Access & Reimbursement Guide

Information on Distribution, Patient Support, Coverage, and Access
# Access & Reimbursement Tool Kit

## Table of Contents

### GAVRETO Product Information
- Indications & Important Safety Information ........................................... 3
- Dosing & Administration ................................................................. 4
- Ordering Information .................................................................. 5

### Provider & Patient Support Services with YourBlueprint
- Overview of Support Services Provided for Eligible Patients by Blueprint Medicines ........................................... 6

### Navigating the Approval Process
- Overview .......................................................................................... 10
- Prior Authorization Documentation Checklist ................................... 10

### Denials & Appeals
- Payer Processes ................................................................................. 11
- Sample Coverage Determination Request Letter ............................. 12
- Appeals Documentation Checklist ..................................................... 13

### Coverage for Diagnostic Tests & Related Coding
- Information Related to RET Diagnostic Testing and Coding .......... 14

Please see the Important Safety Information on page 3 and click here to see the full Prescribing Information for GAVRETO.
INDICATIONS
GAVRETO® (pralsetinib) is a kinase inhibitor indicated for treatment of:

- Adult patients with metastatic rearranged during transfection (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-mutant medullary thyroid cancer (MTC) who require systemic therapy
- 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)

These indications are approved under accelerated approval based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

IMPORTANT SAFETY INFORMATION

Interstitial Lung Disease (ILD)/Pneumonitis occurred in 10% of patients who received GAVRETO, including 2.7% with Grade 3/4, and 0.5% with fatal reactions. Monitor for pulmonary symptoms indicative of ILD/pneumonitis. Withhold GAVRETO and promptly investigate for ILD in any patient who presents with acute or worsening of respiratory symptoms (e.g., dyspnea, cough, and fever). Withhold, reduce dose or permanently discontinue GAVRETO based on severity of confirmed ILD.

Hypertension occurred in 29% of patients, including Grade 3 hypertension in 14% of patients. Overall, 7% had their dose interrupted and 3.2% had their dose reduced for hypertension. Treatment-emergent hypertension was most commonly managed with anti-hypertension medications. Do not initiate GAVRETO in patients with uncontrolled hypertension. Optimize blood pressure prior to initiating GAVRETO. Monitor blood pressure after 1 week, at least monthly thereafter and as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue GAVRETO based on the severity.

Hepatotoxicity: Serious hepatic adverse reactions occurred in 2.1% of patients treated with GAVRETO. Increased aspartate aminotransferase (AST) occurred in 69% of patients, including Grade 3/4 in 5% and increased alanine aminotransferase (ALT) occurred in 46% of patients, including Grade 3/4 in 6%. The median time to first onset for increased AST was 15 days (range: 5 days to 1.5 years) and increased ALT was 22 days (range: 7 days to 1.7 years). Monitor AST and ALT prior to initiating GAVRETO, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose or permanently discontinue GAVRETO based on severity.

Grade ≥ 3 hemorrhagic events occurred in 2.5% of patients treated with GAVRETO including one patient with a fatal hemorrhagic event. Permanently discontinue GAVRETO in patients with severe or life-threatening hemorrhage.

Tumor Lysis Syndrome (TLS): Cases of TLS have been reported in patients with medullary thyroid carcinoma receiving GAVRETO. Patients may be at risk of TLS if they have rapidly growing tumors, a high tumor burden, renal dysfunction, or dehydration. Closely monitor patients at risk, consider appropriate prophylaxis including hydration, and treat as clinically indicated.

Impaired wound healing can occur in patients who receive drugs that inhibit the vascular endothelial growth factor (VEGF) signaling pathway. Therefore, GAVRETO has the potential to adversely affect wound healing. Withhold GAVRETO for at least 5 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of GAVRETO after resolution of wound healing complications has not been established.

Based on findings from animal studies and its mechanism of action, GAVRETO can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with GAVRETO and for 2 weeks after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with GAVRETO and for 1 week after the final dose. Advise women not to breastfeed during treatment with GAVRETO and for 1 week after the final dose.

Common adverse reactions (≥25%) were constipation, hypertension, fatigue, musculoskeletal pain and diarrhea.

