BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

LAZCLUZE™ (lazertinib) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Lazcluze (lazertinib) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations

b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. Requested agent will be used in combination with Rybrevant (amivantamab), if tolerated

5. Individual should also receive anticoagulant prophylaxis to prevent venous thromboembolic events (VTE) for the first four months of treatment

6. Individual has completed **ALL** the following **baseline tests** before initiation of treatment and will have continued monitoring as clinically appropriate:
   a. There is documentation of presence of EGFR exon 19 deletions or exon 21 L858R substitution mutations in tumor or plasma specimens
   b. Negative pregnancy test in a woman of childbearing potential
   c. Eastern Co-operative Oncology Group (ECOG) status of 0-1

7. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

8. Individual is not currently taking any drugs which may cause severe adverse reactions or significant drug interactions that may require discontinuation such as strong to moderate CYP3A4 inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, armodafinil, bexarotene, bosentan, others)

9. Individual does not have severe renal impairment or end-stage renal disease (eGFR < 30 mL/min)

10. Individual does not have severe hepatic impairment (total bilirubin > 3×ULN and any AST)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Lazcluze (lazertinib) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual has documentation of positive clinical response to therapy defined as the following:
   a. There is no disease progression
   b. There is no unacceptable toxicity

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
    a. Venous thromboembolic events (VTE) that is recurrent despite therapeutic anticoagulation
    b. Interstitial Lung Disease (ILD)/Pneumonitis
    c. Dermatologic adverse reactions such as severe rash, acneiform dermatitis that has not recovered or improved with dose adjustment
    d. New or worsening signs and symptoms of ocular adverse reactions, including keratitis
    e. Adverse reaction that recurs after two dose reductions

6. Individual is not currently taking any drugs which may cause severe adverse reactions or significant drug interactions that may require discontinuation such as strong to moderate CYP3A4 inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, armodafinil, bexarotene, bosentan, others)

7. Individual does not have severe renal impairment or end-stage renal disease (eGFR < 30 mL/min)

8. Individual does not have severe hepatic impairment (total bilirubin > 3×ULN and any AST)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

    1. **Off-Label Use of Non-Cancer Medications**

    2. **Off-Label Use of Cancer Medications**

Description:

Lazcluze (lazertinib) is a kinase inhibitor indicated in combination with amivantamab for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.

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 wild-type EGFR. Treatment with lazertinib in combination with amivantamab increased in vivo anti-tumor activity compared to either agent alone in a mouse xenograft model of human NSCLC with an EGFR L858R mutation.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer Version 10.2024 – Updated September 23, 2024

Molecular and biomarker-directed therapy for advanced or metastatic disease:

EGFR Exon 19 Deletion or Exon 21 L858R Mutations

- First-line therapy
  - Osimertinib (preferred)
  - Other recommended (category 1)
    - Osimertinib + pemetrexed + (cisplatin or carboplatin) (nonsquamous)
    - Amivantamab-vmjw + lazertinib
  - Useful in certain circumstances
    - Afatinib (category 1)
    - Dacomitinib (category 1)
    - Erlotinib (category 1)
    - Gefitinib (category 1)
    - Erlotinib + ramucirumab
    - Erlotinib + bevacizumabc (nonsquamous)
- Subsequent therapy
  - Osimertinib
  - Amivantamab-vmjw + carboplatin + pemetrexed (nonsquamous)

Resources:

Lazcluze (lazertinib) product information, revised by Janssen Biotech, Inc. 08-2024 Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 24, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer Version 08.2025 – Updated August 15, 2025. Available at https://www.nccn.org. Accessed October 07, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.