NSCLC=non–small cell lung cancer; RET=rearranged during transfection.

DOSING & ADMINISTRATION GUIDE

Learn more about managing treatment with GAVRETO.

INDICATIONS

GAVRETO (pralsetinib) is indicated for the 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 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).

SELECT SAFETY INFORMATION

WARNING: SERIOUS INFECTIONS, INCLUDING OPPORTUNISTIC INFECTIONS

GAVRETO may increase the risk for serious infections, including bacterial, fungal, viral and opportunistic infections, which can lead to hospitalization or death. Withhold, reduce the dose or permanently discontinue GAVRETO based on severity.

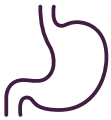
Please see additional Important Safety Information throughout and the accompanying Full Prescribing Information, including Boxed Warning.

The only once-daily RET inhibitor[1]

Recommended starting dose: 400 mg once daily

Four 100-mg capsules

Capsules are not actual size.



Patients should take GAVRETO on an empty stomach (no food intake for at least 2 hours before and at least 1 hour after taking GAVRETO).

- Continue treatment until disease progression or until unacceptable toxicity
- If a dose of GAVRETO is missed, it can be taken as soon as possible on the same day. Resume the regular daily dose schedule for GAVRETO the next day
- Advise patients not to take an additional dose if vomiting occurs after taking GAVRETO but continue with the next dose as scheduled
- Select patients for treatment with GAVRETO based on the presence of a RET gene fusion
- An FDA-approved test for the detection of RET gene fusion (thyroid cancer) is not currently available

SELECT SAFETY INFORMATION

Warnings and Precautions

Serious Infections, Including Opportunistic Infections: GAVRETO may increase the risk for serious infections, including fatal and opportunistic infections. In the AcceleRET-Lung trial, infections occurred in 72% of patients who received GAVRETO, including 18% with Grade 3 and 3.7% with Grade 4 and 7% with fatal outcomes. Among the patients who received chemotherapy/immunotherapy, infections occurred in 52%, including 10% with Grade 3. Infections in the GAVRETO arm included pneumonia, urinary tract infection, opportunistic infections (such as pneumocystis jirovecii pneumonia and fungal infections) and others. Monitor patients for signs and symptoms of infection and treat appropriately. Withhold, reduce the dose, or permanently discontinue GAVRETO based on severity.

Interstitial Lung Disease (ILD)/Pneumonitis: Severe, life-threatening, and fatal ILD/pneumonitis can occur in patients treated with GAVRETO. Pneumonitis occurred in 12% of patients who received GAVRETO, including 3.3% with Grade 3-4, and 0.2% 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.

Please see additional Important Safety Information throughout and the accompanying Full Prescribing Information, including Boxed Warning.

GAVRETO® pralsetinib 100mg capsules

Dosage modifications with GAVRETO[1]

GAVRETO is available in 100-mg capsules, giving you the opportunity to modify dosage based on individual patient needs

First reduction:
300 mg once daily

Second reduction:
200 mg once daily

Final reduction:
100 mg once daily

Capsules are not actual size.

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

SELECT SAFETY INFORMATION

Warnings and Precautions (cont'd)

Hypertension: Occurred in 35% of patients, including Grade 3 hypertension in 18% of patients. Overall, 8% had their dose interrupted and 4.8% 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 1.5% of patients treated with GAVRETO. Increased aspartate aminotransferase (AST) occurred in 49% of patients, including Grade 3 or 4 in 7% and increased alanine aminotransferase (ALT) occurred in 37% of patients, including Grade 3 or 4 in 4.8%. The median time to first onset for increased AST was 15 days (range: 5 days to 2.5 years) and increased ALT was 24 days (range: 7 days to 3.7 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.

Hemorrhagic Events: Serious, including fatal, hemorrhagic events can occur with GAVRETO. Grade ≥3 events occurred in 4.1% of patients treated with GAVRETO including one patient with a fatal hemorrhagic event. Permanently discontinue GAVRETO in patients with severe or life-threatening hemorrhage.

