

Retevmo™ (selpercatinib) (Oral)

Document Number: IC-0537

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Dates Reviewed: 06/2020, 05/2021, 05/2022, 10/2022

I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Retevmo 40 mg capsules: 2 capsules per day
- Retevmo 80 mg capsules: 4 capsules per day

B. Max Units (per dose and over time) [HCPCS Unit]:

- 320 mg per day

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); **AND**

Universal Criteria ¹

- Used as a single agent; **AND**
- Patient does not have uncontrolled hypertension; **AND**
- Patient must not have had major surgery within the preceding 14 days or have a surgical wound that has not fully healed; **AND**
- Therapy will not be used concomitantly with other RET-type targeted therapies (i.e., cabozantinib, vandetanib, pralsetinib, etc.)
- Patient will avoid concomitant therapy with all of the following:
 - Coadministration with acid-reducing agents, or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **OR**
 - Coadministration with strong or moderate CYP3A inhibitors (e.g., diltiazem, fluconazole, verapamil, itraconazole, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **OR**

- Coadministration with strong and moderate CYP3A inducers (e.g., rifampin, bosentan, efavirenz, etc.); **AND**

Non-Small Cell Lung Cancer (NSCLC) † ‡ Φ^{1-3,7}

- Patient has RET gene fusion/rearrangement positive disease as detected by an FDA-approved or CLIA compliant test❖; **AND**
- Patient has recurrent, advanced, or metastatic disease (*excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease*) or mediastinal lymph node recurrence with prior radiation therapy

Thyroid Cancer † ‡ Φ^{1,2,4,6}

- Patient has RET-fusion positive Follicular, Hürthle Cell, or Papillary carcinoma as detected by an FDA-approved or CLIA compliant test❖; **AND**
 - Patient is at least 12 years of age; **AND**
 - Patient has metastatic, advanced, or unresectable locoregional recurrent or persistent disease; **AND**
 - Patient is radioactive iodine (RAI) therapy refractory or is not amenable to RAI therapy; **OR**
- Patient has RET-mutation positive medullary thyroid cancer (MTC) as detected by an FDA-approved or CLIA compliant test❖; **AND**
 - Patient is at least 12 years of age; **AND**
 - Patient has symptomatic or progressive unresectable locoregional disease ‡; **OR**
 - Patient has advanced or metastatic disease †; **OR**
- Patient has RET-fusion positive Anaplastic carcinoma as detected by an FDA-approved or CLIA compliant test❖‡; **AND**
 - Used as neoadjuvant therapy for borderline resectable locoregional disease; **OR**
 - Used as first- or second-line therapy for metastatic disease

RET Fusion-Positive Solid Tumors †¹

- Patient has locally advanced or metastatic RET-fusion positive solid tumors other than NSCLC and thyroid cancer; **AND**
 - Disease has progressed on or following prior systemic therapy; **OR**
 - Patient has no satisfactory alternative treatment options; **AND**
- Patient has, but is not limited to*, one of the following tumor types:
 - Pancreatic Adenocarcinoma
 - Colorectal
 - Salivary
 - Unknown primary
 - Breast

- Soft tissue sarcoma
- Bronchial carcinoid
- Cholangiocarcinoma
- Ovarian
- Small intestine

**Note: Solid tumors not listed, that are RET-fusion positive, will be reviewed on a case-by-case basis and considered medically necessary when all other relevant medication and indication specific criteria are met.*

Histiocytic Neoplasms ‡ ^{2,8}

- Disease has the presence of a RET gene fusion; **AND**
- Patient has one of the following sub-types of disease:
 - Langerhans Cell Histiocytosis (LCH); **AND**
 - Used for multisystem disease with symptomatic or impending organ dysfunction; **OR**
 - Used for pulmonary LCH; **OR**
 - Patient has multifocal single system bone disease not responsive to treatment with a bisphosphonate and more than 2 lesions; **OR**
 - Patient has CNS lesions; **OR**
 - Used for relapsed/refractory disease; **OR**
 - Erdheim-Chester Disease; **AND**
 - Patient has symptomatic disease; **OR**
 - Used for relapsed or refractory disease; **OR**
 - Rosai-Dorfman Disease; **AND**
 - Patient has symptomatic disease that is multifocal or unresectable unifocal; **OR**
 - Used for relapsed or refractory disease

❖ *If confirmed using an immunotherapy assay-<http://www.fda.gov/companiondiagnostics>*

† FDA Approved Indication(s); ‡ Compendia recommended indication(s); Ⓢ Orphan Drug

IV. Renewal Criteria ¹

Coverage can be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe hepatotoxicity, severe hypersensitivity, QT interval prolongation, impaired wound

healing, severe or life-threatening hemorrhagic events, uncontrolled hypertension, tumor lysis syndrome, etc.

V. Dosage/Administration ^{1,9}

Indication	Dose
All Indications	Administer orally twice daily, until disease progression or unacceptable toxicity. <ul style="list-style-type: none">• Weight < 50 kg: 120 mg per dose• Weight ≥ 50 kg: 160 mg per dose

VI. Billing Code/Availability Information

HCPCS Code(s):

- J8999 – Prescription drug, oral, chemotherapeutic, nos
- C9399 – Unclassified drugs or biologicals (*for hospital outpatient use ONLY*)

NDC(s):

- Retevmo 40 mg capsules: 00002-3977-xx
- Retevmo 80 mg capsules: 00002-2980-xx

VII. References

1. Retevmo [package insert]. Indianapolis, IN; Lilly USA, LLC., September 2022. Accessed September 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for selpercatinib. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed September 2022.
3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer Version 4.2022. National Comprehensive Cancer Network, 2022. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed September 2022.
4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Thyroid Carcinomas Version 2.2022. National Comprehensive Cancer Network, 2022. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed September 2022.
5. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Date: 5/17/17. Identifier NCT03157128: A Phase 1/2 Study of Oral LOXO-292 in Patients With Advanced Solid Tumors, Including RET Fusion-Positive Solid Tumors, Medullary Thyroid Cancer, and Other Tumors With RET Activation (LIBRETTO-001); [Accessed 5/12/20];

[about 4 screens]. Available from:

<https://clinicaltrials.gov/ct2/show/NCT03157128?term=NCT03157128&draw=2&rank=1>.

