selpercatinib (Retevmo™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO192

Description

Selpercatinib (Retevmo) is an orally administered kinase inhibitor of RET.

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
selpercatinib (Retevmo)	RET Fusion-Positive Non-Small Cell Lung Cancer (NSCLC) RET-Mutant Medullary Thyroid Cancer (MTC) RET Fusion-Positive Thyroid Cancer, who require systemic therapy and radioactive iodine refractory RET Fusion-Positive Solid Tumors, locally advanced or metastatic	40 mg capsules	90 capsules/30 days
		80 mg capsules	60 capsules/30 days
		40 mg tablets	90 tablets/30 days
		80 mg tablets	60 tablets/30 days
		120 mg tablets	60 tablets/30 days
		160 mg tablets	60 tablets/30 days

Initial Evaluation

I. **Selpercatinib (Retevmo)** may be considered medically necessary when the following criteria are met:
   A. Medication is prescribed by, or in consultation with, an oncologist or hematologist; **AND**
   B. Member has not previously progressed on a selective RET kinase inhibitor (e.g., pralsetinib (Gavreto)); **AND**
   C. Medication will be used as monotherapy (i.e., not in combination with other oncologic agents); **AND**
   D. Presence of a RET- fusion as detected by an FDA-approved test; **AND**
   E. A diagnosis of one of the following:
      1. **Locally advanced or metastatic non-small cell lung cancer (NSCLC); OR**
      2. **Recurrent, advanced, or metastatic thyroid cancer; AND**
         i. Member has locally recurrent, advanced, or metastatic thyroid carcinoma; **AND**
            a. Treatment with radioactive iodine (RAI) therapy has been ineffective, contraindicated, or not tolerated; **OR**

3. **Recurrent, or metastatic medullary thyroid carcinoma**; **AND**
    i. Member had disease progression after surgical resection; **OR**
        a. Provider attests that the tumor is unresectable; **OR**
4. **Locally advanced or metastatic solid tumors; AND**
    i. Documented diagnosis of RET-fusion positive solid tumor (e.g., pancreatic adenocarcinoma, colorectal, salivary, breast, soft tissue, cholangiocarcinoma or rectal neuroendocrine tumor etc.); **AND**
    ii. Member has had a disease progression on, or after, prior systemic therapy (e.g., platinum-based chemotherapy, paclitaxel, immunotherapy, radiation); **OR**
        a. Provider attests that the member has no satisfactory alternative treatment options.

II. Selpercatinib (Retevmo) is considered investigational when used for all other conditions, including but not limited to:
    A. Selpercatinib (Retevmo) used in combination with another oncology therapy
    B. Selpercatinib (Retevmo) used for the treatment of tumors not harboring RET-fusions or mutations

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms (e.g., tumor response or disease stability)

Supporting Evidence

I. Rearranged during transfection (RET), a transmembrane receptor protein, is present at the surface of several tissue types. Alterations include fusions and point mutations – both are oncogenic drivers. Selpercatinib (Retevmo) is the first FDA-approved therapy that targets RET gene fusion alterations specifically.
II. Selpercatinib (Retevmo) is a kinase inhibitor of RET. It is FDA-approved for adults with metastatic RET fusion-positive non-small-cell lung cancer (NSCLC), advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy in patients aged two years and older, advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate) in patients aged 2 years and older, and locally advanced or metastatic solid tumors with a RET gene fusion that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options in patients two years of age and older.

III. Selpercatinib (Retevmo) was evaluated in clinical trials as monotherapy and has not been sufficiently studied in combination with other oncology therapy in any disease setting. There are currently no active or completed clinical trials to evaluate selpercatinib (Retevmo) used in combination with other oncology agents, therefore use is limited to monotherapy only.

IV. Selpercatinib (Retevmo) was evaluated in clinical trials in the first-line setting, and following progression on systemic chemotherapy, surgical resection, and/or radioactive iodine (RAI) therapy. There are currently no active or completed clinical trials to evaluate the safety and efficacy of selpercatinib (Retevmo) following progression on another selective RET kinase inhibitor (e.g., pralsetinib (Gavreto)). The benefit of selpercatinib (Retevmo) after progression on another RET kinase inhibitor is unknown, and guidelines do not make recommendations to use another RET kinase inhibitor after progression on one.

V. The National Comprehensive Cancer Network (NCCN) guidelines version 07.2026 for NSCLC have been updated to recommend pralsetinib (Gavreto) (category 2A) or selpercatinib (Retevmo) (category 1A) as first line therapy if the *RET* gene was discovered prior to initiation of first-line therapy. If the *RET* gene was discovered during first-line systemic therapy, guidelines recommend to interrupt current systemic therapy and start pralsetinib (Gavreto) or selpercatinib (Retevmo) (category 2A).

