

Drug Policy:

Gavreto™ (pralsetinib)

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| POLICY NUMBER UM ONC_1414 | SUBJECT Gavreto™ (pralsetinib) | DEPT/PROGRAM UM Dept | PAGE 1 OF 3 |
| DATES COMMITTEE REVIEWED 10/14/20, 01/13/21, 02/16/21, 11/15/21, 01/12/22, 05/11/22, 01/11/23, 01/10/24, 01/08/25 | APPROVAL DATE January 08, 2025 | EFFECTIVE DATE January 31, 2025 | COMMITTEE APPROVAL DATES 10/14/20, 01/13/21, 02/19/21, 11/15/21, 01/12/22, 05/11/22, 01/11/23, 01/10/24, 01/08/25 |
| 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 | |

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. A list of 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.

I. PURPOSE

To define and describe the accepted indications for Gavreto (pralsetinib) 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 member has not experienced disease progression on the requested medication **AND**

2. The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization **AND**
3. Additional medication(s) are not being added to the continuation request.

B. Non-Small Cell Lung Cancer (NSCLC)

1. The member has RET fusion positive advanced, recurrent, or metastatic NSCLC and Gavreto (pralsetinib) may be used as a single agent as initial or subsequent therapy.

C. Thyroid Cancer

1. Gavreto (pralsetinib) may be used in adult and pediatric members greater than or equal to 12 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 greater than or equal to 12 years of age with RET-fusion/RET-mutation positive non-Medullary thyroid cancer (e.g., papillary, follicular, Hurthle cell, or anaplastic thyroid cancer) 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. Gavreto (pralsetinib) will be used as a single agent.

III. EXCLUSION CRITERIA

- A. Disease progression while taking Gavreto (pralsetinib) or another RET inhibitor (e.g., seliprecatinib).
- B. Dosing exceeds single dose limit of Gavreto (pralsetinib) 400 mg.
- C. Treatment exceeds the maximum limit of 120 (100 mg) capsules/month.
- D. Investigational use of Gavreto (pralsetinib) 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. CODING INFORMATION

| HCP Code | Description |
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| C9399 | pralsetinib |
| J8999 | pralsetinib |

V. MEDICATION MANAGEMENT

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

VI. APPROVAL AUTHORITY

- A. Review – Utilization Management Department
B. Final Approval – Utilization Management Committee

VII. ATTACHMENTS

- A. None

VIII. REFERENCES

- A. Gainor JF, et al. Pralsetinib for RET fusion-positive non-small-cell lung cancer (ARROW): a multi-cohort, open-label, phase 1/2 study. *Lancet Oncol*. 2021 Jul;22(7):959-969.
- B. Gavreto prescribing information 2024. Rigel Pharmaceuticals, Inc. South San Francisco, CA
- C. Clinical Pharmacology Elsevier Gold Standard 2025.
- D. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, CO 2025.
- E. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
- F. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs Bethesda, MD 2025.
- G. 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.
- H. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services:
<https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf>.
- I. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA:
<http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>.