Effective Date: 01/2019
Last P&T Approval/Version: 01/26/2022
Next Review Due By: 01/2023
Policy Number: C16017-A

Vitrakvi (larotrectinib)

PRODUCTS AFFECTED

Vitrakvi (larotrectinib)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This 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 Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
solid tumors that: have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. SOLID TUMOR WITH NEUROTROPHIC RECEPTOR TYROSINE KINASE (NTRK) GENE FUSION:
1. Documentation of diagnostically confirmed solid tumors that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation – Lab result confirming a positive test for NTRK gene fusion using RT-PCR, FISH, or NGS testing methodology must be submitted (reviewed through MCP-051)

AND

2. Documentation of presences of metastatic disease or where surgical resection is likely to result in severe morbidity
AND
3. Documentation of member's prior therapies with start and stop dates and that there are no satisfactory alternative treatments, or the member has progressed following treatment.
AND
4. Documentation of radiographically measurable disease
AND
5. Documentation member has fully recovered from toxic effects of prior chemotherapy

CONTINUATION OF THERAPY:

A. SOLID TUMOR WITH NEUROTROPHIC RECEPTOR TYROSINE KINASE (NTRK) GENE FUSION

1. Documentation within chart notes of member's clinical benefit since starting Vitrakvi (larotrectinib) therapy
AND
2. Current chart notes detailing response and adherence to therapy
AND
3. Documentation that member is not having intolerable or unacceptable toxicity

DURATION OF APPROVAL:

Initial authorization: 3 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with an oncologist. [If prescribed in consultation, consultation notes must be submitted within initial request and reauthorization requests]

AGE RESTRICTIONS:

No requirement

QUANTITY:

Maximum quantities of 60/30 for 100mg capsules, 90/30 for 25 mg capsules, 300ml/30 days for the20mg/ml solution.
A split fill program will apply to new starts receiving Vitrakvi capsules. An override to bypass the split- fill program will be provided for existing users that have been maintained on Vitrakvi capsules

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral

DRUG CLASS:

FDA-APPROVED USES:

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

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Solid Tumors with TRK Gene Fusion
TRK fusion cancer occurs when a neurotrophic tyrosine receptor kinase (NTRK) gene fuses with another unrelated gene, producing an altered tropomyosin receptor kinase (TRK) protein.
The altered protein, or TRK fusion protein, is constantly active, triggering a permanent signal cascade. These proteins become the primary driver of the spread and growth of tumors in patients with TRK fusion cancer. TRK fusion cancer is not limited to certain types of cells or tissues and can occur in any part of the body. NTRK gene fusions occur in various adult and pediatric solid tumors with varying prevalence, including appendiceal cancer, breast cancer, cholangiocarcinoma, colorectal cancer, GIST, infantile fibrosarcoma, lung cancer, mammary analogue secretory carcinoma of the salivary gland, melanoma, pancreatic cancer, thyroid cancer, and various sarcomas. It may affect greater than 60% of both adult and pediatric patients with certain rare tumor types, such as secretory breast, secretory salivary gland and infantile fibrosarcoma, while only affecting 1% of colorectal cancer patients.

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Lab Testing
Oncogenic fusions involving TRK proteins have been implicated in various cancer types, prompting clinical development of therapies targeting the aberrations across histologies rather than their body site of origin. This “tumor-agnostic” development approach includes research into fluorescence is situ hybridization (FISH) testing, reverse transcriptase polymerase chain reaction testing (RT-PCR),next-generation sequencing (NGS), and immunohistochemistry (IHC) assays for the detection of TRK fusions.
FISH testing has been a commonly used method of detecting gene fusions but has limited potential when searching for TRK fusions. This is because FISH testing looks for 2 genes that should be next to each other

but are not; however, with TRK fusions there are 3 genes to look for on 3 chromosomes. Therefore, a lab would have to run 3 separate tests. Additionally, FISH is a relatively subjective testing method that requires interpretation and an experienced pathologist to produce an accurate result.

NGS testing could offer a comprehensive approach for identifying any actionable gene amplifications, mutations, or fusion, including TRK fusion, in a definitive readout. NGS will also test for many other genes in the tumor sample at the same time and may identify a different therapeutic option. Since NGS can be done in a multiplexed fashion, you can do sequencing for EGFR, ALK, ROS1, TRK fusions, and many others all at once. Many of the panels that are used either commercially or by individual institutions will include many genes for gene sequencing, as well as being able to detect fusions involving a variety of fusion proteins. Historical disadvantages with NG Shave included the cost of the test and a lack of regulation and standardization.

IHC also represents a potential option to test for TRK fusions with a staining method. IHC testing has the advantage of being a less expensive test that is reimbursed by most insurance companies, and any laboratory has the capability of conducting the test. The disadvantage in using IHC testing is that laboratories can only run one test at a time. Although currently there is not a preferred diagnostic test to be used to identify NTRK gene fusion mutation, some oncologists suggest using a multiplexed NGS-based sequencing platform is the best way to detect these fusions because you can test for different alterations in a single assay.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Vitrakvi (larotrectinib) that are not an FDA-approved indication or not included in this policy are considered experimental/investigational or not a covered benefit of this policy. This subject to change based on research and medical literature, or at the discretion of Molina Healthcare.

OTHER SPECIAL CONSIDERATIONS:

Dosing Information

Adult and Pediatric Patients with Body Surface Area of at Least 1.0 Meter-Squared: 100 mg orally twice daily

Pediatric Patients with Body Surface Area of Less Than 1.0 Meter-Squared: 100 mg/m2 orally twice daily

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:

Vitrakvi CAPS 25MG, Vitrakvi CAPS 100MG, Vitrakvi SOLN 20MG/ML

REFERENCES

1. VITRAKVI(R) oral capsules, oral solution, larotrectinib oral capsules, oral solution.LoxoOncology Inc (per FDA), Stamford, CT March 2021
2. Gatalica, Z., Xiu, J., Swensen, J., & Vranic, S. (2018). Molecular characterization of cancers with NTRK gene fusions. Modern Pathology, 32(1), 147-153. doi:10.1038/s41379-018-0118-3
3. Expanded Access to Provide Larotrectinib (LOXO-101) for the Treatment of Cancers With a NTRK Gene Fusion - Full Text View - ClinicalTrials.gov. (2019). Retrieved from https://clinicaltrials.gov/ct2/show/NCT03025360