BlueCross BlueShield
Federal Employee Program

ROZLYTREK
(entrectinib)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Rozlytrek (entrectinib) is an inhibitor of the tropomyosin receptor kinases (TRK) TRKA, TRKB, and TRKC, proto-oncogene tyrosine-protein kinsase ROS1, and anaplastic lymphoma kinase (ALK) with IC_{50} values of 0.1 to 2 nM. TRKA, B, and C are encoded by the genes *NTRK1*, *NTRK2*, and *NTRK3,* respectively. Rozlytrek also inhibits JAK2 and TNK2 with IC_{50} values > 5nM. Fusion proteins that include TRK, ROS1, or ALK kinase domains can drive tumorigenic potential through hyperactivation of downstream signaling pathways leading to unconstrained cell proliferation (1).

Regulatory Status

FDA-approved indications: Rozlytrek is a kinase inhibitor indicated for the treatment of:
(1)

1. Adult patients with *ROS1*-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.
2. Adult and pediatric patients older than 1 month of age with solid tumors that:
    a. Have a neurotrophic tyrosine receptor kinase (*NTRK*) gene fusion as detected by an FDA-approved test without a known acquired resistance mutation,
    b. Are metastatic or where surgical resection is likely to result in severe morbidity, and
    c. Have progressed following treatment or have no satisfactory alternative therapy.

Hepatotoxicity may occur in patients on Rozlytrek 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).

Monitoring should occur in patients who have or who are at risk for QTc interval prolongation, including assessing QT interval and electrolytes at baseline and periodically during treatment. For those patients with symptoms of known risk factors for congestive heart failure, assessment of left ventricular ejection fraction should be completed prior to initiation of Rozlytrek (1).

Females of reproductive potential should be advised to avoid becoming pregnant while being treated, as Rozlytrek may cause fetal harm. Females of reproductive potential should be advised to use effective contraception during treatment with Rozlytrek and for 5 weeks after the final dose.

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Males with a female partner of reproductive potential should be advised to use effective contraception during treatment with Rozlytrek and for 3 months after the final dose (1).

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

The safety and effectiveness of Rozlytrek in pediatric patients less than 1 month of age with solid tumors who have an NTRK gene fusion have not been established. The safety and effectiveness of Rozlytrek in pediatric patients less than 18 years of age with ROS1-positive NSCLC have not been established (1).

Summary

Rozlytrek (entrectinib) is an inhibitor of the tropomyosin receptor kinases (TRK) TRKA, TRKB, and TRKC, proto-oncogene tyrosine-protein kinsase ROS1, and anaplastic lymphoma kinase (ALK) with IC_{50} values of 0.1 to 2 nM. TRKA, B, and C are encoded by the genes *NTRK1*, *NTRK2*, and *NTRK3,* respectively. Rozlytrek also inhibits JAK2 and TNK2 with IC_{50} values > 5nM. Fusion proteins that include TRK, ROS1, or ALK kinase domains can drive tumorigenic potential through hyperactivation of downstream signaling pathways leading to unconstrained cell proliferation. The safety and effectiveness of Rozlytrek in pediatric patients less than 1 month of age with solid tumors who have an NTRK gene fusion have not been established. The safety and effectiveness of Rozlytrek in pediatric patients less than 18 years of age with ROS1-positive NSCLC have not been established (1).

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

References

1. Rozlytrek [package insert]. South San Francisco, CA: Genentech USA, Inc.; January 2024.
2. NCCN Drugs & Biologics Compendium® Entrectinib 2024. National Comprehensive Cancer Network, Inc. Accessed on July 19, 2024.