Clinical Policy: Adagrasib (Krazati)

Reference Number: CP.PHAR.605
Effective Date: 03.01.23
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Adagrasib (Krazati®) is an inhibitor of the RAS GTPase family.

FDA Approved Indication(s)

Krazati is indicated:

- 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*.

**This indication is approved under accelerated approval based on objective response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of a clinical benefit in a confirmatory trial(s).*

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Krazati is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Small Cell Lung Cancer (must meet all)**:**

1. Diagnosis of recurrent, advanced, or metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For Krazati requests, member must use adagrasib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Disease is positive for *KRAS* G12C mutation;
6. Member meets one of the following (a or b):
    a. Both of the following (i and ii):
        i. Member has received at least one systemic therapy (not including Lumakras) *(see Appendix B)*;
        ii. Member must use Lumakras®, unless contraindicated, clinically significant adverse effects are experienced, or request is for treatment associated with

cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix D)*;*
**For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*

b. Member has brain metastases;

7. Prescribed as monotherapy;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed 1,200 mg (6 tablets) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Colorectal Cancer (must meet all)**:**
1. Diagnosis of locally advanced or metastatic CRC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For Krazati requests, member must use adagrasib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Disease is positive for *KRAS* G12C mutation;
6. Member has had previous treatment with a fluoropyrimidine- (e.g., 5-fluorouracil, capecitabine), oxaliplatin-, and irinotecan-containing chemotherapy (*see Appendix B*);
7. Member must use Lumakras, unless contraindicated, clinically significant adverse effects are experienced, or request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (*see Appendix D*);*
   **For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
8. Krazati is prescribed in one of the following ways (a, b, or c):
   a. In combination with Vectibix® (*off-label*);
   b. In combination with Erbitux®;
   c. As monotherapy if member is unable to tolerate epidermal growth factor receptor (EGFR) inhibitor (e.g., Erbitux, Vectibix) due to toxicity;
9. Request meets one of the following (a or b):*
   a. Dose does not exceed 1,200 mg (6 tablets) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. NCCN Compendium Indications (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a, b, or c):
   a. Pancreatic adenocarcinoma that is locally advanced, recurrent, or metastatic;
   b. Ampullary adenocarcinoma;

c. One of the following biliary tract cancers that is unresectable, resected gross residual (R2), or metastatic (i, ii, or iii) as subsequent therapy:
   i. Extrahepatic cholangiocarcinoma;
   ii. Intrahepatic cholangiocarcinoma;
   iii. Gallbladder cancer;

2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For Krazati requests, member must use adagrasib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Prescribed as monotherapy;
6. Disease is positive for *KRAS* G12C mutation;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 1,200 mg (6 tablets) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

D. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Krazati for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Krazati requests, member must use adagrasib, if available, unless contraindicated or clinically significant adverse effects are experienced;

4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 1,200 mg (6 tablets) per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CRC: colorectal cancer
EGFR: epidermal growth factor receptor
FDA: Food and Drug Administration
NSCLC: non-small cell lung cancer