VI. NCCN guidelines version 02.2026 for thyroid carcinoma recommend surgical resection as first-line therapy for medullary thyroid carcinoma (MTC) (Category 1). Systemic treatment may be warranted for high volume, symptomatic or progressive MTC if the patient progresses on, or is not a candidate for surgery. Guidelines have been updated to prefer selpercatinib (Retevmo) (Category 1A) if the *RET* gene is identified following progression on surgical resection, or in the setting of in unresectable disease.

VII. NCCN guidelines 02.2026 for Thyroid carcinoma recommend radioactive iodine (RAI) is recommended as first-line therapy for differentiated thyroid cancer (Category 1A). Systemic treatment may be warranted if the patient progresses on RAI. Guidelines have been updated to prefer selpercatinib (Retevmo) or pralsetinib (Gavreto) (Category 2A) if the RET gene is identified.

VIII. **Clinical Trial in the setting of NSCLC, MTC, and Thyroid Cancer:**
Selpercatinib (Retevmo) was evaluated in a Phase 1/2, interventional, open-label, single-arm (LIBRETTO-001) trial in patients with advanced RET-altered malignancies, including RET fusion-positive non-small cell lung cancer (NSCLC), RET-mutant medullary thyroid cancer (mTC), and RET fusion-positive thyroid cancer. Patients received selpercatinib (Retevmo) until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR), with key secondary endpoints including duration of response (DoR), progression-free survival (PFS), and overall survival (OS).

- RET fusion-positive NSCLC: Patients were advanced or metastatic, progressed on platinum-based chemotherapy or were systemic treatment naïve. Over half (58%) of pretreated patients also received anti-PD1/PD-L1 therapy.
- RET-mutant MTC: 98% had metastatic disease, and patients were previously treated with cabozantinib (Cometriq) and/or vandetanib (Caprelsa) or were treatment naïve to both. Ten patients were previously treated with platinum chemotherapy or anti-PD1/PD-L1 therapy.

- RET fusion-positive TC: Patients were not amenable to RAI therapy and may have been treated with lenvatinib (Lenvima) and/or sorafenib (Nexavar), or were naïve to both.

Clinical Efficacy in Pretreated Patients*			
Outcome	**RET Fusion+ NSCLC (n=247)**	**RET-Mutant MTC (n=152)**	**RET Fusion-Positive TC (n=41)**
ORR (n)	62 (55-68%)	118 (77.6%)	35 (85.4%)
CR (n)	20 (8.1%)	19 (12.5%)	5 (12.2%)
PR (n)	132 (53.4%)	99 (65.1%)	30 (73.2%)
PFS (months)	26.2 (19.3-35.7)	41.4% (30.2-NR)	27.4 (14.5-NR)
OS (months)	47.6	64.3 (48.3-NR)	NR
Clinical Efficacy in Treatment-Naïve Patients*			
Outcome	**RET Fusion+ NSCLC (n=69)**	**RET-Mutant MTC (n=143)**	**RET Fusion-Positive TC (n=24)**
ORR (n)	83 (72-91%)	118 (82.5%)	23 (95.8%)
CR (n)	5 (7.2%)	34 (23.8%)	5 (20.8%)
PR (n)	52 (75.4%)	84 (58.7%)	18 (75.0%)
PFS (months)	22 (16.5-24.9)	NR (53.1-NR)	NR (44.2-NR)
OS, (months)	NR	NR	NR
**Data available as of Sept. 2026*			

  - As of February 2025, long term efficacy results have been posted from LIBRETTO-001. The update extends the data cut-off for up to three-years, however LIBRETTO-001 is still ongoing and is estimated to be completed in 2027. Results from up to three years of follow-up are similar to initial efficacy data.
  - Selpercatinib (Retevmo) is being studied in an ongoing, pivotal Phase 3, interventional, randomized, open-label trial (LIBRETTO-431). The OS has not yet been reached in either cohort. Based on results from LIBRETTO-431, the FDA allowed for traditional approval of selpercatinib (Retevmo) for treatment of locally advanced or metastatic NSCLC with a RET gene fusion, as detected by an approved test, in adults. Salpercatinib (Retevmo) met its primary endpoint 31 months, with PFS of 24.8 months CI 95% (16.9-NE) vs 11.2 months 95% CI (8.77-16.76) for pemetrexed and platinum with pembrolizumab.
  - Although NCCN guidelines does not specify stage of disease for treatment, only that confirmation of the RET-fusion gene is confirmed before treatment, selpercatinib (Retevmo) is also being evaluated in early-stage RET fusion-positive NSCLC in a Phase 3, randomized, double-blind, placebo-controlled study (LIBRETTO-432). The primary endpoint was event-free survival which was met at 92% with selpercatinib (Retevmo) and 61% with placebo 95% CI (0.06-0.51) P<0.001. OS has not yet been reached, and the study is estimated to be completed in 2028. Despite reaching the primary endpoint, The FDA has not approved selperactinib (Retevmo) in early stage RET fusion-positive NSCLC and use of selperactinib (Retevmo) should be limited to advanced/metastatic disease.

