Drug Policy:

Retevmo™ (selpercatinib)

POLICY NUMBER UM ONC_1405	SUBJECT Retevmo™ (selpercatinib)		DEPT/PROGRAM UM Dept	PAGE 1 of 3
DATES COMMITTEE REVIEWED 06/10/20, 10/14/20, 02/16/21, 11/15/21, 01/12/22, 05/11/22, 11/09/22, 11/08/23, 07/10/24, 11/13/24	**APPROVAL DATE** November 13, 2024	**EFFECTIVE DATE** November 29, 2024	**COMMITTEE APPROVAL DATES** 06/10/20, 10/14/20, 02/19/21, 11/15/21, 01/12/22, 05/11/22, 11/09/22, 11/08/23, 07/10/24, 11/13/24	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Evolent Specialty Services Clinical Guideline Review Committee		
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. 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.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

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

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND
3. Additional medication(s) are not being added to the continuation request.

B. Non-Small Cell Lung Cancer

1. The member has advanced/recurrent/metastatic Non-Small Cell Lung Cancer that is positive for a RET- genomic alteration confirmed by a gene sequencing test AND Retevmo (selpercatinib) will be used as a single agent as first or subsequent line of therapy.

C. Solid Tumors with a RET Gene Fusion

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

D. Thyroid Cancer

1. 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
2. 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
3. Retevmo (selpercatinib) will be used as a single agent.

III. EXCLUSION CRITERIA

A. Lack of confirming documentation of a positive RET- genomic alteration (fusion or mutation) by genomic testing.

B. Disease progression while receiving Retevmo or another RET inhibitor (e.g., pralsetinib)

C. Concurrent use with other anti-cancer therapy including targeted therapy, immunotherapy and/or chemotherapy.

D. 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.

E. Pediatric patients 2 to less than 12 years of age with body surface area less than 0.33 m2.

F. Treatment exceeds the maximum limit of:

   a. 90 (40 mg) or 60 (80 mg) capsules or tablets/month

   b. 60 (120 mg) or 60 (160 mg) tablets/month

G. 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:

   1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
   2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
   3. 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.
   4. 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).

5. 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.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. 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.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. 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.

B. 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

C. 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

D. Retevmo prescribing information. Lilly USA, LLC, Indianapolis, IN 2024.

E. Clinical Pharmacology Elsevier Gold Standard 2024.

F. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, CO 2024.

G. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2024.

H. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2024.

I. 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.

J. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.

K. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.