* gene fusion is **without** a known acquired resistance mutation such as, G595R, G623R, G696A, or F617L

5. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. Neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion test
   b. Liver function tests (alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and bilirubin)
   c. Negative pregnancy test in a woman of childbearing potential
   d. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-2

6. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Vitrakvi (larotrectinib) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual's condition has responded while on therapy with response defined as the following:
   a. Documented evidence of efficacy, disease stability and/or improvement
   b. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
   a. Severe neurotoxicity such as dizziness, cognitive impairment, mood disorders, sleep disturbances, delirium
   b. Severe hepatotoxicity
   c. Any adverse effect that has not resolved within 4 weeks of with-holding Vitrakvi

d. Individual who is unable to tolerate Vitrakvi after 3 dose modifications

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Vitrakvi (larotrectinib) 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.

Vitrakvi (larotrectinib) is an inhibitor of the tropomyosin receptor kinases (TRK), TRKA, TRKB, and TRKC. TRKA, B, and C are encoded by the genes *NTRK1, NTRK2,* and *NTRK3.* Chromosomal rearrangements involving fusions of these genes with other genes can result in constitutively-activated chimeric TRK fusion proteins that act as an oncogenic driver, promoting cell proliferation and survival in tumor cell lines.

NTRK fusions are rare but occur in sites where no other treatments are available for cancers that frequently express this mutation, like mammary analogue secretory carcinoma, cellular or mixed congenital mesoblastic nephroma and infantile fibrosarcoma.

Larotrectinib has minimal activity in cell lines with point mutations in the TRKA kinase domain, including the clinically identified acquired resistance mutation, G595R. Point mutations in the TRKC kinase domain with clinically identified acquired resistance to larotrectinib include G623R, G696A, and F617L.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Resources:

Vitrakvi (larotrectinib) cap & oral solution product information, revised by Bayer HealthCare Pharmaceuticals, Inc. 11/2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 09, 2024.

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Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.

ORIGINAL EFFECTIVE DATE: 02/21/2019 | ARCHIVE DATE: | LAST REVIEW DATE: 02/20/2025 | LAST CRITERIA REVISION DATE: 02/15/2024