Oscar Clinical Guideline: Lazcluze (lazertinib) (PG251, Ver. 3)

Lazcluze (lazertinib)

Summary

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for about 80-85% of all cases. NSCLC can be further classified based on genetic mutations, with approximately 10-15% of cases in Western populations and 30-40% in Asian populations harboring mutations in the epidermal growth factor receptor (EGFR) gene. The most common EGFR mutations are exon 19 deletions and exon 21 L858R substitutions, which account for about 85-90% of all EGFR mutations in NSCLC.

Treatment options for EGFR-mutated NSCLC have evolved significantly in recent years. The standard first-line treatment has been EGFR tyrosine kinase inhibitors (TKIs), with osimertinib being the preferred option due to its efficacy and ability to penetrate the blood-brain barrier. However, resistance to EGFR TKIs eventually develops in almost all patients.

Lazcluze (lazertinib) is indicated in combination with amivantamab (Rybrevant) 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.

Definitions

"EGFR" is the Epidermal Growth Factor Receptor, a protein on the surface of cells that, when mutated, can lead to uncontrolled cell growth in some cancers.

"Locally advanced" refers to cancer that has spread from where it started to nearby tissue or lymph nodes.

"Metastatic" is cancer that has spread from its original site to other parts of the body.

"NSCLC" refers to Non-Small Cell Lung Cancer, a type of lung cancer that includes adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.

"RECIST criteria" refers to Response Evaluation Criteria in Solid Tumors, a standard way to measure how well a cancer patient responds to treatment.

"Tyrosine Kinase Inhibitor (TKI)" is a type of targeted therapy that blocks specific enzymes called tyrosine kinases, which are involved in cancer cell growth and survival.

Medical Necessity Criteria for Initial Authorization

The Plan considers Lazcluze (lazertinib) medically necessary when ALL of the following criteria are met:

1. The medication is prescribed by or in consultation with an oncologist; *AND*
2. The member is 18 years of age or older; *AND*
3. The member has a diagnosis of locally advanced or metastatic non-small cell lung cancer (NSCLC); *AND*
4. The member has EGFR exon 19 deletions or exon 21 L858R substitution mutations, as confirmed by FDA-approved testing[*]; *AND*

   [*]*Information on FDA-approved tests is available at: http://www.fda.gov/CompanionDiagnostics.*
5. Lazcluze (lazertinib) is being used for treatment consistent with NCCN category 1, 2A, or 2B recommendations for EGFR-mutated NSCLC (see Appendix A, Table 1); *AND*
6. Lazcluze (lazertinib) is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.

If the above prior authorization criteria are met, the requested product will be authorized for up to 6-months

Medical Necessity Criteria for Reauthorization

Reauthorization for up to 12-months will be granted if the member has recent (within the last 3 months) clinical chart documentation demonstrating ALL of the following criteria:

1. The requested medication is prescribed by or in consultation with an oncologist; *AND*
2. The member has experienced a documented clinical benefit from therapy, as evidenced by at least ONE (1) of the following:
    a. Tumor response with a decrease in tumor size or tumor burden; *or*
    b. Stable disease (no disease progression); *or*
    c. Improvement in cancer-related symptoms; *or*
    d. Improvement in Eastern Cooperative Oncology Group (ECOG) performance status; *AND*
3. There is no clinical evidence indicating disease progression, as defined by RECIST (Response Evaluation Criteria in Solid Tumors) criteria or other standardized criteria for NSCLC progression; *AND*
4. Lazcluze (lazertinib) is being used for treatment consistent with NCCN category 1, 2A, or 2B recommendations for EGFR-mutated NSCLC (see Appendix A, Table 1); *AND*
5. Lazcluze is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.

Experimental or Investigational / Not Medically Necessary

Lazcluze (lazertinib) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Used in combination with therapies other than amivantamab (Rybrevant) for the first-line treatment of EGFR-mutated NSCLC, unless supported by high-quality clinical evidence and recommended by clinical practice guidelines.
- Used for the treatment of NSCLC without confirmed EGFR exon 19 deletions or exon 21 L858R substitution mutations.
- Used for the treatment of other types of cancer or non-cancer conditions, unless supported by high-quality clinical evidence and recommended by clinical practice guidelines.
- Use in pediatric members (under 18 years of age), as safety and efficacy have not been established in this population.
- Used at doses exceeding the FDA-approved maximum dose of 240 mg once daily.

References

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Appendix A

Table 1: Recommended Indications by the National Comprehensive Cancer Network (NCCN)

Indication	NCCN Recommendation Category
Brain Metastases [Central Nervous System Cancers - Limited Brain Metastases] Used in combination with amivantamab-vmjw (preferred) for limited brain metastases in non-small cell lung cancer with exon 19 deletion or L858R • may be considered as initial treatment in select cases (eg, small	2A

asymptomatic brain metastases) for newly diagnosed or stable systemic disease or if reasonable systemic treatment options exist ● consider as treatment for recurrent brain metastases	
Brain Metastases [Central Nervous System Cancers - Extensive Brain Metastases] Used in combination with amivantamab-vmjw (preferred) for extensive brain metastases in non-small cell lung cancer with exon 19 deletion or L858R ● may be considered as primary treatment in select cases (eg, small asymptomatic brain metastases) ● as treatment for recurrent disease with stable systemic disease or reasonable systemic treatment options	2A
Adenocarcinoma (with mixed subtypes), Large cell carcinoma, Squamous cell carcinoma [Non-Small Cell Lung Cancer] In combination with amivantamab-vmjw for EGFR exon 19 deletion or exon 21 L858R recurrent, advanced, or metastatic disease as ● first-line therapy ● continuation of therapy following disease progression on amivantamab-vmjw + lazertinib for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression Single-agent therapy for EGFR exon 19 deletion or L858R mutation recurrent, advanced, or metastatic disease as ● first-line therapy (useful in certain circumstances) ● continuation of therapy following disease progression on single-agent lazertinib for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression Useful in certain circumstances as subsequent therapy for EGFR exon 19 deletion or L858R mutation* positive recurrent, advanced, or metastatic disease in combination with amivantamab-vmjw (if not previously given) following disease progression on osimertinib for symptomatic systemic disease with multiple lesions *not an option for EGFR S768I, L861Q, and/or G719X mutations	1 - for first line therapy if EGFR mutation discovered prior to first-line systemic therapy 2A - for all others
Adenocarcinoma (with mixed subtypes) Large cell carcinoma [Non-Small Cell Lung Cancer] Subsequent systemic therapy in combination with amivantamab-vmjw for recurrent, advanced, or metastatic disease in those with performance status 0-2 and EGFR exon 19 deletion or L858R mutation and nonsquamous histology if progression on (carboplatin or cisplatin)/osimertinib/pemetrexed (if not previously given)	2A
NCCN recommendation categories 1, 2A, and 2B will be considered medically necessary if all applicable medical necessity criteria above are met. The above table is representative of the NCCN guideline recommendations as of the time of policy review. For the most up to date information refer to NCCN.	

Category 1: Based upon high-level evidence (≥1 randomized phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.
Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.
Category 2B: Based upon lower-level evidence, there is NCCN consensus (≥50%, but <85% support of the Panel) that the intervention is appropriate.

Clinical Guideline Revision / History Information

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