Common Grade 3/4 laboratory abnormalities (≥2%) were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased phosphate, decreased calcium (corrected), decreased sodium, increased AST, increased ALT, decreased platelets and increased alkaline phosphatase.

Avoid coadministration of GAVRETO with strong CYP3A inhibitors or combined P-gp and strong CYP3A inhibitors. If coadministration cannot be avoided, reduce the GAVRETO dose. Avoid coadministration of GAVRETO with strong CYP3A inducers. If coadministration cannot be avoided, increase the GAVRETO dose.
DOSSING

The recommended starting dose is 400 mg orally once daily on an empty stomach (no food intake for at least 2 hours before and at least 1 hour after taking GAVRETO).

Select patients for treatment with GAVRETO based on the presence of RET positivity.

Recommended dosage reductions for GAVRETO for adverse reactions

<table>
<thead>
<tr>
<th>Dose Reduction</th>
<th>Recommended Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>300 mg once daily</td>
</tr>
<tr>
<td>Second</td>
<td>200 mg once daily</td>
</tr>
<tr>
<td>Third</td>
<td>100 mg once daily</td>
</tr>
</tbody>
</table>

Permanently discontinue GAVRETO in patients who are unable to tolerate 100 mg taken orally once daily.

Recommended dosage modifications for adverse reactions

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Severity*</th>
<th>Dosage Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILD/Pneumonitis</td>
<td>Grade 1 or 2</td>
<td>Withhold GAVRETO until resolution. Resume by reducing the dose by 100 mg. Permanently discontinue GAVRETO for recurrent ILD/pneumonitis.</td>
</tr>
<tr>
<td></td>
<td>Grade 3 or 4</td>
<td>Permanently discontinue for confirmed ILD/pneumonitis.</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Grade 3</td>
<td>Withhold GAVRETO for Grade 3 hypertension that persists despite optimal antihypertensive therapy. Resume at a reduced dose when hypertension is controlled.</td>
</tr>
<tr>
<td></td>
<td>Grade 4</td>
<td>Discontinue GAVRETO.</td>
</tr>
<tr>
<td>Hepatotoxicity</td>
<td>Grade 3 or 4</td>
<td>Withhold GAVRETO and monitor AST/ALT once weekly until resolution to Grade 1 or baseline. Resume at reduced dose. If hepatotoxicity recurs at Grade 3 or higher, discontinue GAVRETO.</td>
</tr>
<tr>
<td>Hemorrhagic Events</td>
<td>Grade 3 or 4</td>
<td>Withhold GAVRETO until recovery to baseline or Grade 0 or 1. Discontinue GAVRETO for severe or life-threatening hemorrhagic events.</td>
</tr>
<tr>
<td>Other Adverse Reactions</td>
<td>Grade 3 or 4</td>
<td>Withhold GAVRETO until improvement to ≤ Grade 2. Resume at reduced dose. Permanently discontinue for recurrent Grade 4 adverse reactions.</td>
</tr>
</tbody>
</table>

Recommended dosage modifications for GAVRETO for coadministration with combined P-gp and strong CYP3A inhibitors

<table>
<thead>
<tr>
<th>Current GAVRETO Dosage</th>
<th>Recommended GAVRETO Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>400 mg orally once daily</td>
<td>200 mg orally once daily</td>
</tr>
<tr>
<td>300 mg orally once daily</td>
<td>200 mg orally once daily</td>
</tr>
<tr>
<td>200 mg orally once daily</td>
<td>100 mg orally once daily</td>
</tr>
</tbody>
</table>

Recommended dosage modification for use with strong CYP3A inducers

Avoid coadministration of GAVRETO with strong CYP3A inducers. If coadministration with a strong CYP3A inducer cannot be avoided, increase the starting dose of GAVRETO to double the current GAVRETO dosage starting on Day 7 of coadministration of GAVRETO with the strong CYP3A inducer. After the inducer has been discontinued for at least 14 days, resume GAVRETO at the dose taken prior to initiating the strong CYP3A inducer.

*Adverse reactions graded by the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03
GAVRETO Ordering Information

GAVRETO is available through a select network of specialty pharmacies and distributors.

**Specialty Pharmacy Provider Network**

To prescribe GAVRETO, please complete the YourBlueprint™ Enrollment Form and fax it to 1-866-370-3082 or send your patient’s prescription to one of the authorized specialty pharmacies listed below. Please do not fax the YourBlueprint Enrollment Form directly to the specialty pharmacy.

