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| **Section:** | Prescription Drugs | **Effective Date:** | January 1, 2025 |
| **Subsection:** | Antineoplastic Agents | **Original Policy Date:** | January 6, 2023 |
| **Subject:** | Krazati | **Page:** | 1 of 4 |

***Last Review Date:*** December 13, 2024

# Krazati

## Description

### Krazati (adagrasib)

**Background**

Krazati (adagrasib) is an irreversible inhibitor of KRAS G12C that covalently binds to the mutant cysteine in KRAS G12C and locks the mutant KRAS protein in its inactive state and prevents downstream signaling without affecting wild-type KRAS protein. Krazati inhibits tumor cell growth and viability in cells harboring KRAS G12C mutations and results in tumor regression in KRAS G12C-mutated tumor xenograft models with minimal off-target activity (1).

**Regulatory Status**

FDA-approved indications: Krazati is an inhibitor of the RAS GTPase family indicated for: (1)

- As a single agent, for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy.
- In combination with cetuximab, for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic colorectal cancer (CRC), as determined by an FDA-approved test, who have received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy.

Krazati has warnings regarding gastrointestinal adverse reaction, QTc interval prolongation, hepatotoxicity, and interstitial lung disease (ILD)/pneumonitis. Liver function tests (ALT, AST, alkaline phosphatase, and total bilirubin) should be monitored prior to the start of Krazati and monthly for 3 months or as clinically indicated (1).

The safety and effectiveness of Krazati in pediatric patients less than 18 years of age have not been established (1).

**Related policies**
Lumakras

## Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Krazati may be considered **medically necessary** if the conditions indicated below are met.

Krazati may be considered **investigational** for all other indications.

## Prior-Approval Requirements

**Age** 18 years of age or older

**Diagnoses**

Patient must have **ONE** of the following:

1. Locally advanced or metastatic non-small cell lung cancer (NSCLC)
   a. Used as a single agent
   b. Patient has received at least one prior systemic therapy
2. Locally advanced or metastatic colorectal cancer (CRC)
   a. Used in combination with Erbitux (cetuximab)
   b. Patient has received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy

**AND ALL** of the following for **ALL** indications:

1. Presence of KRAS G12C mutation as determined by an FDA-approved test
2. Prescriber agrees to monitor AST, ALT, alkaline phosphatase, and total bilirubin
3. Prescriber agrees to monitor for QTc prolongation as clinically indicated

## Prior – Approval *Renewal* Requirements

**Age** 18 years of age or older

**Diagnoses**

Patient must have **ONE** of the following:

1. Locally advanced or metastatic non-small cell lung cancer (NSCLC)
    a. Used as a single agent
2. Locally advanced or metastatic colorectal cancer (CRC)
    a. Used in combination with Erbitux (cetuximab)

**AND ALL** of the following for **ALL** indications:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to monitor AST, ALT, alkaline phosphatase, and total bilirubin
3. Prescriber agrees to monitor for QTc prolongation as clinically indicated

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

**Quantity** 1,200 mg per day

**Duration** 12 months

### Prior – Approval *Renewal* Limits

Same as above

## Rationale

**Summary**

Krazati (adagrasib) is an inhibitor of the RAS GTPase family indicated for the treatment of adult patients with KRAS G12C-mutated non-small cell lung cancer (NSCLC) and colorectal cancer (CRC). Krazati contains warnings regarding gastrointestinal adverse reactions, QTc interval prolongation, hepatotoxicity, and interstitial lung disease (ILD)/pneumonitis. The safety and effectiveness of Krazati in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Krazati while maintaining optimal therapeutic outcomes.

**References**

1. Krazati [package insert]. San Diego, CA: Mirati Therapeutics, Inc.; July 2024.
2. NCCN Drugs & Biologics Compendium® Adagrasib 2024. National Comprehensive Cancer Network, Inc. Accessed on October 28, 2024.

## Policy History

| Date | Action |
|---|---|
| January 2023 | Addition to PA |
| March 2023 | Annual review and reference update |
| March 2024 | Annual review and reference update |
| July 2024 | Per PI update, added indication of colorectal cancer in combination with Erbitux. Also changed quantity limit to 1,200 mg per day |
| September 2024 | Annual review and reference update |
| December 2024 | Annual review and reference update |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.**