Clinical Policy: Selpercatinib (Retevmo)

Reference Number: CP.PHAR.478
Effective Date: 09.01.20
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Selpercatinib (Retevmo®) is a kinase inhibitor.

FDA Approved Indication(s)

Retevmo is indicated for the treatment of:

- Adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a rearranged during transfection (*RET)* gene fusion, as detected by an FDA-approved test
- Adult and pediatric patients 2 years of age and older with advanced or metastatic medullary thyroid cancer (MTC) with a *RET* mutation, as detected by an FDA-approved test, who require systemic therapy
- Adult and pediatric patients 2 years of age and older with advanced or metastatic thyroid cancer with *RET* gene fusion, as detected by an FDA-approved test, who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)
- Adult and pediatric patients 2 years of age and older with locally advanced or metastatic solid tumors with a *RET* gene fusion, as detected by an FDA-approved test, that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options*

**This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).*

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Retevmo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Small Cell Lung Cancer (must meet all)**:**

1. Diagnosis of recurrent, advanced, or metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Documentation of *RET* fusion-positive disease (e.g., KIF5B-RET);
5. Retevmo is not prescribed concurrently with Gavreto™;
6. Member has not received prior *RET* targeted therapy (e.g., Gavreto);
7. Prescribed as a single agent;

8. For brand Retevmo requests, member must use generic selpercatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
9. Request meets one of the following (a, b, or c):*
   i. Weight < 50 kg: Dose does not exceed both (i and ii):
      1) 240 mg per day;
      2) One of the following (1 or 2):
         a) 6 capsules per day;
         b) 2 tablets per day;
   ii. Weight ≥ 50 kg: Dose does not exceed both (i and ii):
      1) 320 mg per day;
      2) One of the following (1 or 2):
         a) 4 capsules per day;
         b) 2 tablets per day;
   iii. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Thyroid Cancer (must meet all)**:**
1. Diagnosis of one of the following (a, b, or c):
   a. MTC;
   b. Differentiated thyroid carcinoma (DTC; oncocytic [formerly Hurthle cell], papillary, follicular);
   c. Anaplastic thyroid carcinoma (ATC);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 2 years;
4. For age ≥ 2 years to < 12 years, body surface area (BSA) ≥ 0.33 m^2;
5. Disease is recurrent, advanced, or metastatic;
6. For MTC, documentation of *RET* mutant-positive disease (e.g., RET M918T);
7. For DTC or ATC, both of the following (a and b):
   a. Documentation of *RET* fusion-positive disease (e.g., CCDC6-RET, KIF5B-RET);
   b. Member is radioactive iodine-refractory (if radioactive iodine is appropriate);
8. Retevmo is not prescribed concurrently with Gavreto;
9. Member has not received prior *RET* targeted therapy (e.g., Gavreto);
10. Prescribed as a single agent;
11. For brand Retevmo requests, member must use generic selpercatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
12. Request meets one of the following (a, b, or c):*
   a. For age ≥ 12 years, one of the following (i or ii):
      i. Weight < 50 kg: Dose does not exceed both (1 and 2):
         1) 240 mg per day;
         2) One of the following (a or b):
            a) 6 capsules per day;
            b) 2 tablets per day;

ii. Weight ≥ 50 kg: Dose does not exceed both (1 and 2):
1) 320 mg per day;
2) One of the following (a or b):
a) 4 capsules per day;
b) 2 tablets per day;

b. For age 2 years to < 12 years, one of the following (i, ii, iii, or iv):
i. BSA 0.33 to 0.65 m^2: Dose does not exceed both (1 and 2):
1) 120 mg per day;
2) 3 capsules or tablets per day;
ii. BSA 0.66 to 1.08 m^2: Dose does not exceed both (1 and 2):
1) 160 mg per day;
2) 2 capsules or tablets per day;
iii. BSA 1.09 to 1.52 m^2: Dose does not exceed both (1 and 2):
1) 240 mg per day;
2) One of the following (a or b):
a) 6 capsules per day;
b) 2 tablets per day;
iv. BSA ≥ 1.53 m^2: Dose does not exceed both (1 and 2):
1) 320 mg per day;
2) One of the following (a or b):
a) 4 capsules per day;
b) 2 tablets per day;

c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. RET Fusion-Positive Solid Tumors (must meet all)**:**
1. Diagnosis of a locally advanced, recurrent, or metastatic solid tumor (*see Appendix D for examples*);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 2 years;
4. For age ≥ 2 years to < 12 years, BSA ≥ 0.33 m^2;
5. Documentation of *RET* fusion-positive disease;
6. One of the following (a, b, or c):
   a. Disease has progressed on or following prior systemic treatment;
   b. Member has no satisfactory alternative treatment options;
   c. For ampullary adenocarcinoma, biliary tract cancer, pancreatic adenocarcinoma, soft tissue sarcoma, or uterine sarcoma: as first line therapy;
7. Retevmo is not prescribed concurrently with Gavreto;
8. Member has not received prior RET targeted therapy (e.g., Gavreto);
9. Prescribed as a single agent;
10. For brand Retevmo requests, member must use generic selpercatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;