**Biologics**

Phone: 1-800-850-4306
Fax: 1-800-823-4506

**PANTHERx Rare Pharmacy**

Phone: 1-833-918-2015
Fax: 1-866-984-0627

**Specialty Distribution Network**

The following specialty distributors are authorized to drop-ship GAVRETO to qualified accounts.

**Physician Dispensing Offices**

Cardinal Health Specialty Distribution
Phone: 1-855-855-0708
Email: GMB-SPD-Specialty @cardinalhealth.com

McKesson Specialty Health
Phone: 1-855-477-9800
Email: mshcustomercareteam @mckesson.com

Oncology Supply
Phone: 1-800-633-7555
Email: custserv@oncologysupply.com

Blueprint Medicines and Genentech do not endorse the use of any particular specialty pharmacy or specialty distributor listed above and make no representation or guarantee of services or coverage of any product.

**GAVRETO Product Information**

GAVRETO capsules are supplied in the following quantities based on daily dosage. The recommended starting dose of GAVRETO is 400 mg (4 capsules) once daily, which is equivalent to two 60-count bottles for a 30-day supply. Please see full Prescribing Information for complete dosing instructions.

<table>
<thead>
<tr>
<th>Dosage Strength</th>
<th>Capsules per Bottle</th>
<th>NDC Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 mg</td>
<td>60</td>
<td>10-digit code: 72064-210-60 11-digit code: 72064-0210-60</td>
<td>100 mg, light blue opaque, immediate-release hydroxypropyl methylcellulose (HPMC) hard capsule, printed with &quot;BLU-667&quot; on the body and &quot;100 mg&quot; on the cap, available in bottles of 60 capsules.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10-digit code: 72064-210-90 11-digit code: 72064-0210-90</td>
<td>100 mg, light blue opaque, immediate-release hydroxypropyl methylcellulose (HPMC) hard capsule, printed with &quot;BLU-667&quot; on the body and &quot;100 mg&quot; on the cap, available in bottles of 90 capsules.</td>
</tr>
</tbody>
</table>

The blue zero converts the 10-digit NDC code to the 11-digit NDC code. Some payers may require each NDC to be listed on the claim. Payer requirements regarding the use of NDCs may vary. Electronic data exchange generally requires use of the 11-digit NDC.

Storage: Store at 20°C to 25°C (68°F to 77°F); excursions are permitted from 15°C to 30°C (59°F to 86°F). Protect from moisture.

Please visit GAVRETOHCP.com to see the full Prescribing Information for GAVRETO.

These codes are not all-inclusive; appropriate codes can vary by patient, setting of care and payer; correct coding is the responsibility of the provider submitting the claim for the item or service; please check with the payer to verify codes and special billing requirements; Blueprint Medicines and Genentech do not make any representation or guarantee concerning reimbursement or coverage for any item.
Provider & Patient Support Services with YourBlueprint

ACCESS SUPPORT FOR YOUR OFFICE
YourBlueprint Case Managers work with you and your patients to provide seamless support throughout the journey to access treatment.

Your dedicated Case Manager can help with:

- Reimbursement Assistance including investigating your patient’s insurance benefits, including prescription drug coverage, out-of-pocket costs, and pharmacy options
- Guidance and support through the prior authorization and appeals process
- Connecting patients with financial assistance options
- Supplying helpful resources, such as sample letters of medical necessity
- Ensure that you are kept up to date throughout the process

FINANCIAL ASSISTANCE OPTIONS

- Co-Pay Assistance Program – Provides assistance for eligible, commercially insured patients that reduces their out-of-pocket costs (co-pay, co-insurance, or deductible) to as little as $0
- Patient Assistance Program – Provides GAVRETO at no cost for eligible patients who are uninsured or have limited coverage

TEMPORARY TREATMENT PROGRAMS

- QuickStart Program – Provides newly-prescribed, eligible patients a 15-day no cost supply of GAVRETO in the event of a coverage-related delay
- Coverage Interruption Program – Provides existing prescribed eligible patients a short-term supply of GAVRETO at no cost in the event of a temporary lapse in coverage

