BlueCross BlueShield Federal Employee Program

VITRAKVI (larotrectinib)

RATIONALE FOR INCLUSION IN PA PROGRAM

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).

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.; November 2023.
2. NCCN Drugs & Biologics Compendium® Vitrakvi 2024. National Comprehensive Cancer Network, Inc. May 2021. Accessed on July 22, 2024.