PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Gavreto Prior Authorization Policy
- Gavreto® (pralsetinib capsules – Blueprint Medicines)

REVIEW DATE: 09/18/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Gavreto, a kinase inhibitor, is indicated for the following uses:[1]
- **Non-small cell lung cancer**, with metastatic *RET* fusion-positive disease in adults, as detected by an FDA approved test.
- **Thyroid cancer**, with advanced or metastatic *RET* fusion-positive disease in adults and pediatric patients ≥ 12 years of age who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). This thyroid cancer indication was approved under accelerated approval based on overall response rate and duration of response. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Guidelines

Gavreto is addressed in the National Comprehensive Cancer Network (NCCN) guidelines:
- **Non-Small Cell Lung Cancer:** Guidelines (version 9.2024 – September 9, 2024) recommend Gavreto and Retevmo® (selpercatinib capsules) as "preferred" first-line therapies for *RET* rearrangement-positive recurrent, advanced, or metastatic disease (both category 2A).[2] For patients who were started on other systemic therapy options and had disease progression,

Gavreto and Retevmo are recommended as "preferred" subsequent therapies (category 2A). The NCCN compendium recommend Gavreto for locoregional recurrence or symptomatic local disease with *RET* rearrangement with no evidence of disseminated disease (both category 2B).[4]

- **Thyroid Carcinoma:** Guidelines (version 4.2024 – August 19, 2024) recommend the use of Gavreto and Retevmo in a variety of therapy settings.[3] The guidelines recommend Gavreto and Retevmo for differentiated thyroid carcinoma (papillary, follicular, oncocytic carcinoma) with *RET* fusion-positive tumors for unresectable locoregional recurrent or persistent disease, or distant metastatic disease that is not amenable to radioactive therapy as "useful in certain circumstances" (category 2A). For recurrent, persistent, locoregional or metastatic medullary thyroid cancer, Gavreto (category 2B) or Retevmo (category 2A) are listed as "preferred" options for positive *RET* pathogenic variant. For anaplastic carcinoma, Gavreto or Retevmo can be used for *RET*-fusion positive tumors as neoadjuvant therapy for locoregional disease (category 2A). For metastatic anaplastic carcinoma, molecular testing for actionable mutations is recommended; if positive for *RET* fusion, Gavreto or Retevmo can be considered (category 2A).[3]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Gavreto. All approvals are provided for the duration noted below.

- **Gavreto® (pralsetinib capsules (Blueprint Medicines)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Differentiated Thyroid Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C and D):
   Note: Differentiated thyroid cancer includes papillary, follicular, and oncocytic thyroid cancer; see below for other types of thyroid cancer.
   A) Patient is ≥ 12 years of age; AND
   B) Patient has unresectable, recurrent, or metastatic disease; AND
   C) Patient has rearranged during transfection (*RET*) fusion-positive or *RET*-mutation-positive disease; AND
   D) Patient meets both of the following (i and ii):
      i. The disease requires treatment with systemic therapy; AND
      ii. The disease is radioactive iodine-refractory.

2. **Non-Small Cell Lung Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has recurrent, advanced, or metastatic disease; AND

C) Patient has rearranged during transfection (*RET*) fusion-positive disease as detected by an approved test.

Other Uses with Supportive Evidence

3. **Anaplastic Thyroid Cancer**. Approve for 1 year if the patient meets ALL of the following (A, B and C):
   A) Patient is ≥ 12 years of age; AND
   B) Patient has unresectable, recurrent, or metastatic disease; AND
   C) Patient has rearranged during transfection (*RET*) fusion-positive or *RET*-mutation-positive disease.

4. **Medullary Thyroid Cancer**. Approve for 1 year if the patient meets ALL of the following (A, B, C and D):
   A) Patient is ≥ 12 years of age; AND
   B) Patient has unresectable, recurrent, or metastatic disease; AND
   C) The disease is positive for rearranged during transfection (*RET*) pathogenic variant; AND
   D) Patient is continuing therapy with Gavreto.

CONDITIONS NOT COVERED

- **Gavreto® (pralsetinib capsules (Blueprint Medicines)**

is(are) considered experimental, investigational or unproven for ANY other use(s); criteria will be updated as new published data are available.

REFERENCES

1. Gavreto® capsules [prescribing information]. Cambridge, MA: Blueprint Medicines; March 2024.
2. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 9.2024– September 9, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed September 16, 2024.
3. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (version 4.2024 – August 19, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 16, 2024.
4. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 15, 2024. Search term: pralsetinib.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	The indication of "medullary thyroid cancer, in adults and pediatric patients ≥ 12 years of age with advanced or metastatic rearranged during transfection (RET)-mutant disease who require systemic therapy" was removed from the overview section because this indication has been removed from labeling. **Non-Small Cell Lung Cancer:** Criteria was added for patients with recurrent and advanced disease.	09/13/2023

	Differentiated Thyroid Cancer: This condition of approval was previously titled "thyroid cancer." The requirement that the patient has unresectable, recurrent, or metastatic disease was added. The criteria for anaplastic and medullary thyroid cancer were moved to "other uses with supportive evidence" section. A note was added with types of differentiated thyroid cancer. **Anaplastic Thyroid Cancer.** This indication was separated from the previous condition of approval of thyroid cancer and added to "other uses with supportive evidence." The requirement that the patient has unresectable, recurrent, or metastatic disease was added. **Medullary Thyroid Cancer.** This indication was separated from the previous condition of approval of thyroid cancer and added to "other uses with supportive evidence." Two requirements: 1) the patient has unresectable, recurrent, or metastatic disease and 2) the patient is currently receiving Gavreto were added.	
Annual Revision	**Medullary Thyroid Cancer:** Based on guideline changes, "Patient has rearranged during transfection (*RET*) fusion positive or *RET* mutation-positive disease" was changed to "The disease is positive for rearranged during transfection (*RET*) pathogenic variant."	09/18/2024