Please see additional Important Safety Information throughout and the accompanying Full Prescribing Information, including Boxed Warning.

GAVRETO® pralsetinib 100mg capsules

GAVRETO dosing can be modified in response to adverse reactions[1]

Recommended dosage modifications for adverse reactions

Adverse Reaction	Severity*	Dosage Modification
Serious Infections, including Opportunistic Infections	Grade 2 or 3	Withhold GAVRETO until resolution Resume at a reduced dose.
	Grade 4	Permanently discontinue GAVRETO
ILD/Pneumonitis	Grade 1 or 2	Withhold GAVRETO until resolution. Resume by reducing the dose as shown in Table 1 of the GAVRETO full Prescribing Information. Permanently discontinue GAVRETO for recurrent ILD/pneumonitis.
	Grade 3 or 4	Permanently discontinue for confirmed ILD/pneumonitis.

Pneumonitis occurred in 12% of 540 patients who received GAVRETO at 400 mg once daily. Median time to onset was 16.1 weeks and median time to resolution was 4.3 weeks (95% CI: 6.3-22.4).[2]

Hypertension	Grade 3	Withhold GAVRETO for Grade 3 hypertension that persists despite optimal antihypertensive therapy. Resume at a reduced dose when hypertension is controlled.
	Grade 4	Discontinue GAVRETO.
Hepatotoxicity	Grade 3 or 4	Withhold GAVRETO and monitor AST/ALT once weekly until resolution to Grade 1 or baseline. Resume at reduced dose (Table 1). For recurrent events at Grade 3 or higher, discontinue GAVRETO.
Hemorrhagic Events	Grade 3 or 4	Withhold GAVRETO until recovery to baseline or Grade 0 or 1. Discontinue GAVRETO for severe or life-threatening hemorrhagic events.
Other Adverse Reactions	Grade 3 or 4	Withhold GAVRETO until improvement to ≤ Grade 2. Resume at reduced dose (Table 1). Permanently discontinue for recurrent Grade 4 adverse reactions.

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

ALT=alanine aminotransferase; AST=aspartate aminotransferase; CI=confidence interval.

Please see additional Important Safety Information throughout and the accompanying Full Prescribing Information, including Boxed Warning.

GAVRETO® pralsetinib 100mg capsules

Recommended dose modification for coadministration[1]

Coadministration with CYP3A and/or P-gp inhibitors

Avoid coadministration of GAVRETO with strong or moderate CYP3A inhibitors, P-gp inhibitors, combined P-gp and moderate CYP3A inhibitors, and/or combined P-gp and strong CYP3A inhibitors. If coadministration with any of the above inhibitors cannot be avoided, reduce the current dose of GAVRETO as recommended below. After the inhibitor has been discontinued for 3 to 5 elimination half-lives, resume GAVRETO at the dose taken prior to initiating the inhibitor.

Current GAVRETO Dosage	Recommended GAVRETO Dosage When Coadministered With:	
	Combined P-gp and strong CYP3A inhibitors	• Strong CYP3A inhibitors • Moderate CYP3A inhibitors • P-gp inhibitors • Combined P-gp and moderate CYP3A inhibitors
400 mg orally once daily	200 mg orally once daily	300 mg orally once daily
300 mg orally once daily	200 mg orally once daily	200 mg orally once daily
200 mg orally once daily	100 mg orally once daily	100 mg orally once daily

Coadministration with CYP3A inducers

Avoid coadministration of GAVRETO with strong or moderate CYP3A inducers. If coadministration with any of the above inducers cannot be avoided, increase the current dose of GAVRETO as recommended below starting on Day 7 of coadministration of GAVRETO with the inducer. After the inducer has been discontinued for at least 14 days, resume GAVRETO at the dose taken prior to initiating the inducer.

Current GAVRETO Dosage	Recommended GAVRETO Dosage When Coadministered With:	
	Strong CYP3A inducers	Moderate CYP3A inducers
400 mg orally once daily	800 mg orally once daily	600 mg orally once daily
300 mg orally once daily	600 mg orally once daily	500 mg orally once daily
200 mg orally once daily	400 mg orally once daily	300 mg orally once daily

CYP=cytochrome P450; P-gp=P-glycoprotein.

SELECT SAFETY INFORMATION

Warnings and Precautions (cont'd)

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.

Please see additional Important Safety Information throughout and the accompanying Full Prescribing Information, including Boxed Warning.

Safety of GAVRETO was evaluated in 540 patients with RET-altered tumors[1]

- The most common adverse reactions (≥25%) were musculoskeletal pain, constipation, hypertension, diarrhea, fatigue, edema, pyrexia, and cough
- The most common Grades 3-4 laboratory abnormalities (≥2%) were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased phosphate, decreased leukocytes, decreased sodium, increased AST, increased ALT, decreased calcium (corrected), decreased platelets, increased alkaline phosphatase, increased potassium, decreased potassium, and increased bilirubin
- In 34 patients with RET-altered solid tumors, no large mean increase in QTc (>20 ms) was detected in the study

Safety of GAVRETO in 281 patients with RET+ mNSCLC[1]

20% of patients permanently discontinued GAVRETO due to any adverse reaction;
9.6% discontinued due to adverse reactions considered treatment-related by the trial investigator[1,2]

Adverse reactions resulting in permanent discontinuation, which occurred in ≥2% of patients, included pneumonitis (3.2%) and pneumonia (2.8%).

Serious adverse reactions occurred in 65% of patients who received GAVRETO. The most frequent serious adverse reactions (in ≥2% of patients) were pneumonia, anemia, pneumonitis, pyrexia, sepsis, urinary tract infection, coronavirus infection, pleural effusion, dyspnea, musculoskeletal pain, pulmonary embolism, and seizure. Fatal adverse reactions occurred in 7% of patients; fatal adverse reactions, which occurred in >1 patient, included pneumonia (n=8), sepsis (n=3), and COVID (n=3).

51% of patients treated with GAVRETO experienced dose reductions due to adverse reactions

Adverse reactions requiring dosage reductions in ≥2% of patients included anemia, neutropenia, pneumonitis, increased blood creatine phosphokinase, leukopenia, hypertension, fatigue, pneumonia, and lymphopenia.

73% of patients treated with GAVRETO experienced dosage interruptions due to an adverse reaction

Adverse reactions requiring dosage interruption in ≥2% of patients included anemia, pneumonia, pneumonitis, neutropenia, hypertension, increased blood creatine phosphokinase, fatigue, pyrexia, increased AST, increased ALT, coronavirus infection, diarrhea, hypophosphatemia, musculoskeletal pain, thrombocytopenia, dyspnea, hemorrhage, leukopenia, lymphopenia, edema, sepsis, and vomiting.

mNSCLC=metastatic non–small cell lung cancer.

SELECT SAFETY INFORMATION

Warnings and Precautions (cont'd)

Risk of Impaired Wound Healing: 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.

Please see additional Important Safety Information throughout and the accompanying Full Prescribing Information, including Boxed Warning.

Safety of GAVRETO was evaluated in 540 patients with RET-altered tumors[1] (cont'd)

Safety of GAVRETO in 138 patients with RET-altered thyroid cancer[1]*

9% of patients permanently discontinued GAVRETO due to any adverse reaction;

3.6% discontinued due to adverse reactions considered treatment-related by the trial investigator[1,2]

Adverse reactions resulting in permanent discontinuation, which occurred in >1 patient, included fatigue, pneumonia, and anemia.

Serious adverse reactions occurred in 39% of patients who received GAVRETO. The most frequent serious adverse reactions (in ≥2% of patients) were pneumonia, pneumonitis, urinary tract infection, pyrexia, fatigue, diarrhea, dizziness, anemia, hyponatremia, and ascites. Fatal adverse reactions occurred in 2.2% of patients; fatal adverse reactions that occurred in >1 patient included pneumonia (n=2).

44% of patients treated with GAVRETO experienced dose reductions due to adverse reactions

Adverse reactions requiring dosage reductions in ≥2% of patients included neutropenia, anemia, hypertension, increased blood creatine phosphokinase, decreased lymphocyte count, pneumonitis, fatigue, and thrombocytopenia.

67% of patients treated with GAVRETO experienced dosage interruptions due to an adverse reaction

Adverse reactions requiring dosage interruption in ≥2% of patients included neutropenia, hypertension, diarrhea, fatigue, pneumonitis, anemia, increased blood creatine phosphokinase, pneumonia, urinary tract infection, musculoskeletal pain, vomiting, pyrexia, increased AST, dyspnea, hypocalcemia, cough, thrombocytopenia, abdominal pain, increased blood creatinine, dizziness, headache, decreased lymphocyte count, stomatitis, and syncope.

*Includes 19 patients with RET fusion-positive thyroid cancer.

SELECT SAFETY INFORMATION

Warnings and Precautions (cont'd)

Embryo-Fetal Toxicity: 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 last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with GAVRETO and for 1 week after the last dose.

Please see additional Important Safety Information throughout and the accompanying Full Prescribing Information, including Boxed Warning.

GAVRETO® pralsetinib 100mg capsules

Support is available for you and your patients taking GAVRETO

GAVRETO® pralsetinib 100mg capsules

Enroll your current and new patients into RIGEL ONECARE for ongoing support

The Patient Support Team at RIGEL ONECARE is fully trained to support patients prescribed GAVRETO, whether their GAVRETO is fulfilled through integrated, in-office dispensing or specialty pharmacies.

Download the RIGEL ONECARE Enrollment Form or enroll in Copay Assistance at RigelONECARE.com

rigel onecare®

1-833-RIGELOC (1-833-744-3562)
Monday-Friday, 8 am to 8 pm ET

With GAVRETO financial assistance, eligible patients pay as little as $0†

The GAVRETO copay assistance program can help eligible patients with commercial insurance pay as little as $0 per prescription fill. Enroll your patients now by answering a few eligibility questions.

*All Rigel programs are subject to eligibility requirements. Restrictions may apply.

†Eligible patients, aged 12 or older and with a valid prescription, may receive GAVRETO at a $0 copay for each prescription fill if they pay through commercial insurance. Full program criteria are not displayed and can be found at RigelONECARE.com.

RIGEL ONECARE is a patient support center sponsored by Rigel Pharmaceuticals, Inc.

SELECT SAFETY INFORMATION

Adverse Reactions

Common adverse reactions (≥25%) were musculoskeletal pain, constipation, hypertension, diarrhea, fatigue, edema, pyrexia, and cough. **Common Grade 3/4 laboratory abnormalities (≥2%)** were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased phosphate, decreased leukocytes, decreased sodium, increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT), decreased calcium (corrected), decreased platelets, increased alkaline phosphatase, increased potassium, decreased potassium, and increased bilirubin.

Drug Interactions

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

Lactation: Advise women not to breastfeed during treatment with GAVRETO and for 1 week after the last dose.

Pediatric Use: Monitor open growth plates in adolescent patients. Consider interrupting or discontinuing GAVRETO if abnormalities occur.

You may report side effects to the FDA at **1-800-FDA-1088** or **www.fda.gov/medwatch**.

Please see additional Important Safety Information throughout and the accompanying Full Prescribing Information, including Boxed Warning.

References: 1. GAVRETO® [Package insert], South San Francisco, CA: Rigel Pharmaceuticals, Inc.
2. GAVRETO: Data on file, Rigel Pharmaceuticals, Inc. June 2024.

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