DRUG QUANTITY MANAGEMENT POLICY – PER RX

POLICY: Oncology (Oral – Rearranged During Transfection-Targeting Agent) – Gavreto Drug Quantity Management Policy – Per Rx
- Gavreto® (pralsetinib capsules – Rigel)

REVIEW DATE: 05/02/2025

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 WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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 treatment of:[1]
- **Non-small cell lung cancer**, in adults with metastatic *RET* fusion-positive disease as detected by an FDA approved test.
- **Thyroid cancer**, in adults and pediatric patients ≥ 12 years of age with advanced or metastatic *RET* fusion-positive disease who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

Dosing

The recommended dose of Gavreto is 400 mg once daily (QD) given on an empty stomach.[1] Treatment should be continued until disease progression or unacceptable toxicity. If vomiting occurs after Gavreto, the patient should not take

an additional dose but continue with the next dose as scheduled. Dose reductions to either 300 mg, 200 mg, or 100 mg QD may be needed to manage adverse events or drug interactions. Patients taking Gavreto should avoid coadministration with moderate or strong cytochrome P450 (CYP)3A inducers, moderate or strong CYP3A inhibitors, P-gp inhibitors, combined P-gp and moderate/strong CYP3A inhibitors. However, if coadministration with any of these agents cannot be avoided, the dose of Gavreto should be adjusted based on the recommendations in Table 1 and Table 2.

Table 1. Recommended Dose Modifications for Gavreto for Coadministration with CYP3A and/or P-gp Inhibitors.[1]

Current Gavreto Dose	Recommended Dose	
	Combined P-gp and Strong CYP3A Inhibitors	Moderate CYP3A Inhibitors Strong CYP3A Inhibitors P-gp Inhibitors Combined P-gp and Moderate CYP Inhibitors
400 mg QD	200 mg QD	300 mg QD
300 mg QD	200 mg QD	200 mg QD
200 mg QD	100 mg QD	100 mg QD

CYP – Cytochrome P450; QD – Once daily.

Table 2. Recommended Dose Modifications for Gavreto for Coadministration with CYP3A Inducers.[1]

Current Gavreto Dose	Recommended Dose	
	Strong CYP3A Inducers	Moderate CYP3A Inducers
400 mg QD	800 mg QD	600 mg QD
300 mg QD	600 mg QD	500 mg QD
200 mg QD	400 mg QD	300 mg QD

CYP – Cytochrome P450; QD – Once daily.

Gavreto was previously approved for 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.[1] This indication was removed from the label in 2023. However, current thyroid carcinoma guidelines from the National Comprehensive Cancer Network (NCCN) (version 1.2025 – March 27, 2025 recommend the use of Gavreto in several settings at doses similar to the FDA-approved doses.[2]

Availability

Gavreto is available as 100 mg capsules supplied in bottles of 60 or 90 capsules.[1]

POLICY STATEMENT

This Drug Quantity Management program has been developed to promote the safe, effective, and economic use of Gavreto. If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. All approvals are provided for 1 year in duration.

Drug Quantity Limits

Product	Strength and Dosage Form	Retail Maximum Quantity per Rx	Home Delivery Maximum Quantity Per Rx
Gavreto® (pralsetinib capsules)	100 mg capsules	120 capsules	360 capsules

EXCEPTIONS TO THE QUANTITY LIMITS LISTED ABOVE ARE COVERED AS MEDICALLY NECESSARY WHEN THE FOLLOWING CRITERIA ARE MET. ANY OTHER EXCEPTION IS CONSIDERED NOT MEDICALLY NECESSARY.

CRITERIA

1. If the patient is taking a moderate or strong cytochrome P450 (CYP)3A inducer, approve the requested quantity, not to exceed 240 tablets per dispensing at retail or 720 tablets per dispensing per home delivery.
Note: Examples of moderate/strong CYP3A4 inducers include, but are not limited to, apalutamide, carbamazepine, efavirenz, enzalutamide, mitotane, modafinil, phenytoin, rifampin, rifabutin, and St. John's wort.

REFERENCES

1. Gavreto® capsules [prescribing information]. South San Francisco, CA: Rigel; June 2024.
2. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (version 1.2025 – March 27, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 17, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	Policy was updated to reflect the existing quantity limits when a product is obtained via home delivery. No criteria changes.	05/11/2023
Annual Revision	**Gavreto 100 mg capsules:** Override criteria were revised to approve an additional quantity for a patient taking a moderate or strong cytochrome P450 (CYPP)3A inducer. Previously, this criteria approved an additional quantity for a patient taking a strong CYP3A inducer only.	05/22/2024
Annual Revision	The name of the policy was updated to "Oncology (Oral – Rearranged During Transfection-Targeting Agent) – Gavreto Drug Quantity Management Policy – Per Rx". Previously, the policy was named "Oncology – Gavreto Drug Quantity Management Policy – Per Rx". There were no other changes to criteria.	05/02/2025