



An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 2/21/2019
LAST REVIEW DATE: 2/17/2022
LAST CRITERIA REVISION DATE: 2/17/2022
ARCHIVE DATE:

VITRAKVI® (larotrectinib) oral capsule & solution

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the [request form](#) in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**



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Criteria:

- **Criteria for initial therapy:** Vitrakvi (larotrectinib) is considered *medically necessary* and will be approved when **ALL** of 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. 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. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
 - a. Neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion test
 - b. Negative pregnancy test in a woman of childbearing potential
 - c. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-2
 6. There are no significant interacting drugs

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Vitrakvi (larotrectinib) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:
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
 - a. Response is defined as:
 - i. Documented evidence of efficacy, disease stability and/or improvement
 - ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use



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3. Individual has been adherent with the medication
4. Individual has not developed any significant adverse drug effects that may exclude continued use
 - a. Significant adverse effect such as:
 - i. Severe neurotoxicity such as encephalopathy, severe gait disturbances, or delirium
 - ii. Severe hepatotoxicity
 - iii. Any adverse effect that has not resolved within 4 weeks of with-holding Vitrakvi
 - iv. Individual who is unable to tolerate Vitrakvi after 3 dose modifications
5. There are no significant interacting drugs

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.



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Resources:

Vitakvi (larotrectinib) product information, revised by Bayer HealthCare Pharmaceuticals, Inc. 08-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed December 11, 2021.

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.