

PHARMACY COVERAGE GUIDELINE

TAGRISO™ (osimertinib) 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/or 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.

Medical Necessity Requirements for TAGRISO (osimertinib)

Criteria for Initial Therapy:

Prescriber Qualifications

- Prescribed by an Oncologist or in consultation with an Oncologist

Indication

- Diagnosis of non-small cell lung cancer (NSCLC) with **ONE** of the following:
 - Adjuvant therapy after tumor resection with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations

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- First-line treatment of metastatic tumors with EGFR exon 19 deletions or exon 21 L858R mutations
- First-line treatment of locally advanced or metastatic tumors with EGFR exon 19 deletions or exon 21 L858R mutations, used in combination with pemetrexed and platinum-based chemotherapy
- Treatment of metastatic EGFR T790M mutation-positive tumor, progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy (e.g., afatinib, dacomitinib, erlotinib, gefitinib)
- Treatment of locally advanced, unresectable (stage III) NSCLC with no disease progression during or following platinum-based chemoradiation therapy and tumors with EGFR exon 19 deletions or exon 21 L858R mutations
- Other oncologic direct treatment uses listed in National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement

- 18 years or older

Baseline Clinical Evaluation

- FDA-approved test confirming EGFR exon deletions or mutations in tumor specimens
- Left ventricular ejection fraction (LVEF) by echocardiogram or multigated acquisition scan
- Negative pregnancy test for women of reproductive potential
- Eastern Cooperative Oncology Group (ECOG) Performance status of 0–1
- Complete blood count with differential

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- No end-stage renal disease (creatinine clearance less than 15 mL/min)
- No severe hepatic impairment (total bilirubin greater than 3 times ULN and any AST value)

Documentation Requirements

- A completed request form must be submitted, including:
 - Chart notes
 - Lab results (EGFR mutation test, LVEF, pregnancy test, complete blood count)
 - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

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Criteria for Continuation of Therapy (renewal therapy)

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications

- Continues to be seen by a physician specializing in or is in consultation with an Oncologist

Clinical Response

- No evidence of disease progression or unacceptable toxicity

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- No end-stage renal disease (creatinine clearance less than 15 mL/min)
- No severe hepatic impairment (total bilirubin greater than 3 times ULN and any AST value)
- No development of adverse drug effects that exclude continued use, including:
 - Interstitial lung disease or pneumonitis
 - Symptomatic congestive heart failure or QTc prolongation with life-threatening arrhythmia
 - Erythema multiforme major, Stevens-Johnson syndrome, or toxic epidermal necrolysis
 - Aplastic anemia
 - Cutaneous vasculitis
 - Any adverse reaction not improving within 3 weeks of dose modification

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values confirming safe use (e.g., renal and hepatic function, blood counts)

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year
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Criteria for Off-Label Use Requests:

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

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2. Off-Label Use of Cancer Medications

Description:

Tagrisso (osimertinib) is a kinase inhibitor indicated for adjuvant therapy of adults patients with metastatic non-small cell lung cancer (NSCLC) after tumor resection whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test; and for first-line treatment of adult patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test; and for first-line treatment of adult patients with locally advanced or metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test, used in combination with pemetrexed and platinum-based chemotherapy; and for the treatment of adult patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive NSCLC, as detected by an FDA-approved test, who have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy.

Osimertinib is kinase inhibitor of the EGFR, which binds irreversibly to certain mutant forms of EGFR (T790M, L858R, and exon 19 deletion). It exhibits anti-tumor activity against NSCLC lines harboring EGFR-mutations (T790M/L858R, L858R, T790M/exon 19 deletion, and exon 19 deletion) and to a lesser extent, wild-type EGFR amplifications.

Lung cancer:

- Lung cancer is the second most common cancer in the United States and it is the leading cause of cancer-related mortality
- There are two main types of lung cancer:
 - Small cell lung cancer (SCLC)
 - SCLC is also known as “oat-cell” cancer because the cells look like oats under the microscope
 - Non-small cell lung cancer (NSCLC)
 - NSCLC is the most common type of lung cancer and is seen in 85-90% of lung cancers
 - NSCLC can be either squamous or non-squamous type
 - Classification:
 - Adenocarcinoma
 - Adenosquamous carcinoma
 - Large-cell undifferentiated carcinoma
 - Sarcomatoid carcinoma which includes pleomorphic carcinoma, carcinosarcoma, and pulmonary blastoma
 - Squamous cell carcinoma
 - Squamous (epidermoid) cells are thin, flat cells that look like fish scales
 - Squamous cells are seen in the tissues that line the larger airways
 - Non-squamous cancers usually begin in more distal airway
- Distribution of various NSCLC types:
 - About 40% of lung cancers are adenocarcinomas
 - About 25-30% of lung cancers are squamous cell carcinomas
 - About 10-15% of lung cancers are large cell undifferentiated carcinomas

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- Brain metastases are a frequent complication of NSCLC, with 25-40% of patients developing brain metastases during the course of the disease
 - Many patients with brain metastases are not eligible for radiation therapy due to poor performance status
- An estimated 2-7% NSCLC are found to have ALK gene rearrangements and 15% of NSCLC cases have epidermal growth factor receptor (EGFR) mutations
 - ALK rearrangements and sensitizing EGFR mutations are generally mutually exclusive
 - Central nervous system progression is common with ALK gene rearrangements and accounts for significant morbidity and mortality among these patients
 - Individuals who are relatively young, never or light smokers with adenocarcinoma are most likely to have ALK gene rearrangements

Definitions:

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

NCCN recommendation definitions:

Category 1:

Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:

Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:

Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:

Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead

Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982

Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
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Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to AE
U.S. department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

Resources:

Tagrisso (osimertinib) product information, revised by AstraZeneca Pharmaceuticals LP 02-2024. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed February 21, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-small Cell Lung Cancer Version 3.2025 – Updated January 14, 2025. Available at <https://www.nccn.org>. Accessed April 18, 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.