Clinical Policy: Lorlatinib (Lorbrena)

Reference Number: CP.PHAR.406
Effective Date: 03.01.19
Last Review Date: 05.23
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Lorlatinib (Lorbrena®) is a kinase inhibitor.

FDA Approved Indication(s)

Lorbrena is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

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 Lorbrena 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. Disease is ALK or ROS1 positive;
5. If disease is ROS1 positive, failure of Rozlytrek™, Xalkori®, or Zykadia®, unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for Rozlytrek, Xalkori and Zykadia.*
6. Prescribed as a single agent;
7. For Lorbrena requests, member must use generic lorlatinib, 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 both (i and ii):
      i. 100 mg per day;
      ii. 1 tablet 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. Additional NCCN Recommended Uses (off-label) (must meet all)**:**

1. Prescribed for one of the following diagnoses (a - d):
   a. Diffuse large B-cell lymphoma and (i):
      i. Disease is relapsed or refractory;
   b. Erdheim-Chester disease and (i):
      i. Disease is symptomatic or relapsed/refractory;
   c. Inflammatory myofibroblastic tumor (IMT; a soft tissue sarcoma)
   d. Uterine sarcoma and both (i and ii):
      i. Presence of IMT;
      ii. Disease is advanced, recurrent, metastatic, or inoperable;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Disease is ALK positive;
5. Prescribed as a single agent;
6. For Lorbrena requests, member must use generic lorlatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed both (i and ii):
      i. 100 mg per day;
      ii. 1 tablet per day;
   b. Requested 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. 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 Lorbrena for NSCLC and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Lorbrena requests, member must use generic lorlatinib, 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 both (i and ii):
      i. 100 mg per day;
      ii. 1 tablet 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 policy – 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

ALK: anaplastic lymphoma kinase
FDA: Food and Drug Administration

IMT: inflammatory myofibroblastic tumor
NCCN: National Comprehensive Cancer Network
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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Rozlytrek® (entrectinib)	600 mg PO QD	600 mg/day
Zykadia® (ceritinib)	450 mg PO QD	450 mg/day
Xalkori® (crizotinib)	250 mg PO BID	500 mg/day

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
- Contraindication(s): concomitant use with strong CYP3A inducers
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ALK-positive NSCLC	100 mg PO QD	100 mg/day

VI. Product Availability
Tablets: 25 mg, 100 mg

VII. References
1. Lorbrena Prescribing Information. New York, NY: Pfizer Inc; March 2021. Available at: www.pfizer.com. Accessed January 31, 2023.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 4, 2023.
3. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed February 4, 2023.
4. Clinical Pharmacology [database online]. Tampa, FL: Elsevier, Inc. Updated periodically. Accessed February 4, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2019 annual review: no significant changes; references reviewed and updated.	02.19.19	05.19
No significant changes; finalized line of business to apply to HIM.	04.18.19	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2020 annual review: per NCCN Compendium added Xalkori as a possible redirect option for ALK-positive disease; added Rozlytrek as a possible redirect option for ROS1-positive disease; added quantity limit of 3 tablets to allow for dose adjustments; references reviewed and updated.	02.12.20	05.20
2Q 2021 annual review: RT4: updated FDA-approved indication for NSCLC removing disease progression on specific prior therapies; per NCCN Compendium which supports Lorbrena as first-line therapy in ALK positive NSCLC, removed requirement for use of prior therapies; oral oncology generic redirection language added; revised reference to HIM off-label use policy from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	03.23.21	05.21
2Q 2022 annual review: added criterion for use as single-agent therapy for NSCLC; maximum dose corrected to "100 mg (1 tablet per day)" in criteria; Commercial approval durations revised from "Length of Benefit" to "12 months or duration of request, whichever is less"; references reviewed and updated.	04.15.22	05.22
Template changes applied to other diagnoses/indications.	09.23.22	
2Q 2023 annual review: added off-label NCCN-supported indications of diffuse large B-cell lymphoma, Erdheim-Chester disease, IMT, and uterine sarcoma; references reviewed and updated.	02.04.23	05.23

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.