UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2024 P 1404-3
Program	Prior Authorization/Notification
Medication	Krazati™ (adagrasib)
P&T Approval Date	2/2023, 2/2024, 8/2024
Effective Date	11/1/2024

1. Background:

Krazati™ (adagrasib) is an inhibitor of the RAS GTPase family indicated for as a single agent, for the treatment of adult patients with *KRAS* G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy. Krazati is also indicated in combination with cetuximab, for the treatment of adult patients with *KRAS* G12C-mutated locally advanced or metastatic colorectal cancer (CRC) who have received prior treatment with fluorpyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy.
The National Comprehensive Cancer Network (NCCN) recommends the use of Krazati as a single agent for the treatment of KRAS G12C mutation positive progressive ampullary adenocarcinoma, as subsequent therapy for KRAS G12 mutation positive locally advanced or metastatic pancreatic adenocarcinoma, for the treatment of brain metastases in *KRAS G12C*-mutated NSCLC, as subsequent therapy for KRAS G12C mutation positive recurrent NSCLC, as subsequent therapy for KRAS G`12 mutation positive unresectable or resected gross residual (R2) disease, or biliary tract cancer. NCCN also recommends the use of Krazati in combination with panitumumab or as a single agent for patients with KRAS G12C-mutated unresectable metastatic CRC and previous FOLFOX (fluorauracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin), and as adjuvant, second-line and subsequent therapy in combination with cetuximab or panitumumab or as a single agent, if not previously given, for progression of advanced or metastatic colorectal cancer, or patient is ineligible for or progressed on checkpoint inhibitor immunotherapy.
Coverage Information:
Members will be required to meet the criteria below for coverage. For members under the age of 19 years, the prescription will automatically process without a coverage review.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

2. Coverage Criteria[a]:

A. <u>Patients less than 19 years of age</u>

1. **Krazati** will be approved based on the following criterion:

   a. Patient is less than 19 years of age

   Authorization will be issued for 12 months.

B. <u>Non-Small Cell Lung Cancer (NSCLC)</u>

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1. **Initial Authorization**

   a. **Krazati** will be approved based on the following criteria:

      (1) Diagnosis of non-small cell lung cancer (NSCLC)

      -AND-

      (2) Presence of *KRAS G12C* mutation

      -AND-

      (3) Disease is **one** of the following:

         (a) Recurrent
         (b) Advanced
         (c) Metastatic

      -AND-

      (4) Patient has received at least one prior systemic therapy

      Authorization will be issued for 12 months.

2. **Reauthorization**

   a. **Krazati** will be approved based on the following criterion:

      (1) Patient does not show evidence of progressive disease while on Krazati therapy

      Authorization will be issued for 12 months.

C. Colorectal Cancer

1. **Initial Authorization**

   a. **Krazati** will be approved based on the following criteria:

      (1) Diagnosis of colorectal cancer

      -AND-

      (2) Presence of *KRAS G12C* mutation

      -AND-

      (3) Disease is **one** of the following:

         (a) Recurrent

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(b) Advanced
(c) Metastatic

-AND-

(4) Patient has received at least one prior systemic therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Krazati** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Krazati therapy

Authorization will be issued for 12 months.

D. Ampullary Adenocarcinoma

1. **Initial Authorization**

a. Krazati will be approved based on the following criteria:

(1) Diagnosis of ampullary adenocarcinoma

-AND-

(2) Presence of *KRAS G12C* mutation

-AND-

(3) Disease is one of the following:

(a) Recurrent
(b) Advanced
(c) Metastatic

-AND-

(4) Patient has received at least one prior systemic therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Krazati** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Krazati therapy

Authorization will be issued for 12 months.

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E. Pancreatic Adenocarcinoma

1. **Initial Authorization**

   a. **Krazati** will be approved based on the following criteria:

      (1) Diagnosis of pancreatic adenocarcinoma

      -AND-

      (2) Presence of *KRAS G12C* mutation

      -AND-

      (3) Disease is one of the following:

         (a) Recurrent
         (b) Advanced
         (c) Metastatic

      -AND-

      (4) Patient has received at least one prior systemic therapy

      Authorization will be issued for 12 months.

2. **Reauthorization**

   a. **Krazati** will be approved based on the following criterion:

      (1) Patient does not show evidence of progressive disease while on Krazati therapy

      Authorization will be issued for 12 months.

F. Biliary Tract Cancers

1. Initial Authorization

   a. Krazati will be approved based on the following criteria:

      (1) Diagnosis of **one** of the following:

         (a) Gallbladder Cancer
         (b) Intrahepatic cholangiocarcinoma
         (c) Extrahepatic cholangiocarcinoma

      -AND-

      (2) Presence of KRAS G12C mutation

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-AND-

(3) Disease is one of the following:

(a) Unresectable
(b) Resected gross residual (R2)
(c) Metastatic

-AND-

(4) Patient has received at least one prior systemic therapy

Authorization will be issued for 12 months.

2. Reauthorization

a. Krazati will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Krazati therapy

Authorization will be issued for 12 months.

G. NCCN Recommended Regimens

The drug has been recognized for treatment of the cancer indication by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a Category of Evidence and Consensus of 1, 2A, or 2B

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits and/or step therapy may be in place.

4. References:

1. Krazati [package insert]. San Diego, CA: Mirati Therapeutics, Inc.; June 2024.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at https://www.nccn.org. Accessed on July 10, 2024.

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Program	Prior Authorization/Notification – Krazati (adagrasib)
Change Control	
2/2023	New program
2/2024	Annual review. Added criteria for NCCN recommended use of Krazati in colon cancer, rectal cancer, ampullary adenocarcinoma and pancreatic adenocarcinoma. Updated background and references.
8/2024	Combined criteria for colon and rectal cancer in one section – Colorectal Cancer. Added criteria for NCCN recommended use of Krazati in biliary tract cancer. Updated background and references.

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