Evolent Clinical Guideline 3223 for Retevmo™ (selpercatinib)

Guideline Number:	Applicable Codes	
Evolent_CG_3223		
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Original Date:	**Last Revised Date:**	**Implementation Date:**
June 2020	November 2025	November 2025

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STATEMENT

Purpose

To define and describe the accepted indications for Retevmo (selpercatinib) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Non-Small Cell Lung Cancer (NSCLC)

- Retevmo (selpercatinib) may be used as a single agent as first or subsequent line therapy in adult members with locally advanced/recurrent/metastatic Non-Small Cell Lung Cancer that is positive for a RET-genomic alteration confirmed by a gene sequencing test.

Solid Tumors with a RET Gene Fusion

- Retevmo (selpercatinib) may be used as monotherapy in adult and pediatric members ≥ 2 years of age with recurrent, unresectable or metastatic solid tumors that are positive for RET Gene Fusions as detected by an FDA approved test, and the disease has progressed following one or more prior systemic therapies.

Thyroid Cancer

- Retevmo (selpercatinib) will be used in adult and pediatric members ≥ 2 years of age with advanced/metastatic RET-mutation /RET-fusion positive Medullary Thyroid Cancer who require systemic therapy OR
- In adult and pediatric members ≥ 2 years of age with RET-fusion/RET-mutation positive thyroid cancer (all non-Medullary histologies are included - Anaplastic/Follicular/Hurthle Cell/Papillary Carcinoma) who require systemic therapy and have disease that is refractory to radioactive iodine (if radioactive iodine is appropriate therapy for their thyroid cancer and the cancer is positive for radioactive

iodine uptake on appropriate scanning) AND

- Retevmo (selpercatinib) will be used as a single agent.

CONTRAINDICATIONS/WARNINGS

- None

EXCLUSION CRITERIA

- Lack of confirming documentation of a positive RET-genomic alteration (fusion or mutation) by genomic testing.
- Disease progression while receiving Retevmo or another RET inhibitor (e.g., pralsetinib).
- Concurrent use with other anti-cancer therapy including targeted therapy, immunotherapy and/or chemotherapy.
- Dosing exceeds single dose limit of Retevmo (selpercatinib) 120 mg (for weight less than 50 kg) or 160 mg (for weight greater than or equal to 50kg) in adult and adolescent patients 12 years of age or older based on body weight. Dosing exceeds single dose limit of Retevmo (selpercatinib) 160 mg in pediatric patients 2 to less than 12 years of age based on body surface area.
- Pediatric patients 2 to less than 12 years of age with body surface area less than 0.33 m2.
- Treatment exceeds the maximum limit of:
    - 90 (40 mg) or 60 (80 mg) capsules or tablets/month
    - 60 (120 mg) or 60 (160 mg) tablets/month
- Investigational use of Retevmo (selpercatinib) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
    - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
    - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
    - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
    - Whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).

- That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J8999 - selpercatinib

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
November 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1405 Retevmo (selpercatinib) • Updated indication section • Updated references
November 2024	• Added new tablet strengths to exclusion criteria • Updated maximum dosage form quantities in exclusion criteria • Updated references

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Zhou C, et al; LIBRETTO-431 Trial Investigators. First-Line Selpercatinib or Chemotherapy and Pembrolizumab in *RET* Fusion-Positive NSCLC. *N Engl J Med*. 2023 Nov 16;389(20):1839-1850. doi: 10.1056/NEJMoa2309457.
2. Gautschi O, et al. 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.
3. Drilon A, 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.
4. Wirth LJ, et al. LIBRETTO-531: a phase III study of selpercatinib in multikinase inhibitor-naïve *RET*-mutant medullary thyroid cancer. *Future Oncol*. 2022 Sep;18(28):3143-3150. doi: 10.2217/fon-2022-0657.
5. Morgenstern D, et al. Safety and efficacy of selpercatinib in pediatric patients with RET-altered solid tumors: Updated results from LIBRETTO-121. *J Clin Onc*. 2024 May 29; 42(16). https://doi.org/10.1200/JCO.2024.42.16_suppl.10022**.**
6. Retevmo prescribing information. Lilly USA, LLC. Indianapolis, IN 2024.
7. Clinical Pharmacology Elsevier Gold Standard 2025.
8. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
9. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
10. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
11. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.

12. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: **https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf**.
13. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: **http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm**.