IX. **Clinical Trial in the setting solid tumors with RET-fusion:**

- Selpercatinib (Retevmo) was initially FDA-approved under the accelerated approval pathway for the treatment of locally advanced or metastatic solid tumors with a RET gene fusion, based on phase 1/ 2 single-arm, open-label clinical trial (basket trial, LIBRETTO-001). As of July 2026, the FDA granted traditional approval of selpercatinib (Retevmo) this indication in adult and pediatric patients two years of age and older that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options based on the matured efficacy data from the ongoing LIBRETTO-001 study. LIBRETTO-001 recruited additional participants, totaling 75 patients with *RET* fusion-positive tumors other than NSCLC and thyroid cancer with disease progression on or following prior systemic treatment or who had no satisfactory alternative treatment options. The primary efficacy endpoint, ORR was 47% (95% CI: 35, 59), with a median DOR of 24.5 months (95% CI: 11.2, 49.1). These results are similar to the initial efficacy results.
- The FDA references LIBRETTO-121 (see below) for supportive pediatric evidence, combined with adult and pediatric efficacy data from LIBRETTO-001 for granting selpercatinib (Retevmo) traditional FDA-approval.
    i. Selpercatinib (Retevmo) was administered to a tumor agnostic cohort of 41 patients with solid tumors harboring RET fusions, which consisted of following tumor types: pancreatic cancer (12), colon (10), salivary gland (4), sarcoma (3), unknown primary (3), breast (2), skin carcinoma (2), cholangiocarcinoma (2), xanthogranuloma (2), and carcinoid, ovarian, pulmonary sarcoma, rectal neuroendocrine, and small intestinal tumors (1 patient each). Majority of these patients were pre-treated and progressed after one to two lines of systemic therapies.
        1. Solid tumors may include the following, but not limited to: appendiceal neoplasms and cancers, breast cancer, cervical cancer, colorectal cancer, including anal adenocarcinoma, epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, esophageal and esophagogastric junction cancers, gastric cancer, intrahepatic and extrahepatic cholangiocarcinoma, salivary gland tumors, small bowel adenocarcinoma, vaginal cancer
- The efficacy of salpercatinib (Retevmo) is being further studied in a multicenter, open-label, multi-cohort trial (LIBRETTO-121) in pediatric patients from six months to 12 years of age with locally advanced refractory *RET* fusion-positive solid tumors who are unresponsive to available therapies or have no standard systemic curative therapy available. Results from LIBRETTO-121 has not been published, and the study is estimated to be completed in 2029.

X. In the setting of advanced solid tumors, NCCN guidelines recommend treatment according to the specific cancer histology and stage. Standard of care typically consists of surgery, radiation, systemic chemotherapy and immunotherapy (e.g., platinum-based chemotherapy, taxanes, fluoropyrimidines, immune checkpoint inhibitors), and/or tumor-specific targeted therapy, as

clinically appropriate. RETEVMO may be considered following progression on prior therapy or when no satisfactory alternative treatment options exist.

XI. Per the package insert, for patients who cannot swallow whole capsules or tablets, selpercatinib (Retevmo) 40 mg tablets may be used to create a dispersion and/or be administer orally or via gastrostomy or nasogastric tube. Quantity limit exceptions may be allowed on a case-by-case basis if medical necessity is met for use.

Investigational or Not Medically Necessary Uses

I. Selpercatinib (Retevmo) has not been sufficiently studied for safety and efficacy when used in combination with other oncology therapies, and for tumors not harboring RET fusions or mutations.

