CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Lazertinib (Lazcluze®)

Version: 1.0

EFFECTIVE DATE: 5/5/2024

NantHealth® | Eviti®

Please note the following:

For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within 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.

Lazertinib (Lazcluze®)

Discussion

Lazertinib is a kinase inhibitor of epidermal growth factor receptor (EGFR) that inhibits EGFR exon 19 deletions and exon 21 L858R substitution mutations at lower concentrations than wildtype EGFR.[1] It forms an irreversible covalent bond to the Cys797 residue in the ATP-binding site of the EGFR kinase domain. Lazertinib exhibits high selectivity for sensitizing and T790M EGFR mutations. Treatment with lazertinib in combination with amivantamab increased in vivo anti-tumor activity compared to either agent alone.[1,2]

Clinically significant adverse reactions include venous thromboembolic events, interstitial lung disease (ILD)/pneumonitis, dermatologic reactions, and ocular toxicity. The most common adverse reactions (≥ 20%) were rash, nail toxicity, infusion-related reaction (amivantamab-vmjw), musculoskeletal pain, edema, stomatitis, VTE, paresthesia, fatigue, diarrhea, constipation, COVID-19, hemorrhage, dry skin, decreased appetite, pruritus, nausea, and ocular toxicity.[1]

Lazertinib is approved by the Food and Drug Administration (FDA) and National Comprehensive Cancer Network (NCCN) for non-small cell lung cancer.[1,3]

Definitions

- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.[4]
- **National Comprehensive Cancer Network (NCCN)** - An alliance of over 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.[5]

Policy

Coverage will be considered for FDA approved indications and for NCCN category 1, 2A, or 2B recommendations when the following criteria are met:

Non-Small Cell Lung Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. First-line treatment in combination with amivantamab-vmjw for patients with locally advanced or metastatic disease with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations;[1] OR

For **NCCN** required criteria coverage:

4. In combination with amivantamab-vmjw for EGFR exon 19 deletion or exon 21 L858R recurrent, advanced, or metastatic disease for one of the following:
   a) First-line therapy
   b) Continuation of therapy following disease progression on amivantamab-vmjw + lazertinib for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression.[3]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Coding (CPT®, ICD-10 and HCPCS)

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C34	Malignant neoplasm of bronchus and lung
J8999	Prescription drug, oral, chemotherapeutic, not otherwise specified

Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	5/5/2025
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee:	5/5/2025
6	Revision Changes:	

References

[1] Lazaertinib (Lazcluze) [Package Insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/219008s000lbledt.pdf. Accessed March 25, 2025.

[2] Lee J, Hong MH, Cho BC. Lazertinib: on the Way to Its Throne. *Yonsei Med J*. 2022;63(9):799-805. https://pubmed.ncbi.nlm.nih.gov/36031779/. Accessed March 25, 2025.

[3] National Comprehensive Cancer Network. NCCN Guidelines. Non-Small Cell Lung Cancer. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed March 25, 2025.

[4] U.S. Food & Drug Administration. https://www.fda.gov/about-fda/what-we-do. Accessed April 23, 2025.

[5] National Comprehensive National Cancer Network. https://www.nccn.org/home. Accessed April 23, 2025.