Clinical Policy: Sotorasib (Lumakras)

Reference Number: CP.PHAR.549
Effective Date: 09.01.21
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Sotorasib (Lumakras®) is an inhibitor of the RAS GTPase family.

FDA Approved Indication(s)

Lumakras 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 panitumumab for the treatment of adult patients with *KRAS* G12C-mutated metastatic colorectal cancer (CRC), as determined by an FDA-approved test, who have received prior fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy.

**This indication is approved under accelerated approval based on overall response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of 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 Lumakras 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, locally advanced, or metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is positive for *KRAS* G12C mutation;
5. Prescribed as monotherapy;
6. Member has received at least one systemic therapy *(see Appendix B)*;
7. Member has not received prior treatment with Krazati™;
8. For Lumakras requests, member must use generic sotorasib, if available, unless contraindicated or clinically significant adverse effects are experienced;
9. Request meets one of the following (a or b):*
   a. Dose does not exceed 960 mg 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 advanced or metastatic CRC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is positive for *KRAS* G12C mutation;
5. Member has received prior therapy *(see Appendix B)*;
6. Lumakras is prescribed in one of the following ways (a, b, or c):
   a. In combination with Vectibix®;
   b. In combination with Erbitux® (*off-label*);
   c. As monotherapy if member is unable to tolerate epidermal growth factor receptor (EGFR) inhibitor (e.g., Erbitux, Vectibix) due to toxicity (*off-label*);
7. For Lumakras requests, member must use generic sotorasib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed 960 mg 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 Recommended Uses (off-label) (must meet all)**:**
1. Prescribed for one of the following diagnoses (a – c):
   a. Ampullary adenocarcinoma;
   b. Pancreatic adenocarcinoma that is locally advanced, recurrent, or metastatic;
   c. Small bowel adenocarcinoma that is advanced or metastatic;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is positive for *KRAS* G12C mutation;
5. Member has received prior therapy;
6. Prescribed as monotherapy;
7. For Lumakras requests, member must use generic sotorasib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose is within FDA maximum limit for any FDA approved indication or 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 Lumakras for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. NSCLC and CRC: New dose does not exceed 960 mg 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
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
NSCLC		
cisplatin- or carboplatin-containing chemotherapy	Varies	Varies
Imfinzi® (durvalumab)	10 mg/kg IV every 2 weeks or 1,500 mg every 4 weeks	1,500 mg every 4 weeks
Keytruda® (pembrolizumab)	200 mg IV every 3 weeks OR 400 mg every 6 weeks up to 24 months	400 mg every 6 weeks
Libtayo® (cemiplimab-rwlc)	350 mg IV every 3 weeks	350 mg every 3 weeks
Opdivo® (nivolumab)	240 mg IV every 2 weeks or 480 mg IV every 4 weeks	480 mg every 4 weeks
Tecentriq® (atezolizumab)	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)	In combination with Opdivo: 1 mg/kg IV every 6 weeks	1 mg/kg every 6 weeks
Imjudo® (tremelimumab)	Patients ≥ 30 kg: 75 mg IV on day 1 every 3 weeks for cycles 1 through 4 in combination with durvalumab and platinum-based	See dosing regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	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	
CRC, Ampullary Adenocarcinoma, Small Bowel Adenocarcinoma		
fluoropyrimidine-containing regimens (e.g., 5-fluorouracil, capecitabine, FOLFOX, CAPEOX, FOLFIRINOX	Varies	Varies
oxaliplatin-containing regimens (e.g., FOLFOX, CAPEOX, FOLFIRINOX)	Varies	Varies
irinotecan-containing regimens (e.g., FOLFIRI, FOLFIRINOX)	Varies	Varies
Pancreatic Adenocarcinoma		
Examples include gemcitabine-based regimens (gemcitabine, gemcitabine + erlotinib, gemcitabine + albumin-bound paclitaxel) and fluoropyrimidine-containing regimens (e.g., 5-fluorouracil, capecitabine, FOLFOX, CAPEOX, FOLFIRINOX, NALIFIROX)	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

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CRC	960 mg PO QD in combination with panitumumab	960 mg/day
NSCLC	960 mg PO QD	960 mg/day

VI. Product Availability

Tablets: 120 mg, 240 mg, 320 mg

VII. References

1. Lumakras Prescribing Information. Thousand Oaks, CA: Amgen Inc.; January 2025. Available at: www.lumakras.com. Accessed April 10, 2025.
2. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer. Version 4.2025. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed May 25, 2025.
3. National Comprehensive Cancer Network. Colon Cancer Version 3.2025. Available at: http://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed May 25, 2025.
4. National Comprehensive Cancer Network. Rectal Cancer Version 2.2025. Available at: http://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed May 25, 2025.
5. National Comprehensive Cancer Network. Pancreatic Adenocarcinoma Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed May 25, 2025.
6. National Comprehensive Cancer Network. Ampullary Adenocarcinoma Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ampullary.pdf. Accessed May 25, 2025.
7. National Comprehensive Cancer Network. Small Bowel Adenocarcinoma Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/small_bowel.pdf. Accessed May 25, 2025.
8. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/. Accessed May 25, 2025.
9. Skoulidis F, Li BT, Dy GK, et al. Sotorasib for lung cancers with KRAS p.G12C mutation. N Engl J Med 2021 Jun 4; 384:2371-2381. doi: 10.1056/NEJMoa2103695.
10. Clinical Pharmacology [database online]. Philadelphia, PA: Elsevier; 2025. Available at: https://www.clinicalkey.com/pharmacology/. Accessed May 25, 2025.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	06.14.21	08.21
3Q 2022 annual review: no significant changes; added option for recurrent disease per NCCN; removed option to bypass failure of at least one systemic therapy if contraindicated or clinically significant adverse effects are experienced per prescribing information; references reviewed and updated.	04.14.22	08.22
Template changes applied to other diagnoses/indications.	10.06.22	
Added requirement that member has not received prior treatment with Krazati per NCCN; revised Commercial approval durations	01.04.23	02.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
from length of benefit to "12 months or duration of request, whichever is less."		
RT4: Addition of new strength (320 mg); references reviewed and updated.	02.08.23	
3Q 2023 annual review: added standard oral oncology generic redirection language; references reviewed and updated.	05.09.23	08.23
3Q 2024 annual review: added disclaimer that indication is approved under accelerated approval to FDA Approved Indications section; added NCCN recommended off-label use criteria for ampullary adenocarcinoma, pancreatic adenocarcinoma, rectal cancer, appendiceal adenocarcinoma, and colon cancer; references reviewed and updated.	05.13.24	08.24
RT4: added newly approved 240 mg strength tablet.	11.19.24	
RT4: added new FDA-approved indication of CRC and removed requirement for previous use of a fluoropyrimidine- (e.g., 5-fluorouracil, capecitabine), oxaliplatin-, and irinotecan-containing chemotherapy per NCCN and as Appendix B now lists previous CRC regimens; removed colon, appendiceal, and rectal cancers from NCCN-recommended off-label uses section as these are now encompassed within the CRC section; for NCCN-recommended off-label uses, added requirements for positive *KRAS* G12C mutation, previous therapy, and Lumakras monotherapy use per NCCN Compendium; for ampullary adenocarcinoma, added requirement for disease progression per NCCN; for small bowel adenocarcinoma, added requirement for advanced or metastatic disease per NCCN; for pancreatic adenocarcinoma, added requirement for locally advanced, recurrent, or metastatic disease; for NSCLC, added monotherapy requirement.	02.07.25	
3Q 2025 annual review: no significant changes; references reviewed and updated.	04.10.25	08.25

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.