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Lumakras (sotorasib)	NSCLC: 960 mg PO QD	960 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	CRC: 960 mg PO QD in combination with panitumumab	
cisplatin- or carboplatin-containing chemotherapy	NSCLC: Varies	Varies
Imfinzi® (durvalumab)	NSCLC: 10 mg/kg IV every 2 weeks or 1,500 mg every 4 weeks	1,500 mg every 4 weeks
Keytruda® (pembrolizumab)	NSCLC: 200 mg IV every 3 weeks OR 400 mg every 6 weeks up to 24 months	400 mg every 6 weeks
Libtayo® (cemiplimab-rwlc)	NSCLC: 350 mg IV every 3 weeks	350 mg every 3 weeks
Opdivo® (nivolumab)	NSCLC: 240 mg IV every 2 weeks or 480 mg IV every 4 weeks	480 mg every 4 weeks
Tecentriq® (atezolizumab)	NSCLC: 840 mg IV every 2 weeks, 1,200 mg IV every 3 weeks, or 1,680 mg IV every 4 weeks	1,680 mg every 4 weeks
Yervoy® (ipilimumab)	NSCLC: In combination with Opdivo: 1 mg/kg IV every 6 weeks	1 mg/kg every 6 weeks
Imjudo® (tremelimumab)	NSCLC: Patients ≥ 30 kg: 75 mg IV on day 1 every 3 weeks for cycles 1 through 4 in combination with durvalumab and platinum-based chemotherapy; cycle 5 no dose; cycle 6 - 75 mg IV on day 1 in combination with durvalumab Patients < 30 kg: 1 mg/kg on day 1 every 3 weeks for cycles 1 through 4 in combination with durvalumab and platinum-based chemotherapy; cycle 5 no dose; cycle 6 - 1 mg/kg IV on day 1 in combination with durvalumab	See dosing regimen
fluoropyrimidine-containing regimens (e.g., 5-fluorouracil, capecitabine, FOLFOX, CAPEOX, FOLFIRINOX	CRC: Varies	Varies
oxaliplatin-containing regimens (e.g., FOLFOX,	CRC: Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
CAPEOX, FOLFIRINOX)		
irinotecan-containing regimens (e.g., FOLFIRI, FOLFIRINOX)	CRC: Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: States with Regulations against Redirections in Cancer

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA
LA	Yes≠	For stage 4 advanced, metastatic cancer or associated conditions. ≠Exception if clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy
MS	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to Commercial and HIM requests only** For stage 4 metastatic cancer and associated conditions
OK	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes^	For stage 4 advanced metastatic cancer, metastatic blood cancer, and associated conditions ^Exception if step therapy is for AB-rated generic equivalent, interchangeable biological product, or biosimilar product to the equivalent brand drug
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NSCLC, CRC	600 mg PO BID	1,200 mg/day

VI. Product Availability

Tablet: 200 mg

VII. References

1. Krazati Prescribing Information. San Diego, CA: Mirati Therapeutics, Inc.; July 2024. Available at: https://packageinserts.bms.com/pi/pi_krazati.pdf. Accessed October 31, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at http://www.nccn.org. Accessed November 11, 2024.
3. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 11.2024. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed November 11, 2024.
4. National Comprehensive Cancer Network. Colon Cancer Version 3.2025. Available at: http://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed June 9, 2025.
5. National Comprehensive Cancer Network. Rectal Cancer Version 2.2025. Available at: http://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed June 9, 2025.
6. Jänne PA, Riely GJ, Gadgeel SM, et al. Adagrasib in non-small-cell lung cancer harboring a *KRASG12C* mutation. N Engl J Med. 2022 Jul 14;387(2):120-131.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	01.04.23	02.23
1Q 2024 annual review: Per NCCN: for NSCLC added monotherapy criterion and added brain metastases as exception to having received ≥ 1 prior therapy; added off-label criteria for pancreatic adenocarcinoma and colorectal cancer; references reviewed and updated.	10.26.23	02.24
RT4: added new FDA-approved indication for the treatment of CRC; updated Appendix B. Ad hoc: added off-label criteria for ampullary adenocarcinoma and biliary tract cancers as subsequent therapy per NCCN compendium.	06.27.24	
1Q 2025 annual review: added generic redirection for initial and continued therapy per template; per NCCN, for NSCLC removed "locally" from "locally advanced" NSCLC option and for CRC added monotherapy option; references reviewed and updated. Per December SDC: for NSCLC, added redirection to Lumakras for members without brain metastases; for all indications, removed requirement that member has not received prior treatment with Lumakras.	12.02.24	02.25
Per SDC for CRC, added redirection to Lumakras; for NCSLC and CRC, added step therapy bypass for IL HIM per IL HB 5395.	06.09.25	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical

policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.