PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Krazati Prior Authorization Policy
- Krazati™ (adagrasib tablets – Mirati Therapeutics)

REVIEW DATE: 12/20/2023

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Krazati, a Kirsten RAt Sarcoma virus (KRAS) inhibitor, is indicated for the following uses[1]:

- **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:** Krazati in combination with Erbitux® (cetuximab intravenous infusion) is indicated 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.[2] 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

The National Comprehensive Cancer Network (NCCN) guidelines recommend Krazati for the following cancer types:

- **Non-Small Cell Lung Cancer:** Guidelines (version 5.2023 – November 8, 2023) 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™ (sotorasib tablets), another *KRAS* inhibitor directed at *KRAS G12C*-mutated NSCLC, should not be treated with Krazati; and vice-versa. The NCCN Central Nervous System Cancers guidelines (version 1.2023 – March 24, 2023) recommend use of Krazati for *KRAS G12C* mutation-positive NSCLC that has metastasized to the brain (category 2A).[3]
- **Colon and Rectal Cancer:** Guidelines for colon cancer (version 4.2024 – July 3, 2024) and rectal cancer (version 3.2024 – July 3, 2024) recommend Krazati for some situations in patients with *KRAS G12C*-mutated disease.[4,5] For initial treatment in combination with Erbitux or Vectibix® (panitumumab intravenous infusion) 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).

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 Therapeutics)**

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 Indication

1. **Non-Small Cell Lung Cancer (NSCLC).** Approve for 1 year if the patient meets the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has *KRAS G12C*-mutated locally advanced or metastatic NSCLC, as determined by an approved test; AND
   - **C)** 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), 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.

2. **Colon or Rectal Cancer.** Approve for 1 year if the patient meets the following (A, B, C, D, and E):
   A) Patient is ≥ 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 for colon or rectal cancer; 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 for colon or rectal cancer.
   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).

CONDITIONS NOT COVERED

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

is(are) considered experimental, investigational, or unproven 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 5.2023 - November 8, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 18, 2023.
3. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2023 – March 24, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 6, 2023.
4. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 4.2024 – July 3, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 12, 2024.
5. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 4.2024 – July 3, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on July 12, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	12/14/2022
Update	DEU Update, 12/27/2022: Updated guidelines section with current NCCN guidelines (version 1.2023 – December 22, 2022) recommendations.	--
Update	DEU Update, 04/06/2023: Updated guidelines section with NCCN central nervous system cancers guideline (version 1.2023 – March 24, 2023) recommendation.	--
Annual Revision	**Colon or Rectal Cancer:** 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.	--