BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

Gefitinib oral
IRESSA® (gefitinib) oral

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 Gefitinib generic and IRESSA (gefitinib)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by an Oncologist or in consultation with an Oncologist

Indication
- Metastatic non small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations detected by an FDA approved test
- Other oncologic direct treatment uses listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

ORIGINAL EFFECTIVE DATE: 01/01/2016 | ARCHIVE DATE: | LAST REVIEW DATE: 08/21/2025 | LAST CRITERIA REVISION DATE: 08/21/2025

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Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Tumors must have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 to 2

Alternative Therapies
- **For brand Iressa (gefitinib)**:
  - Failure (trial for at least three months duration), contraindication, intolerance to: generic gefitinib. Note: Failure, contraindication, or intolerance to the generic should be reported to the United States Food and Drug Administration (FDA)

Additional Requirements
- Does not have tumors that have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations as safety and efficacy of IRESSA have not been established

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results (including EGFR mutation status and ECOG performance status)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration:
- 6 months OR end of plan year

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

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

Clinical Response
- Documentation of positive clinical response to therapy defined as no evidence of disease progression or unacceptable toxicity

Adherence
- Adherence to the prescribed therapy regimen has been documented

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Alternative Therapies

- **For brand Iressa (gefitinib)**:
  - Failure (trial for at least three months duration), contraindication, intolerance to: generic gefitinib. Note: Failure, contraindication, or intolerance to the generic should be reported to the United States Food and Drug Administration (FDA)

Safety

- Individual has not developed any of the following:
  - Confirmed interstitial lung disease
  - Severe hepatic impairment (Child Pugh Class C)
  - Gastrointestinal perforation
  - Persistent ulcerative keratitis or other severe or worsening ocular disorder
  - Severe bullous, blistering, or exfoliative skin disorder

Additional Requirements

- Does not have tumors that have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations as safety and efficacy of IRESSA have not been established

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

Continuation Therapy Criteria Approval Duration:

- 12 months OR end of plan year

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

2. Off-Label Use of Cancer Medications

Description:

Gefitinib (brand Iressa and generic gefitinib) is a tyrosine kinase inhibitor indicated for the first line treatment of metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test. The safety and efficacy of Gefitinib (brand Iressa and generic gefitinib) have not been established in patients with metastatic

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NSCLC whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations.

The epidermal growth factor receptor (EGFR) is expressed on the cell surface of both normal and cancer cells and plays a role in the processes of cell growth and proliferation. Some EGFR activating mutations (exon 19 deletion or exon 21-point mutation L858R) within NSCLC cells have been identified as contributing to the promotion of tumor cell growth, blocking of apoptosis, increasing the production of angiogenic factors and facilitating the processes of metastasis.

Gefitinib reversibly inhibits the kinase activity of wild-type and certain activating mutations of EGFR, preventing autophosphorylation of tyrosine residues associated with the receptor, thereby inhibiting further downstream signaling and blocking EGFR-dependent proliferation.

Gefitinib offers a new chemotherapeutic agent with a unique mechanism of action. It is indicated as monotherapy for the treatment of patients with locally advanced or metastatic NSCLC after failure of both platinum-based and docetaxel chemotherapies. The FDA believes that the potential benefit of this agent in these patients outweighs the risk of its pulmonary toxicity, while some special interest groups do not support this decision.

Definitions:

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

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 housework, 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	

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.

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Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Resources:

Iressa (gefitinib) product information, revised by AstraZeneca Pharmaceuticals, LP 02-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 08, 2025.

Gefitinib product information, revised by Teva Pharmaceuticals, Inc. 02-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 08, 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 May 08, 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.

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