BlueCross BlueShield
Federal Employee Program

RETEVMO
(selpercatinib)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Retevmo (selpercatinib) is a kinase inhibitor. It inhibits wild-type RET and multiple mutated RET isoforms as well as VEGFR1 and VEGFR3. Certain point mutations in *RET* or chromosomal rearrangements involving in-frame fusions of *RET* with various partners can result in constitutively activated chimeric RET fusion proteins that can act as oncogenic drivers by promoting cell proliferation of tumor cell lines. Retevmo demonstrates anti-tumor activity in cells harboring constitutive activation of RET protein resulting from gene fusions and mutations as well as in tumors that are *RET* fusion positive (1).

Regulatory Status

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

- Adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a *rearranged during transfection (RET)* gene fusion, as detected by an FDA-approved test
- Adult and pediatric patients 2 years of age and older with advanced or metastatic medullary thyroid cancer (MTC) with a *RET* mutation, as detected by an FDA-approved test, who require systemic therapy
- Adult and pediatric patients 2 years of age and older with advanced or metastatic thyroid cancer with a *RET* gene fusion, as detected by an FDA-approved test, who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)
- Adult and pediatric patients 2 years of age and older with locally advanced or metastatic solid tumors with a *RET* gene fusion, as detected by an FDA-approved test, that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options

Patients should be selected for treatment with Retevmo based on the presence of a *RET* gene fusion (NSCLC, thyroid cancer, or other solid tumors) or specific *RET* gene mutation (MTC) in tumor specimens (1).

Retevmo has warnings regarding hepatotoxicity and hypertension. AST and ALT should be

monitored prior to initiating Retevmo, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Retevmo should not be initiated in patients with uncontrolled hypertension and blood pressure should be optimized prior to initiation. Blood pressure should be monitored after 1 week, at least monthly thereafter and as clinically indicated (1).

Severe, life-threatening, and fatal interstitial lung disease (ILD)/pneumonitis can occur in patients treated with Retevmo. Patients should be monitored for ILD/pneumonitis. Those who develop symptoms should have their treatment withheld, dose reduced, or discontinued depending upon the severity (1).

Thyroid function should be assessed before starting treatment, and periodically while on Retevmo. The medication can cause hypothyroidism. The dose may be withheld until clinically stable or permanently discontinued, depending upon severity (1).

Retevmo can cause concentration-dependent QT interval prolongation. QT interval, electrolytes, and TSH should be assessed at baseline and periodically during treatment. Hypokalemia, hypomagnesemia, and hypocalcemia should be corrected prior to initiating Retevmo and during treatment (1).

Retevmo can cause fetal harm when administered to a pregnant woman. Females of reproductive potential should be advised to use effective contraception during treatment with Retevmo and for at least 1 week after the final dose. Males with female partners of reproductive potential should be advised to use effective contraception during treatment with Retevmo and for 1 week after the final dose (1).

The safety and effectiveness of Retevmo in pediatric patients less than 2 years of age with thyroid cancer or solid tumors have not been established. The safety and effectiveness of Retevmo in pediatric patients less than 18 years of age with NSCLC have not been established (1).

Summary

Retevmo (selpercatinib) is a kinase inhibitor. It inhibits wild-type RET and multiple mutated RET isoforms as well as VEGFR1 and VEGFR3. Certain point mutations in *RET* or chromosomal

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rearrangements involving in-frame fusions of *RET* with various partners can result in constitutively activated chimeric RET fusion proteins that can act as oncogenic drivers by promoting cell proliferation of tumor cell lines. Retevmo demonstrates anti-tumor activity in cells harboring constitutive activation of RET protein resulting from gene fusions and mutations as well as in tumors that are *RET* fusion positive (1).

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

References

1. Retevmo [package insert]. Indianapolis, IN: Eli Lilly and Company; December 2024.
2. NCCN Drugs & Biologics Compendium® Selpercatinib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 14, 2025.