References

1. Retevmo [Prescribing Information]. Eli Lilly and Company. Indianapolis, IN. July 2026.
2. Adeniran AJ, Ahu Z, Gandhi M, et al. Correlation between genetic alterations and microscopic features, clinical manifestations, and prognostic characteristics of thyroid papillary carcinomas. Am J Surg Pathol. 2006. 30(2): 216-222.
3. Drilon A, Hu ZI, Lai GGY, Tan DSW. Targeting RET-driven cancers: lessons from evolving preclinical and clinical landscapes. Nat Rev Clin Oncol. 2018a Mar;15(3):151-67.
4. Guerra A, Sapio MR, Marotta V, Campanile E, Moretti MI, Deandrea M, et al. Prevalence of RET/PTC rearrangement in benign and malignant thyroid nodules and its clinical application. Endocr J. 2011;58(1):31-8.
5. Prasad ML, Vyas M, Horne MJ, Virk RK, Morotti R, Liu Z, et al. NTRK fusion oncogenes in pediatric papillary thyroid carcinoma in northeast United States. Cancer. 2016;122(7):1097-107.
6. Roy M, Chen H, Sippel RS. Current understanding and management of medullary thyroid cancer. Oncologist. 2013;18(10):1093-100.
7. Tappenden P, Carroll C, Hamilton J, Kaltenthaler E, Wong R, Wadsley J, et al. Cabozantinib and vandetanib for unresectable locally advanced or metastatic medullary thyroid cancer: a systematic review and economic model. Health Technol Assess. 2019 Feb;23(8):1-144.
8. Kato S, Subbiah V, Marchlik E, Elkin SK, Carter JL, Kurzrock R. RET aberrations in diverse cancers: next-generation sequencing of 4,871 patients. Clin Cancer Res. 2017 Apr;23(8):1988-97.
9. Sireci AN, Morosini D, Rothenberg S. Efficacy of immune checkpoint inhibition in RET fusion-positive non-small cell lung cancer patients (poster). Presented at the World Lung Cancer Conference; September 7-10, 2019. Barcelona, Spain. Available at: https://wclc2019.iaslc.org/wp-content/uploads/2019/08/WCLC2019-Abstract-Book_web-friendly.pdf. Accessed February 28, 2020.
10. Subbiah V, Wolf J, Konda B, et al. Tumour-agnostic efficacy and safety of selpercatinib in patients with RET fusion-positive solid tumours other than lung or thyroid tumours (LIBRETTO-001): a phase 1/2, open-label, basket trial. Lancet Oncol. 2022 Oct;23(10):1261-1273.
11. Lori J. Wirth et al. Durability of Response With Selpercatinib in Patients With RET-Activated Thyroid Cancer: Long-Term Safety and Efficacy From LIBRETTO-001. J Clin Oncol 42, 3187-3195(2024). DOI:10.1200/JCO.23.02503
12. Gautschi O, Park K, Solomon BJ, Tomasini P, Loong HH, De Braud F, Goto K, Peterson P, Barker S, Liming K, Oxnard GR, Frimodt-Moller B, Drilon A. Selpercatinib in *RET* Fusion-Positive Non-Small Cell Lung Cancer: Final Safety and Efficacy, Including Overall Survival, From the LIBRETTO-001 Phase I/II Trial. J Clin Oncol. 2025 May 20;43(15):1758-1764. doi: 10.1200/JCO-24-02076. Epub 2025 Feb 21. PMID: 39983053; PMCID: PMC12084017.
13. Tsuboi M, Goldman JW, Wu YL, Johnson ML, Paz-Ares L, Yang JC, Besse B, Su W, Chao BH, Drilon A. LIBRETTO-432, a phase III study of adjuvant selpercatinib or placebo in stage IB-IIIA *RET* fusion-positive non-small-cell lung cancer. Future Oncol. 2022 Sep;18(28):3133-3141. doi: 10.2217/fon-2022-0656. Epub 2022 Aug 11. PMID: 35950566.

14. National Comprehensive Cancer Network. Thyroid Carcinoma V2.2026. June 2, 2026. Accessed August 24, 2026. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf
15. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Treatment Guidelines V7.2026. August 7, 2026. Accessed August 24, 2026. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

Related Policies

Currently there are no related policies.

Policy Implementation/Update:

Action and Summary of Changes	Date
Removed selpercatinib (Retevmo) from "Experimental and Investigational Medications" policy (considered investigational when used for all indications) and created new policy with pathway to coverage for selpercatinib (Retevmo) in *RET* fusion-positive non-small cell lung cancer, RET-mutant medullary thyroid cancer, RET fusion-positive thyroid cancer, and other RET fusion-positive solid tumors. Updated supporting evidence and references. Removed split fill. Updated initial authorization to 6 months.	10/2026
Previous History of Retevmo Policy Updates	
General "Experimental & Investigational Medications" policy created and included Retevmo	07/2025
Added 120mg and 360mg tablets to the QL table and updated QL to 60/30. Updated QL for 40mg to 90/30	08/2024
Added tablet variation to the QL table	04/2024
Reviewed expanded indication for Retevmo for the treatment of RET-fusion positive solid tumors; added relevant supporting evidence	03/2023
Added supporting evidence around stage IV metastatic disease and metastases.	10/2021
Policy created	08/2020