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

- N/A

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
selpercatinib (Retevmo)	40 mg capsules	RET Fusion-Positive Non-Small Cell Lung Cancer RET-Mutant Medullary Thyroid Cancer	180 capsules/30 days
	80 mg capsules	RET Fusion-Positive Thyroid Cancer, in those that are radioactive iodine refractory	120 capsules/30 days

Initial Evaluation

I. Selpercatinib (Retevmo) is considered investigational when used for all indications, including but not limited to Non-Small Cell Lung Cancer and Thyroid Cancer.

Renewal Evaluation

I. N/A

Supporting Evidence

I. 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 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) in patients age 12 years and older, and advanced or metastatic RET fusion-positive thyroid cancer who are radioactive iodine (RAI)-refractory in patients age 12 years and older.

III. RET fusion-positive NSCLC, advanced or metastatic: First-line treatment options include cabozantinib (Cometriq®) or vandetanib (Caprelsa®) (not FDA-approved for lung cancer) or combinations of platinum-based chemotherapy, anti-PD-1/PD-L1 therapy, pemetrexed, and bevacizumab. In the second-line setting, additional options include various immunotherapy and chemotherapy treatments (e.g., taxanes, gemcitabine).

IV. RET-mutant MTC, advanced or metastatic: Systemic treatment may be warranted for high volume, symptomatic or progressive MTC. General treatment options include cabozantinib (Cometriq) or vandetanib (Caprelsa).

V. RET fusion-positive thyroid cancer: In persistent/recurrent or metastatic disease, radioactive iodine (RAI) is recommended. In those not amenable to RAI, general treatment options include lenvatinib (Lenvima®) or sorafenib (Nexavar®).

VI. Selpercatinib (Retevmo) is being evaluated in one Phase 1/2, open-label, multi-cohort, single-arm trial in patients with RET abnormal, advanced solid tumors Interim results showed potential antitumor activity, based on objective response rate (ORR), in the three FDA-approved settings. Additional outcomes: progression-free survival (PFS) and overall survival (OS) at 12 months.

- RET fusion-positive NSCLC: Patients were advanced or metastatic, progressed on platinum-based chemotherapy or were systemic treatment naïve. Over half of pretreated patients also received anti-PD1/PD-L1 therapy (n=58).
- 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=105)**	**RET-Mutant MTC (n=55)**	**RET Fusion-Positive TC (n=19)**
ORR (n)	67 (64%)	38 (69%)	15 (79%)
CR (n)	2 (2%)	5 (9%)	1 (5%)
PR (n)	65 (62%)	33 (60%)	14 (74%)
PFS (months)	16.5 (13.7-NE)	NE	20 (9.4-NE)
OS, 12 months (%)	88%	87%	NR
Clinical Efficacy in Treatment-Naïve Patients			
Outcome	**RET Fusion+ NSCLC (n=39)**	**RET-Mutant MTC (n=88)**	**RET Fusion-Positive TC (n=8)**
ORR (n)	33 (85%)	64 (73%)	8 (100%)
CR (n)	0	10 (11%)	1 (12.5%)
PR (n)	33 (85%)	54 (61%)	7 (87.5%)

PFS (months)	NE	23.6 (NE-NE)	NE
OS, 12 months (%)	NR	NR	NR

VII. Selpercatinib (Retevmo) was FDA-approved under the accelerated approval pathway based on ORR. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials. This therapy is being evaluated in multiple other clinical Phase 2 and Phase 3 trials. The quality of the evidence is considered low at this time given the open-label trial design and lack of comparator arm. Given the observational data, medication efficacy remains uncertain. Additionally, the medication has an unfavorable safety profile.

VIII. As of June 2020, safety data are based on a pooled population in 702 patients, 65% were exposed for six months or greater, and 34% were exposed for over one year. Ninety-five percent of patients received 160 mg twice daily.

IX. Warnings and precautions: hepatotoxicity, hypertension, QT interval prolongation, hemorrhagic events, hypersensitivity, impaired wound healing and embryo-fetal toxicity. There are no contraindications. Serious adverse reactions occurred in 33% of patients. The most frequent was pneumonia. Fatal adverse reactions occurred in 3% of individuals due to sepsis (n=1), cardiac arrest (n=3), respiratory failure (N=3).

X. Common adverse reactions (≥25%): increase liver enzymes, laboratory abnormalities (≥25% each, glucose, leukocytes, albumin, calcium, creatinine, alkaline phosphatase, platelets, cholesterol, sodium), dry mouth, diarrhea, hypertension, fatigue, edema, rash, constipation. Permanent discontinuation due to adverse reactions occurred in 5%, dose interruptions in 42%, and dose reduction in 31% of patients.

Investigational or Not Medically Necessary Uses

I. Selpercatinib (Retevmo) has not been sufficiently studied for safety and efficacy for any condition to date.

References

1. Retevmo [Prescribing Information]. Eli Lilly and Company. Indianapolis, IN. May 2020.
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. National Comprehensive Cancer Network. Thyroid Carcinoma Clinical Practice Guidelines V1.2020. June 12, 2020. Available at: https://www.nccn.org/professionals/physician_gls/default.aspx.
11. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Treatment Guidelines V6.2020. June 15, 2020. Available at: https://www.nccn.org/professionals/physician_gls/default.aspx.

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	08/2020