DEDICATED CASE MANAGER

A single point of contact for providers and patients that can:

- Handle patient enrollments into YourBlueprint’s Financial Assistance and Temporary Treatment Programs
- Follow up on missing information
- Provide status and coverage updates to you and your patients
- Conduct one-on-one monthly check-in calls with patients that opt-in to this service

TWO SIMPLE WAYS TO GET STARTED

CALL 1-888-BLUPRNT (1-888-258-7768) Monday—Friday 8 AM—8 PM Eastern Time (ET) to speak with a case manager

OR

Visit: www.YourBlueprint.com/HCP

A completed enrollment form must be submitted for your patient to access reimbursement support, QuickStart, Coverage Interruption, and PAP. Co-pay support does not require enrollment.
YourBlueprint Enrollment

- You may enroll your patient into YourBlueprint via the enrollment form, which can be accessed at: [https://www.yourblueprint.com/wp-content/uploads/GAVRETO_YourBlueprint_Enrollment_Form.pdf](https://www.yourblueprint.com/wp-content/uploads/GAVRETO_YourBlueprint_Enrollment_Form.pdf)
- Be sure to obtain your patient’s consent for enrollment in person, online, or in writing

THE ENROLLMENT FORM CAN BE SUBMITTED IN ANY OF THESE FOUR (4) WAYS:

- Fax the completed forms to 1-866-370-3082
- OR Scan / photograph and email the forms to info@yourblueprint.com
- OR Mail the forms to: YourBlueprint PO Box 15590 Pittsburgh, PA 15244
- OR Log on to covermymeds.com using your account, search prescribed drug name and select Start Enrollment

- A dedicated Case Manager will confirm your patient’s enrollment and initiate the requested services

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YourBlueprint is staffed with dedicated Case Managers who are available at 1-888-BLUPRNT (1-888-258-7768) Monday—Friday 8 AM—8 PM ET. For additional information, please visit www.YourBlueprint.com/HCP

Please see the Important Safety Information on page 3 and click here to see the full Prescribing Information for GAVRETO.
Program Overview and Eligibility

FINANCIAL ASSISTANCE

YourBlueprint Co-Pay Assistance Program

This program helps eligible, commercially insured patients pay as little as $0 for their prescription.
- Patients can pay as little as $0 monthly co-pay if they qualify for the program
- There are no patient income requirements for the Co-Pay Program

Program eligibility criteria are:
- The patient must be a resident of the U.S. or a U.S. territory
- The patient must have commercial or private insurance
- The patient cannot be enrolled in any governmental program, such as patients enrolled in Medicare Part D and patients whose prescription is paid for by Medicare, Medicaid, Medigap, CHAMPUS, Department of Defense (DoD), TRICARE, Veterans Affairs (VA), Children’s Health Insurance Program (CHIP), the Indian Health Service, or a state pharmaceutical assistance program
- The program is not valid where prohibited by law
- This program may not be combined with any third-party rebate, coupon, or offer
- Enroll your patient in the YourBlueprint Co-Pay Program at: https://portaltrialcard.com/yourblueprint/specialty-pharmacy/

YourBlueprint Patient Assistance Program

The YourBlueprint Patient Assistance Program (PAP) helps eligible patients who lack insurance coverage or are ineligible for the Co-Pay Assistance Program to receive GAVRETO at no cost.

The PAP is designed for:
- Uninsured patients
- Patients with commercial insurance or Medicare Part D who do not have coverage for GAVRETO
- Medicare or commercial patients with out of pocket costs that exceed their financial means

YourBlueprint will screen patients to determine their eligibility for the PAP. Program eligibility criteria are:
- The patient must be a resident of the U.S. or a U.S. territory
- The patient must have a valid GAVRETO prescription from their healthcare provider
- The patient must have an enrollment consent and signed HIPAA Authorization on file
- The patient only needs to provide consent on a separate form if they are not in the office to sign the Enrollment Form
- The patient must meet the PAP financial eligibility criteria
TEMPORARY TREATMENT PROGRAMS

YourBlueprint QuickStart

The QuickStart Program provides a no-cost 15-day supply of GAVRETO to eligible patients new to therapy who experience an insurance coverage delay of at least three (3) business days. The initial QuickStart prescription can be refilled 3 times (60 days total supply). Should your patient need an additional number of QuickStart shipments, contact YourBlueprint for next steps.