6. Wirth LJ, Sherman E, Robinson B, et al. Efficacy of Selpercatinib in RET-Altered Thyroid Cancers. *N Engl J Med*. 2020 Aug 27;383(9):825-835. doi: 10.1056/NEJMoa2005651.
7. Drilon A, Oxnard GR, Tan DSW, et al. Efficacy of Selpercatinib in RET Fusion-Positive Non-Small-Cell Lung Cancer. *N Engl J Med*. 2020 Aug 27;383(9):813-824. doi: 10.1056/NEJMoa2005653.
8. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Histiocytic Neoplasms 2.2021. National Comprehensive Cancer Network, 2022. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2022.
9. Durham BH, Lopez Rodrigo E, Picarsic J, et al. Activating mutations in CSF1R and additional receptor tyrosine kinases in histiocytic neoplasms. *Nat Med*. 2019 Dec;25(12):1839-1842. doi: 10.1038/s41591-019-0653-6.
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 Sep 12:S1470-2045(22)00541-1. doi: 10.1016/S1470-2045(22)00541-1.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C06.9	Malignant neoplasm of mouth, unspecified
C07	Malignant neoplasm of parotid gland
C08.0	Malignant neoplasm of submandibular gland
C08.1	Malignant neoplasm of sublingual gland
C08.9	Malignant neoplasm of major salivary gland, unspecified
C17.0	Malignant neoplasm duodenum
C17.1	Malignant neoplasm jejunum
C17.2	Malignant neoplasm ileum
C17.3	Meckel's diverticulum, malignant
C17.8	Malignant neoplasm of overlapping sites of small intestines
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon

RETEVMO™ (selpercatinib) Prior Auth Criteria

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ICD-10	ICD-10 Description
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of large intestines
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C22.1	Intrahepatic bile duct carcinoma
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
C25.0	Malignant neoplasm of head of pancreas
C25.1	Malignant neoplasm of body of the pancreas
C25.2	Malignant neoplasm of tail of pancreas
C25.3	Malignant neoplasm of pancreatic duct
C25.7	Malignant neoplasm of other parts of pancreas
C25.8	Malignant neoplasm of overlapping sites of pancreas
C25.9	Malignant neoplasm of pancreas, unspecified
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C47.0	Malignant neoplasm of peripheral nerves of head, face and neck
C47.10	Malignant neoplasm of peripheral nerves of unspecified upper limb, including shoulder
C47.11	Malignant neoplasm of peripheral nerves of right upper limb, including shoulder
C47.12	Malignant neoplasm of peripheral nerves of left upper limb, including shoulder

ICD-10	ICD-10 Description
C47.20	Malignant neoplasm of peripheral nerves of unspecified lower limb, including hip
C47.21	Malignant neoplasm of peripheral nerves of right lower limb, including hip
C47.22	Malignant neoplasm of peripheral nerves of left lower limb, including hip
C47.3	Malignant neoplasm of peripheral nerves of thorax
C47.6	Malignant neoplasm of peripheral nerves of trunk, unspecified
C47.8	Malignant neoplasm of overlapping sites of peripheral nerves and autonomic nervous
C47.9	Malignant neoplasm of peripheral nerves and autonomic nervous system, unspecified
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck
C49.10	Malignant neoplasm of connective and soft tissue of unspecified upper limb, including
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.20	Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3	Malignant neoplasm of connective and soft tissue of thorax
C49.6	Malignant neoplasm of connective and soft tissue of trunk, unspecified
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right female breast
C50.022	Malignant neoplasm of nipple and areola, left female breast
C50.029	Malignant neoplasm of nipple and areola, unspecified female breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast

ICD-10	ICD-10 Description
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast

ICD-10	ICD-10 Description
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.3	Malignant neoplasm of bilateral ovaries
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C57.10	Malignant neoplasm of unspecified broad ligament
C57.11	Malignant neoplasm of right broad ligament
C57.12	Malignant neoplasm of left broad ligament
C57.20	Malignant neoplasm of unspecified round ligament
C57.21	Malignant neoplasm of right round ligament
C57.22	Malignant neoplasm of left round ligament
C57.3	Malignant neoplasm of parametrium
C57.4	Malignant neoplasm of uterine adnexa, unspecified
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C57.9	Malignant neoplasm of female genital organ, unspecified
C7A.026	Malignant carcinoid tumor of the rectum
C7A.090	Malignant carcinoid tumor of the bronchus and lung
C73	Malignant neoplasm of thyroid gland
C76	Malignant neoplasm of head, face, and neck
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C96.0	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
C96.2	Malignant mast cell neoplasm
C96.5	Multifocal and unisystemic Langerhans-cell histiocytosis
C96.6	Unifocal Langerhans-cell histiocytosis
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
D76.3	Other histiocytosis syndromes
Z85.118	Personal history of other malignant neoplasm of bronchus and lung

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Article (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC