



## PRIOR AUTHORIZATION POLICY

- POLICY:** Oncology (Oral – Kirsten RAt Sarcoma Virus Inhibitor) – Krazati Prior Authorization Policy
- Krazati™ (adagrasib tablets – Mirati)

**REVIEW DATE:** 01/14/2026

### **INSTRUCTIONS FOR USE**

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## **CIGNA NATIONAL FORMULARY COVERAGE:**

### **OVERVIEW**

Krazati, a Kirsten RAt Sarcoma (KRAS) inhibitor, is indicated for the following uses<sup>1</sup>:

- **Non-small cell lung cancer (NSCLC)**, treatment of *KRAS G12C*-mutated locally advanced or metastatic disease, as determined by an FDA-approved test, in adults who have received at least one prior systemic therapy.
- **Colorectal cancer**, in combination with Erbitux® (cetuximab intravenous infusion) for the treatment of *KRAS G12C*-mutated locally advanced or metastatic disease, as determined by an FDA-approved test, in adults who have received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy.

Both the NSCLC and colorectal cancer indications were approved under accelerated approval based on objective response rate and duration of response. Continued

approval for these indications may be contingent upon verification and description of a clinical benefit in confirmatory trials.

Mutations in the *KRAS* gene most commonly occur at codon 12.<sup>2</sup> Data suggest that approximately 30% of patients with NSCLC have *KRAS* mutations. The prognosis of survival of patients with tumors with *KRAS* mutation is poorer compared with that of patients with tumors without *KRAS* mutation.

## Guidelines

National Comprehensive Cancer Network (NCCN) guidelines recommend Krazati in multiple conditions:

- **Ampullary Adenocarcinoma:** Guidelines (version 2.2025 – January 10, 2025) recommend Krazati for *KRAS G12C* mutation-positive disease for subsequent therapy for disease progression under “Useful in Certain Circumstances” for targeted systemic therapies (category 2A).<sup>9</sup>
- **Appendiceal Neoplasms and Cancers:** Guidelines (version 1.2026 – October 30, 2025) recommend Krazati in combination with Erbitux or Vectibix® (panitumumab intravenous infusion) as second-line and subsequent therapy (if not previously given) for *KRAS G12C* mutation-positive disease (category 2A).<sup>11</sup> Monotherapy can be considered if patient is unable to tolerate EGFR inhibitor.
- **Biliary Tract Cancer:** Guidelines (version 2.2025 – July 2, 2025) recommend Krazati for *KRAS G12C* mutation-positive tumors for subsequent-line therapy (category 2A).<sup>6</sup>
- **Central Nervous System (CNS) Cancers:** Guidelines (version 3.2025 – December 5, 2025) recommend Krazati for brain metastases due to *KRAS G12C* mutation-positive NSCLC (category 2A).<sup>3</sup> Lumakras™ (sotorasib tablets) is also recommended (category 2B). The guidelines have a general footnote that if an active agent exists (e.g., cytotoxic, targeted, immune modulating), trial of systemic therapy with good CNS penetration may be considered in select patients (e.g., small asymptomatic metastases) for initial treatment. This is also stated in the Compendium.<sup>10</sup> In addition, the agent can be considered as treatment for recurrent brain metastases and for treatment of relapsed disease with either stable systemic disease or reasonable systemic treatment options. This applies for both limited and extensive brain metastases.
- **Colon and Rectal Cancer:** Guidelines for colon cancer (version 5.2025 – October 30, 2025) and rectal cancer (version 4.2025 – October 31, 2025) recommend Krazati for some situations in patients with *KRAS G12C*-mutated disease.<sup>4,5</sup> For initial treatment in combination with Erbitux or Vectibix or as monotherapy if patient is unable to tolerate Erbitux or Vectibix due to toxicity (category 2A). Krazati is also recommended as subsequent therapy (category 2A) after previous therapy with oxaliplatin, irinotecan, FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin).
- **Non-Small Cell Lung Cancer:** Guidelines (version 3.2026 – December 24, 2025) recommend Krazati as a subsequent treatment option, for use after at least one prior systemic treatment (i.e., second-line and beyond) if the patient has not received previous *KRAS G12C*-targeted therapy (category 2A). Patients who progressed on Lumakras, another *KRAS* inhibitor directed at *KRAS G12C*-

mutated NSCLC, should not be treated with Krazati; and vice-versa due to their similar mechanisms of action.

- **Pancreatic Adenocarcinoma:** Guidelines (version 2.2025 – February 3, 2025) recommend Krazati as “Useful in Certain Circumstances” for subsequent therapy (category 2A) for locally advanced/metastatic disease and therapy for recurrent disease with *KRAS G12C* mutation-positive disease.<sup>8</sup> It is a category 2B recommendation for poor performance status.
- **Small Bowel Adenocarcinoma:** Guidelines (version 4.2025 – October 31, 2025) recommend Krazati as a second-line and subsequent therapy (if not previously given) for *KRAS G12C* mutation-positive disease (category 2A).<sup>7</sup>

## **POLICY STATEMENT**

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

- **Krazati™ (adagrasib tablets - Mirati)**

**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. Non-Small Cell Lung Cancer (NSCLC).** Approve for 1 year if the patient meets ALL of the following (A, B, and C):

**A)** Patient is  $\geq$  18 years of age; AND

**B)** Patient has *KRAS G12C*-mutated locally advanced or metastatic NSCLC; AND

**C)** Patient meets ONE of the following (i or ii):

- i. Patient has been previously treated with at least one systemic regimen; OR  
Note: Examples of systemic regimens include those containing one or more of the following products: Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), Tecentriq (atezolizumab intravenous infusion), Alimta (pemetrexed intravenous infusion), Yervoy (ipilimumab intravenous infusion), Abraxane (albumin-bound paclitaxel intravenous infusion), bevacizumab, cisplatin, carboplatin, docetaxel, gemcitabine, paclitaxel, vinorelbine.

- ii. Patient has brain metastases.

**2. Colon, Rectal, or Appendiceal Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):

**A)** Patient is  $\geq$  18 years of age; AND

**B)** Patient has unresectable, advanced, or metastatic disease; AND

**C)** Patient has *KRAS G12C* mutation-positive disease; AND

**D)** Patient meets ONE of the following (i or ii):

- i. The medication is prescribed as part of a combination regimen; OR  
Note: Examples of combination regimens included Krazati + Erbitux (cetuximab intravenous infusion), Krazati + Vectibix (panitumumab intravenous infusion).

- ii. As per the prescriber, the patient is unable to tolerate combination therapy;  
AND
- E) Patient has previously received a chemotherapy regimen.  
Note: Examples of chemotherapy regimens include a fluoropyrimidine such as 5-fluorouracil (5-FU), capecitabine; oxaliplatin, irinotecan, or an adjunctive chemotherapy regimen such as FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin).

### Other Uses with Supportive Evidence

- 3. **Ampullary Adenocarcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
  - A) Patient is  $\geq$  18 years of age; AND
  - B) Patient has metastatic disease; AND
  - C) Patients has *KRAS G12C* mutation-positive disease; AND
  - D) The medication will be used as subsequent therapy.
  
- 4. **Biliary Tract Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
  - A) Patient is  $\geq$  18 years of age; AND
  - B) Patient has unresectable and metastatic disease; AND
  - C) Patient has *KRAS G12C* mutation-positive disease; AND
  - D) Patient has been previously treated with at least one systemic regimen.  
Note: Examples of systemic regimens include those containing one or more of the following products: Keytruda (pembrolizumab intravenous infusion), Imfinzi (durvalumab intravenous infusion), gemcitabine, cisplatin, carboplatin, capecitabine, oxaliplatin, FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin), 5-fluorouracil, Abraxane (albumin-bound paclitaxel intravenous infusion).
  
- 5. **Pancreatic Adenocarcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
  - A) Patient is  $\geq$  18 years of age; AND
  - B) Patients has *KRAS G12C* mutation-positive disease; AND
  - C) Patient meets ONE of the following (i or ii):
    - i. Patient meets BOTH of the following (a and b):
      - a) Patient has locally advanced or metastatic disease; AND
      - b) Patient has been previously treated with at least one systemic regimen;  
OR  
Note: Examples of systemic regimens include one or more of the following: gemcitabine, albumin-bound paclitaxel, capecitabine, Keytruda (pembrolizumab intravenous infusion), FOLFIRINOX (5-fluorouracil + leucovorin + irinotecan + oxaliplatin).
    - ii. Patient has recurrent disease after resection.

**6. Small Bowel Adenocarcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

- A)** Patient is  $\geq$  18 years of age; AND
- B)** Patient has advanced or metastatic disease; AND
- C)** Patient has *KRAS G12C* mutation-positive disease; AND
- D)** The medication will be used as subsequent therapy.

## CONDITIONS NOT COVERED

- **Krazati™ (adagrasib tablets - Mirati)**

**is(are) considered not medically necessary for ANY other use(s); criteria will be updated as new published data are available.**

## REFERENCES

1. Krazati™ tablets [prescribing information]. San Diego, CA: Mirati Therapeutics; June 2024.
2. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 3.2026 - December 24, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on January 12, 2026.
3. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 3.2025 - December 5, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on January 12, 2026.
4. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 5.2025 - October 30, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on January 12, 2026.
5. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 4.2025 - October 31, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on January 12, 2026.
6. The NCCN Biliary Tract Cancers Clinical Practice Guidelines in Oncology (version 2.2025 - July 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on January 12, 2026.
7. The NCCN Small Bowel Adenocarcinoma Clinical Practice Guidelines in Oncology (version 4.2025 - October 31, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on January 12, 2026.
8. The NCCN Pancreatic Adenocarcinoma Clinical Practice Guidelines in Oncology (version 2.2025 - February 3, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on January 12, 2026.
9. The NCCN Ampullary Adenocarcinoma Clinical Practice Guidelines in Oncology (version 2.2025 - January 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on January 12, 2026.
10. The NCCN Drugs and Biologics Compendium. © 2026 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on January 11, 2026. Search term: adagrasib.
11. The NCCN Appendiceal Neoplasms and Cancers Clinical Practice Guidelines in Oncology (version 1.2026 - October 30, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org/>. Accessed on January 12, 2026.

## HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	<b>Colon or Rectal Cancer:</b> Under "Other Uses with Supportive Evidence" added new condition of approval based on guideline recommendations.	12/20/2023
Update	DEU Update, 7/12/2024: Colon or Rectal Cancer is moved from Other Uses with Supportive Evidence to FDA-approved use for Krazati.	--
Annual Revision	<b>Ampullary Adenocarcinoma:</b> Under "Other Uses with Supportive Evidence" added new condition of approval and criteria. <b>Biliary Tract Cancer:</b> Under "Other Uses with Supportive Evidence" added new condition of approval and criteria. <b>Pancreatic Adenocarcinoma:</b> Under "Other Uses with Supportive Evidence" added new condition of approval and criteria. <b>Small Bowel Adenocarcinoma:</b> Under "Other Uses with Supportive Evidence" added new condition of approval and criteria.	01/08/2025
Update	04/20/2025: The policy name was changed from "Oncology – Krazati PA Policy" to "Oncology (Oral – Kirsten RAat Sarcoma Virus Inhibitor) – Krazati PA Policy".	N/A
Selected Revision	<b>Non-Small Cell Lung Cancer (NSCLC):</b> Added criterion to allow use of Krazati for brain metastases.	05/14/2025
Annual Revision	<b>Non-Small Cell Lung Cancer (NSCLC):</b> Deleted "as determined by an approved test" in reference to KRAS G12C mutation testing. <b>Colon, Rectal, or Appendiceal Cancer:</b> Indication was changed to as written. Previously it was "Colon or Rectal Cancer". In requirements referring to chemotherapy regimen or combination regimen, deleted "for colon or rectal cancer".	01/14/2026

N/A – Not applicable.

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