Program eligibility criteria are:
- The program requires a coverage delay of at least three (3) business days (starting when the PA is submitted) before the patient can qualify
- Patients must have commercial or government insurance to utilize this program
- There are no patient income requirements for the QuickStart Program
- The patient must have a diagnosis of NSCLC, MTC, or thyroid cancer
- The patient must reside in the U.S. or a U.S. territory

YourBlueprint Coverage Interruption Program

The Coverage Interruption Program provides a no-cost 15-day supply of therapy to eligible patients already on therapy who experience a lapse in insurance coverage up to a maximum 60-day supply.

Program eligibility criteria are:
- Patient must be experiencing a temporary lapse in insurance coverage for GAVRETO related to one or more of the following reasons:
  - Lapsed Prior Authorization (PA) with a reasonable expectation that the PA will be renewed by the payer
  - Change in commercial insurance plan and enrollment not completed or coverage is in the process of being confirmed
  - Newly eligible for Medicare, Medicaid, or other government health plan and enrollment not completed or coverage in the process of being confirmed
  - Newly uninsured and the gap in insurance is reasonably expected to be temporary such as a gap associated with a delayed job change or extended foreign travel during which time patient is unable to refill the prescription.
- There are no patient income requirements for the Coverage Interruption Program
- The patient must have a diagnosis of NSCLC, MTC, or thyroid cancer
- The patient must reside in the U.S. or its territories

You may enroll your patient into YourBlueprint via the enrollment form, which can be accessed at www.YourBlueprint.com/HCP

PA, prior authorization

FOR CO-PAY ENROLLMENT, PLEASE VISIT PORTAL.TRIALCARD.COM/YOURBLUEPRINT
Navigating the Approval Process

YourBlueprint can help with questions you may have about the approval process, including prior authorization (PA) and navigating coverage denials for GAVRETO.

Contact a YourBlueprint Case Manager at 1-888-BLUPRNT (1-888-258-7768) for assistance.

**TYPICAL APPROVAL PROCESS**

1. **HCP Prescribes GAVRETO**
2. **Insurance Verification Completed to Confirm Coverage and Benefits**
3. **Prior Authorization for GAVRETO Submitted**
   - **Prior Authorization Approved**
   - **Prior Authorization Denied**
4. **Patient Proceeds with GAVRETO Acquisition**
5. **HCP May Navigate a PA Denial (see below)**

**PRIOR AUTHORIZATION (PA)**

Approval processes and prior authorization requirements vary by payer. This checklist is provided to help simplify the prior authorization process for GAVRETO.

The information shown below may be required by payers to obtain a prior authorization, however individual payers may have their own forms or requirements.

In the case of a prior authorization denial or need for a formulary exception request, detailed information about those processes and documentation requirements are found in the Denials & Appeals section of this tool kit.

**This checklist is provided to help you navigate the approval process in the likely event that GAVRETO requires a prior authorization.**

Complete and submit the prior authorization form as required by the payer that may include:

- Patient’s name
- Patient’s insurance company and policy number
- Patient’s date of birth
- Patient’s diagnosis / ICD-10 code(s)
- Provider details, specialty, contact information, and NPI number
- GAVRETO NDC, dosage, route of administration, and estimated duration of treatment

If not part of the prior authorization form it may be helpful to include the following:

- Full Prescribing Information
- Information related to the treatment decision
- Peer-reviewed journal articles
- Clinical practice guidelines including mutational testing

Include a comprehensive letter of medical necessity written on the provider’s letterhead that includes the following:

- Rationale for Treatment with GAVRETO
- Patient-specific medical history related to the ICD-10 code
- Patient’s diagnostic test results
- Previous treatments (names), duration, and response or reason for discontinuation
- Patient’s current symptoms or condition

If a prior authorization has been denied, see page 13 for an appeals checklist or available for download at www.YourBlueprint.com/HCP

Please see the Important Safety Information on page 3 and click here to see the full Prescribing Information for GAVRETO.
Denials & Appeals

Here are some common reasons for coverage denials that may be resolved through the appeals or formulary exception request processes.

- **New Drug**
  - Not yet reviewed by payer & considered non-formulary

- **Prior Authorization Required**
  - PA not submitted with coverage request

- **Missing Information**
  - Coverage request is missing information or there was a data error

- **Insurance Information**
  - Patient’s insurance changed or coverage has lapsed

If a request for coverage of GAVRETO is denied, it may be resolved through the standard appeals process, which consists of three levels.

1. **1st Level Appeal**
   - Contact payer to request a consideration of the denial. This may include a “peer to peer” discussion with the medical reviewer.

2. **2nd Level Appeal**
   - At this step, the appeal is typically reviewed by a medical director of the plan to determine if the request should be accepted within the coverage guidelines.

3. **Independent External Review**
   - If attempts to appeal a coverage decision have not been successful, an external review can be conducted by an independent third party to make a binding decision.

Patients may also assist with the appeals process.

If a request for coverage of GAVRETO is denied, patients can contact their employer’s benefits administrator or their health plan for additional information on how to appeal the payer’s decision or to request an external review.

In some cases it may be necessary to submit a formulary exception request to the payer.

Common processes for Commercial payers and Medicare Part D are described in this toolkit.
### SAMPLE LETTER OF MEDICAL NECESSITY
For use when submitting a PA (see checklist on page 10)

**Sample Letter of Medical Necessity**

- [Patient's Name]
- [Address]
- [City, State, Zip Code]
- [Name of Insurance Company]
- [NPI]

**To:** [Name of Medical Director]

I am writing to request a formulary exception for [INSERT PRODUCT™ (generic name)] for [Patient's Name]. I am requesting that [the plan] consider [INSERT PRODUCT™ (generic name)] a medically necessary and appropriate drug for [Patient's Name].

**Summary of Medical History**

[Include a brief description of patient's medical history and attach patient's chart notes].

**Treatment Rationale**

[Include a brief description of patient’s medical history and attach patient’s chart notes].

**Please call me or my office staff at [Physician's telephone number OR Practice telephone number] if I need any additional information. I look forward to receiving your timely response and approval for treatment with [INSERT PRODUCT™ (generic name)].**

Sincerely,

[Prescriber’s Name]

[Prescriber’s Signature]

[Attachments: Enclose supporting documentation]

### SAMPLE LETTER OF APPEAL
For use when appealing a coverage denial (see page 11)

**Sample Letter of Appeal**

- [Physician Practice Letterhead at the top of the letter]
- [Date]
- [Name of Medical Director]
- [Name of Insurance Company]
- [City, State, Zip Code]

**To:** [Name of Medical Director]

Please consider this letter an appeal of your decision to deny coverage for [INSERT PRODUCT™ (generic name)] for [Patient's Name]. I am requesting that you review my patient’s file. I am writing to request approval for treatment with [INSERT PRODUCT™ (generic name)] for [Patient's Name].

**Summary of Medical History**

[Include a brief description of patient’s medical history and attach patient’s chart notes].

**Treatment Rationale**

[Include a brief description of patient’s medical history and attach patient’s chart notes].

**Please call me or my office staff at [Physician’s telephone number OR Practice telephone number] if you need any additional information. I look forward to receiving your timely response and approval for treatment with [INSERT PRODUCT™ (generic name)] for [Patient's Name]**

Sincerely,

[Prescriber’s Name]

[Prescriber’s Signature]

[Attachments: Enclose supporting documentation]

### SAMPLE FORMULARY EXCEPTION REQUEST
For use when requesting a coverage exception when a drug is not yet covered on formulary (see page 11)

**Sample Formulary Exception Request**

- [Physician Practice Letterhead at the top of the letter]
- [Date]
- [Name of Medical/Pharmacy Director]
- [Name of Insurance Company]
- [City, State, Zip Code]

**To:** [Name of Medical Director]

I am writing to request a formulary exception for [INSERT PRODUCT™ (generic name)] for [Patient's Name].

**Summary of Medical History**

[Include a brief description of patient’s medical history and attach patient’s chart notes].

**Treatment Rationale**

[Include a brief description of patient’s medical history and attach patient’s chart notes].

**Please call me or my office staff at [Physician’s telephone number OR Practice telephone number] if you need any additional information. I look forward to receiving your timely response and approval for treatment with [INSERT PRODUCT™ (generic name)] for [Patient's Name].**

Sincerely,

[Prescriber’s Name]

[Prescriber’s Signature]

[Attachments: Enclose supporting documentation]

Electronic versions of these sample letters are available on [www.YourBlueprint.com/HCP](http://www.YourBlueprint.com/HCP).
If the patient’s health plan has not established coverage or has denied coverage for GAVRETO it may be necessary to submit an appeal or a formulary exception request.

The information below includes general information, however individual payers may have their own forms or documentation requirements.

REVIEW THE DENIAL LETTER OR NOTIFICATION RECEIVED
Understand why coverage for GAVRETO was denied and consider the following common questions:
- Has coverage for GAVRETO been established for patient’s condition/diagnosis?
- Did the prior authorization include all information as required by the payer or was information missing?
- Was the insurance information correct or did the patient’s insurance change or coverage lapse?

INITIATE THE APPEALS PROCESS
Understand the payer’s specific process or requirements:
- Use payer-specific forms, if available
- Follow payer’s instructions on the appeals submission process and filing timelines
- Include all required documentation such as
  - Letter of medical necessity
  - Biomarker status
  - Treatment rationale

A sample letter is provided in this toolkit and available for download at www.YourBlueprint.com/HCP

The sample letter is provided for information only and supplying the information with requests does not guarantee coverage for GAVRETO and the information is not intended to substitute for or influence the physician’s independent clinical decision.
Diagnostic Testing for RET

GAVRETO™ (pralsetinib) is a kinase inhibitor indicated for treatment of:

- Adult patients with metastatic rearranged during transfection (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-mutant medullary thyroid cancer (MTC) who require systemic therapy
- 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)

These indications are approved under accelerated approval based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

Diagnostic tests for the identification of RET alteration in ARROW

<table>
<thead>
<tr>
<th>RET alteration determined by</th>
<th>Percent of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RET+ NSCLC</td>
</tr>
<tr>
<td></td>
<td>Previously platinum treated (n=87)</td>
</tr>
<tr>
<td>Next Generation Sequencing (NGS)</td>
<td>77%</td>
</tr>
<tr>
<td>Fluorescence in situ hybridization (FISH)</td>
<td>21%</td>
</tr>
<tr>
<td>Polymerase chain reaction (PCR) sequencing</td>
<td>–</td>
</tr>
<tr>
<td>Other</td>
<td>2%</td>
</tr>
</tbody>
</table>

The efficacy and safety of GAVRETO was evaluated in patients with RET-positive metastatic NSCLC, advanced or metastatic RET-positive mutant MTC, and RET-positive advanced or metastatic thyroid cancer in ARROW, a multicenter, non-randomized, open-label, multi-cohort clinical trial. Identification of a RET gene fusion or mutation was determined by local testing.

Next Generation Sequencing (NGS)

NGS is a favorable method for simultaneous detection of mutations and any RET fusions in a single test of solid tumor, blood or plasma within the clinical setting, where a growing number of actionable biomarkers are emerging. Key advantages to NGS include detection and identification of known and unknown fusions; simultaneous detection of multiple targets and alteration types; minimal tissue use; and the inclusion of RET on many panels.

Several commercial reference labs currently offer NGS testing that can detect RET fusions and mutations including: Labcorp/Integrated Oncology, Neogenomics, Foundation Medicine, Caris Life Sciences, Tempus, Quest, Guardant, Mayo Medical Labs, ARUP, PathGroup, Biodesix, and Invata.

Fluorescence in situ hybridization (FISH)

FISH can also be used to detect RET alterations. While FISH can detect any target-specific fusion, it does not detect fusion partners and it cannot detect mutations.

Coverage for diagnostic tests to identify RET alterations may require prior authorization.
OVERVIEW OF COVERAGE BY PAYER TYPE

<table>
<thead>
<tr>
<th>Payer Type</th>
<th>Coverage for Diagnostic Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial</td>
<td>Coverage varies, but trends show an increase in coverage for standardized testing modalities relevant to RET, including NGS</td>
</tr>
<tr>
<td>Medicare</td>
<td>Favorable coverage with a National Coverage Determination</td>
</tr>
<tr>
<td>Medicaid</td>
<td>Varies state by state</td>
</tr>
</tbody>
</table>

Payer restrictions on the use of NGS is variable and may include the following:
- Prior Authorization
- Limit ordering of the tests to specific physician specialties (ex: Oncologist)
- Limited to specific tumor types
- Limit use to cancer patients of a specific stage or severity
- Step edit after first-line treatment failure

Contact your Blueprint Medicines Area Business Manager or Case Manager at YourBlueprint for additional support.