11. Request meets one of the following (a, b, or c):*
    a. For age ≥ 12 years, one of the following (i or ii):
        i. Weight < 50 kg: Dose does not exceed both (1 and 2):
            1) 240 mg per day;
            2) One of the following (a or b):
                a) 6 capsules per day;
                b) 2 tablets per day;
        ii. Weight ≥ 50 kg: Dose does not exceed both (1 and 2):
            1) 320 mg per day;
            2) One of the following (a or b):
                a) 4 capsules per day;
                b) 2 tablets per day;
    b. For age 2 years to < 12 years, one of the following (i, ii, iii, or iv):
        i. BSA 0.33 to 0.65 m^2: Dose does not exceed both (1 and 2):
            1) 120 mg per day;
            2) 3 capsules or tablets per day;
        ii. BSA 0.66 to 1.08 m^2: Dose does not exceed both (1 and 2):
            1) 160 mg per day;
            2) 2 capsules or tablets per day;
        iii. BSA 1.09 to 1.52 m^2: Dose does not exceed both (1 and 2):
            1) 240 mg per day;
            2) One of the following (a or b):
                a) 6 capsules per day;
                b) 2 tablets per day;
        iv. BSA ≥ 1.53 m^2: Dose does not exceed both (1 and 2):
            1) 320 mg per day;
            2) One of the following (a or b):
                a) 4 capsules per day;
                b) 2 tablets per day;
    c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

D. Histiocytic Neoplasms (off-label) (must meet all)**:**
1. Diagnosis of one of the following histiocytic neoplasms (a, b, or c):
    a. Erdheim-Chester disease;
    b. Langerhans cell histiocytosis;
    c. Rosai-Dorfman disease;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Documentation of *RET* fusion-positive disease;
5. Retevmo is not prescribed concurrently with Gavreto;
6. Member has not received prior RET targeted therapy (e.g., Gavreto);

7. Prescribed as a single agent;
8. For brand Retevmo requests, member must use generic selpercatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
9. Request meets one of the following (a, b, or c):*
   a. Weight < 50 kg: Dose does not exceed both (i and ii):
      i. 240 mg per day;
      ii. One of the following (1 or 2):
         1) 6 capsules per day;
         2) 2 tablets per day;
   b. Weight ≥ 50 kg: Dose does not exceed both (i and ii):
      i. 320 mg per day;
      ii. One of the following (1 or 2):
         1) 4 capsules per day;
         2) 2 tablets per day;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

E. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Retevmo for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Retevmo is not prescribed concurrently with Gavreto;

4. Member has not received prior *RET* targeted therapy (e.g., Gavreto);
5. For brand Retevmo requests, member must use generic selpercatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a, b, or c):*
   a. For age ≥ 12 years, one of the following (i or ii):
      i. Weight < 50 kg: Dose does not exceed both (1 and 2):
         1) 240 mg per day;
         2) One of the following (a or b):
            a) 6 capsules per day;
            b) 2 tablets per day;
      ii. Weight ≥ 50 kg: Dose does not exceed both (1 and 2):
         1) 320 mg per day;
         2) One of the following (a or b):
            a) 4 capsules per day;
            b) 2 tablets per day;
   b. For age 2 years to < 12 years, one of the following (i, ii, iii, or iv):
      i. BSA 0.33 to 0.65 m^2: Dose does not exceed both (1 and 2):
         1) 120 mg per day;
         2) 3 capsules or tablets per day;
      ii. BSA 0.66 to 1.08 m^2: Dose does not exceed both (1 and 2):
         1) 160 mg per day;
         2) 2 capsules or tablets per day;
      iii. BSA 1.09 to 1.52 m^2: Dose does not exceed both (1 and 2):
         1) 240 mg per day;
         2) One of the following (a or b):
            a) 6 capsules per day;
            b) 2 tablets per day;
      iv. BSA ≥ 1.53 m^2: Dose does not exceed both (1 and 2):
         1) 320 mg per day;
         2) One of the following (a or b):
            a) 4 capsules per day;
            b) 2 tablets per day;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 of 2):
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ATC: anaplastic thyroid carcinoma
BSA: body surface area
DTC: differentiated thyroid carcinoma
FDA: Food and Drug Administration
MTC: medullary thyroid cancer
NCCN: National Comprehensive Cancer Network
NSCLC: non-small cell lung cancer
RET: rearranged during transfection

