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Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	June 5, 2020
Subject:	Retevmo	**Page:**	1 of 6

Last Review Date: March 7, 2025

Retevmo

Description

Retevmo (selpercatinib)

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).

Related policies
Gavreto

Policy

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

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

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

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Locally advanced or metastatic non-small cell lung cancer (NSCLC)
    a. 18 years of age or older
    b. *RET* fusion-positive, as detected by an FDA-approved test
2. Advanced or metastatic medullary thyroid cancer (MTC)
    a. 2 years of age or older
    b. *RET*-positive mutation, as detected by an FDA-approved test
    c. Patient requires systemic therapy
3. Advanced or metastatic thyroid cancer
    a. 2 years of age or older
    b. *RET* fusion-positive, as detected by an FDA-approved test
    c. Patient requires systemic therapy
    d. Radioactive iodine-refractory (if radioactive iodine is appropriate)
4. Locally advanced or metastatic solid tumors
    a. 2 years of age or older
    b. *RET* fusion-positive, as detected by an FDA-approved test

c. Disease has progressed on or following prior systemic treatment **OR** patient has no satisfactory alternative treatment options

AND ALL of the following:

1. Prescriber agrees to monitor AST, ALT, and blood pressure
2. Prescriber agrees to monitor for QT interval prolongation
3. Any pre-existing hypocalcemia, hypokalemia, or hypomagnesemia will be corrected prior to starting Retevmo therapy
4. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Retevmo and for 1 week after the last dose
5. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Retevmo and for 1 week after the last dose

Prior – Approval *Renewal* Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Locally advanced or metastatic non-small cell lung cancer (NSCLC)
   a. 18 years of age or older
2. Advanced or metastatic medullary thyroid cancer (MTC)
   a. 2 years of age or older
3. Advanced or metastatic thyroid cancer
   a. 2 years of age or older
4. Locally advanced or metastatic solid tumors
   a. 2 years of age or older

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to monitor AST, ALT, and blood pressure
3. Prescriber agrees to monitor for QT interval prolongation
4. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Retevmo and for 1 week after the last dose

5. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Retevmo and for 1 week after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 320 mg per day

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

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 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.

Policy History

Date	Action
June 2020	Addition to PA
September 2020	Annual review
December 2020	Annual review
September 2021	Annual review and reference update
March 2022	Annual review and reference update
October 2022	Per PI update, added indication of advanced or metastatic solid tumors. Also added requirement for the RET mutation or fusion to be confirmed by an FDA-approved test for all indications except for solid tumors. Also, added additional safety information to regulatory section regarding ILD and hypothyroidism
December 2022	Annual review and reference update
September 2023	Annual review and reference update
March 2024	Annual review and reference update
April 2024	Revised quantity limit
June 2024	Annual review and reference update
July 2024	Per PI update, reduced age to 2 and older for MTC, advanced or metastatic thyroid cancer, and advanced or metastatic solid tumors. Also added that solid tumors that are RET fusion-positive must be detected by an FDA-approved test
September 2024	Annual review and reference update
December 2024	Annual review and reference update
March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.