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Section:	Prescription Drugs	**Effective Date:**	October 1, 2023
Subsection:	Antineoplastic Agents	**Original Policy Date:**	December 7, 2018
Subject:	Vitrakvi	**Page:**	1 of 5

Last Review Date: September 8, 2023

Vitrakvi

Description

Vitrakvi (larotrectinib)

Background

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 in-frame fusions of these genes with various partners can result in constitutively-activated chimeric TRK fusion proteins that can act as an oncogenic driver, promoting cell proliferation and survival in tumor cell lines. Vitrakvi demonstrates anti-tumor activity in cells with constitutive activation of TRK proteins resulting from gene fusions, deletion of a protein regulatory domain, or in cells with TRK protein overexpression. Vitrakvi had 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 Vitrakvi include G623R, G696A, and F617L (1).

Regulatory Status

FDA-approved indications: Vitrakvi is a kinase inhibitor indicated for the treatment of adult and pediatric patients with solid tumors that: (1)

1. Have a neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion without a known acquired resistance mutation,
2. Are metastatic or where surgical resection is likely to result in severe morbidity, and
3. Have no satisfactory alternative treatments or that have progressed following treatment.

Patients for treatment with Vitrakvi should be selected based on the presence of a *NTRK* gene fusion in tumor specimens based on an FDA-approved test (1).

Neurotoxicity may occur in patients taking Vitrakvi. Patients and caretakers should be advised of the risk of neurologic adverse reactions. Patients should be advised not to drive or operate hazardous machinery if experiencing neurotoxicity (1).

Hepatotoxicity may also occur in patients on Vitrakvi therapy. Liver tests should be monitored including ALT and AST every 2 weeks during the first month of treatment, then monthly thereafter and as clinically indicated (1).

Vitrakvi may cause fetal harm. Females of reproductive potential should be advised of the potential risk to the fetus and to use effective contraception during treatment and for 1 week after the final dose of Vitrakvi (1).

Patients on Vitrakvi should avoid coadministration with strong CYP3A4 inhibitors, inducers, or with sensitive CYP3A4 substrates (1).

The safety and effectiveness of Vitrakvi in pediatric patients have been established (1).

Related policies
Rozlytrek

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Vitrakvi may be considered **medically necessary** if the conditions indicated below are met.

Vitrakvi may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have the following:

Solid tumors with neurotrophic receptor kinase (*NTRK*) gene fusion

AND ALL of the following:

1. Presence of *NTRK* gene fusion has been detected by an FDA-approved test
2. Solid tumors are metastatic **OR** surgical resection is likely to result in severe morbidity
3. There are no satisfactory alternative treatments **OR** disease has progressed following treatment
4. **NONE** of the following acquired resistance point mutations:
    a. G595R
    b. G623R
    c. G696A
    d. F617L
5. Prescriber agrees to monitor AST and ALT
6. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Vitrakvi and for 1 week after the final dose

Prior – Approval *Renewal* Requirements

Diagnosis

Patient must have the following:

Solid tumors with neurotrophic receptor kinase (*NTRK*) gene fusion

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to monitor AST and ALT
3. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Vitrakvi and for 1 week after the final dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Strength	Quantity Limit
25 mg capsule	540 capsules per 90 days **OR**
100 mg capsule	180 capsules per 90 days **OR**
20 mg/mL oral solution (100mL bottles)	9 bottles per 90 days

***Not to exceed 200 mg per day**

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Vitrakvi (larotrectinib) is a kinase inhibitor indicated for the treatment of adult and pediatric patients with solid tumors with neurotrophic receptor kinase (*NTRK*) gene fusion. Viktravi label cites warnings for neurotoxicity, hepatotoxicity, and embryo-fetal toxicity. Patients on Vitrakvi should avoid coadministration with strong CYP3A4 inhibitors, inducers, or with sensitive CYP3A4 substrates. The safety and effectiveness of Vitrakvi in pediatric patients have been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Vitrakvi while maintaining optimal therapeutic outcomes.

References

1. Vitrakvi [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; December 2022.
2. NCCN Drugs & Biologics Compendium® Vitrakvi 2023. National Comprehensive Cancer Network, Inc. May 2021. Accessed on July 25, 2023.

Policy History

Date	Action
December 2018	Addition to PA
March 2019	Annual review

December 2019	Annual review and reference update
June 2020	Annual review
April 2021	Addition of requirement for *NTRK* gene fusion presence to be detected by an FDA-approved test. Revised contraception requirement
June 2021	Annual editorial review and reference update
December 2022	Annual review and reference update
September 2023	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 8, 2023 and is effective on October 1, 2023.