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: Examples of RET Fusion-Positive Solid Tumors

RET fusion-positive solid tumor types evaluated in the LIBRETTO-001 clinical study (NCT03157128) included:

- Pancreatic adenocarcinoma
- Colorectal
- Salivary
- Breast
- Sarcoma (soft tissue)
- Xanthogranuloma
- Carcinoid (bronchial)
- Carcinoma of the skin
- Cholangiocarcinoma
- Ovarian
- Pulmonary carcinosarcoma
- Rectal neuroendocrine
- Small intestine
- Gastric
- Esophageal and esophagogastric junction

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NSCLC	Adult patients: • Weight < 50 kg: 120 mg PO BID • Weight ≥ 50 kg: 160 mg PO BID	Weight < 50 kg: 240 mg/day Weight ≥ 50 kg: 320 mg/day
Thyroid cancer, RET fusion-positive solid tumors	Adult and adolescent patients 12 years of age or older: • Weight < 50 kg: 120 mg PO BID • Weight ≥ 50 kg: 160 mg PO BID Pediatric patients 2 to less than 12 years of age: The recommended dosage is based on BSA: • 0.33 to 0.65 m^2: 40 mg PO TID • 0.66 to 1.08 m^2: 80 mg PO BID • 1.09 to 1.52 m^2: 120 mg PO BID • ≥ 1.53 m^2: 160 mg PO BID Dosing pediatric patients with BSA < 0.33 m^2 is not recommended.	Age > 12 years: Weight < 50 kg: 240 mg/day Weight ≥ 50 kg: 320 mg/day Age 2 years to < 12 years: 320 mg/day

VI. Product Availability

- Capsules: 40 mg, 80 mg
- Tablets: 40 mg, 80 mg, 120 mg, 160 mg

VII. References

1. Retevmo Prescribing Information. Indianapolis, IN: Lilly USA, LLC; December 2024. Available at http://pi.lilly.com/us/retevmo-uspi.pdf. Accessed January 29, 2025.
2. Selpercatinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed March 10, 2025.
3. National Comprehensive Cancer Network. Thyroid Carcinoma Version 5.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed March 10, 2025.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: no significant changes; added generic redirection language to "must use" since oral oncology product; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	01.26.21	05.21
2Q 2022 annual review: per NCCN added the following: added criterion for use as single-agent therapy for NSCLC and thyroid cancers, added qualifier of recurrent thyroid cancer, removed radioactive iodine criteria for ATC, revised DTC/MTC-specific	02.15.22	05.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
criteria to align with Gavreto, and added indication criteria for histiocytic neoplasms; Commercial approval durations revised from "Length of Benefit" to "12 months or duration of request, whichever is less"; references reviewed and updated.		
RT4: 1) added criteria for new FDA-approved indication of RET fusion-positive solid tumors and 2) revised FDA Approved Indications section to reflect updated label requiring use of an FDA-approved test for all other indications; template changes applied to other diagnoses/indications.	10.04.22	
2Q 2023 annual review: no significant changes; for thyroid cancer, removed requirement that disease is not amenable to radioactive iodine therapy for DTC as this is redundant with immediately preceding criterion; references reviewed and updated.	01.31.23	05.23
2Q 2024 annual review: clarified that Hurthle cell carcinoma is now known as oncocytic carcinoma per NCCN; for *RET* fusion-positive solid tumors added qualifier that tumors can be recurrent and added option for Retevmo use as first-line therapy in pancreatic adenocarcinoma, soft tissue sarcoma, or ampullary adenocarcinoma per NCCN; for *RET* fusion-positive solid tumors, added criterion that member age ≥ 18 years per FDA-labeling; revised maximum capsules corresponding to 240 mg per day dose to 6 capsules per day; references reviewed and updated. RT4: added new tablet formulation.	05.01.24	05.24
RT4: updated to reflect pediatric expanded use down to 2 years of age (previously 12 years of age) for thyroid cancers and new pediatric use in solid tumors; added age restriction for histiocytic neoplasms per NCCN; converted FDA approved indication for thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate) from accelerated approval to full approval per PI.	06.24.24	
RT4: converted FDA approved indication for patients 2 years of age and older with advanced or metastatic MTC with a *RET* mutation who require systemic therapy from accelerated approval to full approval per PI.	10.02.24	
2Q 2025 annual review: for *RET* fusion-positive solid tumors indication, added biliary tract cancer and uterine sarcoma as options for 1st line therapy per NCCN; references reviewed and updated.	01.29.25	05.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional

organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

 Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.