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 \textit{NTRK1}, \textit{NTRK2}, and \textit{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 indication: 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 (\textit{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.
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).

<table>
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<th>Related policies</th>
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<td>Rozlytrek</td>
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**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** in patients with solid tumors with neurotrophic receptor kinase (NTRK) gene fusion and if the conditions indicated below are met.

Vitrakvi is 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. Solid tumors are metastatic **OR** surgical resection is likely to result in severe
morbidity
2. There are no satisfactory alternative treatments OR disease has progressed following treatment
3. **NONE** of the following acquired resistance point mutations:
   a. G595R
   b. G623R
   c. G696A
   d. F617L
4. Prescriber agrees to monitor AST and ALT
5. Prescriber agrees to advise patients of reproductive potential to use effective contraception during therapy 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. Prescriber agrees to advise patients of reproductive potential to use effective contraception during therapy and for 1 week after the final dose

**Policy Guidelines**

**Pre - PA Allowance**

None

**Prior - Approval Limits**

**Quantity**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Quantity Limit per 90 days</th>
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<tbody>
<tr>
<td>25 mg capsule</td>
<td>540 capsules per 90 days <strong>OR</strong></td>
</tr>
<tr>
<td>100 mg capsule</td>
<td>180 capsules per 90 days <strong>OR</strong></td>
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**Rationale**

**Summary**
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. 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**
This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective on January 1, 2020.