Clinical Policy: Pralsetinib (Gavreto)

Reference Number: CP.PHAR.514
Effective Date: 12.01.20
Last Review Date: 05.25
Line of Business: Commercial, Medicaid

Revision Log

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

Description

Pralsetinib (Gavreto®) is an oral tyrosine kinase inhibitor of wild-type rearranged during transfection (RET) and oncogenic *RET* fusions (CCDC6-RET) and mutations (RET V804L, RET V804M, and RET M918T).

FDA Approved Indication(s)

Gavreto is indicated for the treatment of:

- Adult patients with metastatic *RET* fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test.
- Adult and pediatric patients 12 years of age and older with advanced or metastatic *RET* fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).*

**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 Gavreto 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., CCDC6-RET, KIF5B-RET);
5. Gavreto is not prescribed concurrently with Retevmo®;
6. Member has not received prior *RET* targeted therapy (e.g., Retevmo);
7. Prescribed as a single agent;
8. For Gavreto requests, member must use pralsetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
9. Request meets one of the following (a, b, or c):*
   a. Dose does not exceed both of the following (i and ii):
      i. 400 mg per day;

ii. 4 capsules per day;
b. Both of the following (i and ii):
i. Dose does not exceed both of the following (1 and 2):
1) 800 mg per day;
2) 8 capsules per day;
ii. Prescriber attestation of member's inability to avoid concomitant use of CYP3A inducer (e.g., carbamazepine, rifampin, ritonavir, St. John's wort);
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 – 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. Differentiated thyroid carcinoma (DTC; oncocytic/Hurthle cell, papillary, follicular);
   b. Anaplastic thyroid carcinoma (ATC);
   c. Medullary thyroid carcinoma (MTC) [*off-label*];
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. Disease is unresectable, recurrent, advanced, or metastatic;
5. Prescribed as a single agent;
6. For DTC or ATC, documentation of *RET* fusion-positive disease (e.g., CCDC6-RET, KIF5B-RET);
7. For DTC or ATC, member is radioactive iodine-refractory (if radioactive iodine is appropriate);
8. For DTC, disease is not amenable to radioactive iodine therapy;
9. For MTC, documentation of *RET* pathologic variant-positive disease (e.g., RET M918T);
10. Gavreto is not prescribed concurrently with Retevmo;
11. Member has not received prior *RET* targeted therapy (e.g., Retevmo);
12. For Gavreto requests, member must use pralsetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
13. Request meets one of the following (a, b, or c):*
    a. Dose does not exceed both of the following (i and ii):
       i. 400 mg per day;
       ii. 4 capsules per day;
    b. Both of the following (i and ii):
       i. Dose does not exceed both of the following (1 and 2):
          1) 800 mg per day;
          2) 8 capsules per day;
       ii. Prescriber attestation of member's inability to avoid concomitant use of CYP3A inducer (e.g., carbamazepine, rifampin, ritonavir, St. John's wort);

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 – 6 months
Commercial – 12 months or duration of request, whichever is less

C. NCCN Compendium Indications (off-label) (must meet all)**:**

1. Diagnosis of one of the following biliary tract cancers (a, b, or c):
   a. Extrahepatic cholangiocarcinoma;
   b. Intrahepatic cholangiocarcnoma;
   c. Gallbladder cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. Prescribed as a single agent;
5. Documentation of *RET* fusion-positive disease (e.g., CCDC6-RET, KIF5B-RET);
6. Gavreto is not prescribed concurrently with Retevmo;
7. Member has not received prior *RET* targeted therapy (e.g., Retevmo);
8. For Gavreto requests, member must use pralsetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
9. Request meets one of the following (a, b, or c):*
   a. Dose does not exceed both of the following (i and ii):
      i. 400 mg per day;
      ii. 4 capsules per day;
   b. Both of the following (i and ii):
      i. Dose does not exceed both of the following (1 and 2):
         1) 800 mg per day;
         2) 8 capsules per day;
      ii. Prescriber attestation of member's inability to avoid concomitant use of CYP3A inducer (e.g., carbamazepine, rifampin, ritonavir, St. John's wort);
   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 – 6 months
Commercial – 12 months or duration of request, whichever is less

D. 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 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 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 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 Gavreto for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Gavreto is not prescribed concurrently with Retevmo;
4. Member has not received prior *RET* targeted therapy (e.g., Retevmo);
5. For Gavreto requests, member must use pralsetinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. New dose does not exceed both of the following (i and ii):
      i. 400 mg per day;
      ii. 4 capsules per day;
   b. Both of the following (i and ii):
      i. New dose does not exceed both of the following (1 and 2):
         1) 800 mg per day;
         2) 8 capsules per day;
      ii. Prescriber attestation of member's inability to avoid concomitant use of CYP3A inducer (e.g., carbamazepine, rifampin, ritonavir, St. John's wort);
   c. New 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 – 12 months
Commercial – 12 months or duration of request, whichever is less

B. 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 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 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 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 and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ATC: anaplastic thyroid carcinoma
DTC: differentiated thyroid carcinoma
FDA: Food and Drug Administration
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

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NSCLC, thyroid cancer	400 mg PO QD	800 mg/day with coadministration of strong CYP3A inducers

VI. Product Availability

Capsule: 100 mg

VII. References

1. Gavreto Prescribing Information. South San Francisco, CA: Rigel Pharmaceuticals, Inc; June 2024. Available at: https://gavreto.com. Accessed February 5, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 5, 2025.
3. National Comprehensive Cancer Network. Thyroid Carcinoma Version 5.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed February 5, 2025.
4. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed February 5, 2025.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: added that disease must be advanced or metastatic for thyroid cancer; removed HIM line of business as	01.26.21	05.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
formulary alternative Retevmo exists; references reviewed and updated.		
2Q 2022 annual review: added criterion for use as single-agent therapy for NSCLC; for thyroid cancer added qualifier of recurrent thyroid cancer and added criterion for DTC that disease is not amenable to radioactive iodine therapy per NCCN; added oral oncology generic redirection language; Commercial approval durations revised from "Length of Benefit" to "12 months or duration of request, whichever is less"; references reviewed and updated.	02.09.22	05.22
Template changes applied to other diagnoses/indications.	10.03.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	01.05.23	05.23
RT4: removed previously FDA-approved indication for RET-mutant medullary thyroid cancer per PI; added criterion for use as single-agent therapy for thyroid cancer per NCCN; references reviewed and updated.	08.01.23	
RT4: for NSCLC, updated FDA-approved indication for conversion from accelerated approval to regular approval.	08.16.23	
2Q 2024 annual review: no significant changes; references reviewed and updated.	02.12.24	05.24
2Q 2025 annual review: in thyroid cancer per NCCN, added off-label criteria for MTC, added option for unresectable disease; added off-label criteria for biliary tract cancers per NCCN; references reviewed and updated.	02.05.25	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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. 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.