Retevmo™ (selpercatinib)
(Oral)

Document Number: IC-0537

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Dates Reviewed: 06/2020, 05/2021

I. Length of Authorization

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

II. Dosing Limits

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

- Retevmo 40 mg capsules: 2 per day
- Retevmo 80 mg capsules: 4 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 old (unless otherwise specified); **AND**

Universal Criteria [1,4]

- Must be used as a single agent; **AND**
- Patient does not have uncontrolled hypertension; **AND**
- Patient does not have clinically significant active cardiovascular disease or a recent myocardial infarction (i.e., within 6 months prior to start of therapy); **AND**
- Patient does not have a history of prolongation of the QT-interval > 470 msec; **AND**
- Patient has not had recent major surgery within the previous 14 days; **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 any of the following:
  - Coadministration with acid-reducing agents, if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications; **OR**
  - Coadministration with strong or moderate CYP3A4 inhibitors (e.g., fluconazole, itraconazole, etc.), if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications; **OR**

- Coadministration with strong and moderate CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**

Non-Small Cell Lung Cancer (NSCLC) † Φ [1,2,3,7]

- Patient disease has the presence of a RET gene fusion 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; **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); **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; **AND**
  - Used as neoadjuvant therapy for borderline resectable locoregional disease; **OR**
  - Used as first- or second-line therapy for metastatic disease

Histiocytic Neoplasms ‡ [2,8]

- Patient 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); Φ 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

Indication	Dose
All indications	Administer Retevmo orally twice daily, until disease progression or unacceptable toxicity. • Weight < 50 kg: 120 mg per dose • Weight ≥ 50 kg: 160 mg per dose

VI. Billing Code/Availability Information

HCPCS Code:

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

NDC:

- 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., May 2020. Accessed April 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for selpercatinib. National Comprehensive Cancer Network, 2021. 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 April 2021.

3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer Version 4.2021. National Comprehensive Cancer Network, 2021. 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 2021.
4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Thyroid Carcinomas Version 3.2020. National Comprehensive Cancer Network, 2021. 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 2021.
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 1.2021. National Comprehensive Cancer Network, 2021. 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 2021.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
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

ICD-10	ICD-10 Description
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
C73	Malignant neoplasm of thyroid gland
C96.0	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
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
D76.3	Other histiocytosis syndromes

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: http://www.cms.gov/medicare-coverage-database/search/advanced-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