Coding for Diagnostic Tests

That May Identify RET Fusions and/or Mutations

The codes provided below are information only.
Coding is a clinical decision that can only be made by a provider based on the condition of the patient being treated.
The use of the following codes does not suggest or guarantee reimbursement.

CURRENT PROCEDURAL TERMINOLOGY (CPT)¹ CODES FOR RET TESTING MODALITIES

<table>
<thead>
<tr>
<th>Test</th>
<th>CPT Code</th>
<th>Brief Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLA</td>
<td>0022U</td>
<td>Oncomine™ Dx Target Test, Thermo Fisher Scientific: Targeted genomic sequence analysis panel of 23 genes including rearrangements</td>
</tr>
<tr>
<td>NGS</td>
<td>81445</td>
<td>5-50 genes</td>
</tr>
<tr>
<td></td>
<td>81455</td>
<td>&gt; 50 genes</td>
</tr>
<tr>
<td>FISH</td>
<td>88365</td>
<td>Initial single probe stain procedure</td>
</tr>
<tr>
<td></td>
<td>88364</td>
<td>Each additional single probe stain procedure</td>
</tr>
<tr>
<td></td>
<td>88367</td>
<td>Automated, computer-assisted technology, per specimen; initial single probe stain procedure</td>
</tr>
<tr>
<td></td>
<td>88368</td>
<td>Manual, per specimen, initial single probe stain procedure</td>
</tr>
</tbody>
</table>

¹ American Medical Association. CPT® 2020 Professional Edition
## Diagnosis Codes

For the Identification of NSCLC and Thyroid Cancer, Including MTC

Based on the indications for GAVRETO, examples of diagnosis codes that may be appropriate are listed below. The codes provided below are information only. Coding is a clinical decision that can only be made by a provider based on the condition of the patient being treated. The use of the following codes does not suggest or guarantee reimbursement.

### DIAGNOSIS CODES (ICD-10)¹

#### NSCLC

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C34.00</td>
<td>Malignant neoplasm of unspecified main bronchus</td>
</tr>
<tr>
<td>C34.01</td>
<td>Malignant neoplasm of right main bronchus</td>
</tr>
<tr>
<td>C34.02</td>
<td>Malignant neoplasm of left main bronchus</td>
</tr>
<tr>
<td>C34.10</td>
<td>Malignant neoplasm of upper lobe, unspecified bronchus or lung</td>
</tr>
<tr>
<td>C34.11</td>
<td>Malignant neoplasm of upper lobe, right bronchus or lung</td>
</tr>
<tr>
<td>C34.12</td>
<td>Malignant neoplasm of upper lobe, left bronchus or lung</td>
</tr>
<tr>
<td>C34.2</td>
<td>Malignant neoplasm of middle lobe, bronchus or lung</td>
</tr>
<tr>
<td>C34.30</td>
<td>Malignant neoplasm of lower lobe, unspecified bronchus or lung</td>
</tr>
<tr>
<td>C34.31</td>
<td>Malignant neoplasm of lower lobe, right bronchus or lung</td>
</tr>
<tr>
<td>C34.32</td>
<td>Malignant neoplasm of lower lobe, left bronchus or lung</td>
</tr>
</tbody>
</table>

#### Thyroid Cancer, Including MTC

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C73</td>
<td>Malignant neoplasm of thyroid gland</td>
</tr>
<tr>
<td>D09.3</td>
<td>Carcinoma in situ of thyroid and other endocrine glands</td>
</tr>
<tr>
<td>D44. 0</td>
<td>Neoplasm of uncertain behavior of thyroid gland</td>
</tr>
<tr>
<td>Z85.180</td>
<td>Personal history of malignant neoplasm of thyroid</td>
</tr>
</tbody>
</table>

Diagnosis codes shown are not RET alteration specific.


Please see the Important Safety Information on page 3 and the full Prescribing Information for GAVRETO.