BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**1/01/16**
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LAST CRITERIA REVISION DATE:	**3/15/18**
ARCHIVE DATE:	

GILOTRIF™ (afatinib) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

GILOTRIF™ (afatinib) oral tablet (cont.)

Description:

Gilotrif (afatinib) is a tyrosine kinase inhibitor indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test and it is indicated for the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy.

Afatinib covalently binds to the kinase domains of EGFR (ErbB1), HER2 (ErbB2), and HER4 (ErbB4) and irreversibly inhibits tyrosine kinase autophosphorylation, resulting in downregulation of ErbB signaling. Treatment with afatinib results in inhibition of tumor growth.

There are two main types of lung cancer: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). SCLC is also known as “oat-cell” cancer because the cells look like oats under the microscope. NSCLC is the most common type of lung cancer, seen in 85-90% of lung cancers. NSCLC can be divided histopathologically as either squamous or non-squamous type. Squamous (epidermoid) cells are thin, flat cells that look like fish scales and are seen in the tissues that line the larger airways where as non-squamous cancers usually begin in more distal airway. There are three main types of NSCLC: squamous cell carcinoma; adenocarcinoma; and large-cell undifferentiated carcinoma. About 25-30% of all lung cancers are squamous cell carcinomas, 40% are adenocarcinomas, and large cell (undifferentiated) carcinoma accounts for about 10-15% of lung cancers.

Definitions:

Modification of Diet in Renal Disease (MDRD) formula:

$$\text{GFR (mL/min/1.73 m}^2\text{)} = 175 \times (S_{cr})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})$$

P-glycoprotein Inhibitors and Inducers

Inhibitors	Inducers
Amiodarone	Carbamazepine
Cyclosporine A	Phenobarbital
Erythromycin	Phenytoin
Itraconazole	Rifampicin
Ketoconazole	St. John’s wort
Nelfinavir	
Quinidine	
Ritonavir	
Saquinavir	
Tacrolimus	
Verapamil	

GILOTRIF™ (afatinib) oral tablet (cont.)

Gilotrif (afatinib)

Medication class:
Antineoplastic agent, Epidermal growth factor receptor (EGFR) inhibitor, Tyrosine kinase inhibitor

FDA-approved indication(s):
- First-line treatment of metastatic non-small cell lung cancer (NSCLC) in patients whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by a FDA-approved test
- Treatment of previously treated metastatic squamous cell NSCLC that has progressed following platinum-based chemotherapy

Limitations of use:
- For metastatic NSCLC, safety and efficacy have not been established in patients whose tumors express EGFR mutations

Recommended Dose:
- 40 mg orally once daily

Maximum dosage
- Not stated

Available Dosage Forms:
- 20 mg, 30 mg, and 40 mg tablets

Warnings, Precautions, and Clinical Information:
- Dose recommendations cannot be made for patients who have an estimated glomerular filtration rate (eGFR), using the Modification of Diet in Renal Disease (MDRD) formula, of < 15 mL/min/1.73 m^2 or on dialysis
- Adjust dose when used with either a P-glycoprotein inhibitor or P-glycoprotein inducer
- Diarrhea occurs in nearly all patients; every patient should have an anti-diarrheal agent ordered
- Hold for severe and prolonged diarrhea not responsive to anti-diarrheal agents
- Permanently discontinue for life-threatening bullous, blistering, or exfoliative skin lesions including toxic epidermal necrolysis (TEN) and Stevens Johnson syndrome (SJS)
- Permanently discontinue if interstitial lung disease (ILD) is diagnosed
- Hold for severe or worsening liver tests
- Permanently for severe hepatic impairment (Child Pugh C)
- Permanently discontinue for confirmed ulcerative keratitis
- Permanently Discontinue for symptomatic left ventricular dysfunction
- Permanently for severe or intolerable adverse reaction occurring at a dose of 20 mg per day
- Woman of child bearing potential should use effective contraception
- Women who is breast feeding an infant or child should stop breast feeding

GILOTRIF™ (afatinib) oral tablet (cont.)

Criteria:

- **Criteria for initial therapy:** Gilotrif (afatinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is an Oncologist
  2. Individual is 18 years of age or older
  3. A confirmed diagnosis of **ONE** of the following:
     - Metastatic non-small cell lung cancer (NSCLC) and tumors have non-resistant epidermal growth factor receptor (EGFR)
     - Metastatic squamous NSCLC progressing after platinum-based chemotherapy

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Gilotrif (afatinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by an Oncologist
  2. Individual's condition responded while on therapy
     - Response is defined as:
       - Individuals disease has not progressed or worsened while on Gilotrif treatment
  3. Individual has been adherent with the medication
  4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use such as:
     - Diarrhea
       - Signs and symptoms may include: 2 or more consecutive days of severe diarrhea while taking anti-diarrheal agent, dehydration
     - Life-threatening bullous, blistering, or exfoliative skin lesions including toxic epidermal necrolysis (TEN) and Stevens Johnson syndrome (SJS)
     - Interstitial lung disease
       - Some signs & symptoms may include: chest pain, palpitations, tachycardia, shortness of breath at rest dyspnea on exertion, dry cough, fatigue, weakness
     - Hepatic impairment
       - Signs & symptoms may include: right sided abdominal pain, bruising, yellow skin or eyes, dark brown urine, severe nausea or vomiting, fatigue, light colored pale stools, itching, confusion
     - Keratitis
       - Signs & symptoms may include: watery eyes, sensitivity to light, blurred vision, eye pain, eye redness, or vision changes, eye inflammation
     - Left ventricular dysfunction

GILOTRIF™ (afatinib) oral tablet (cont.)

- Signs and symptoms may include: edema, shortness of breath, weight gain, chest pain, shortness of breath

5. There are no significant interacting drugs

Renewal duration: 6 months

Resources:

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.

Gilotrif. Package Insert. Revised by manufacturer 11/2013. Accessed 09-04-2015.

Gilotrif. Package Insert. Revised by manufacturer 10/2016. Accessed 10-19-2016.

Gilotrif. Package Insert. Revised by manufacturer 1/2018. Accessed 02-23-2018.

NCCN Clinical Practice Guidelines in Oncology: Non-small Cell Lung Cancer. Version 9.2017, Sep 28, 2017. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

NCCN Clinical Practice Guidelines in Oncology: Head and Neck Cancers. Version 2.2017, May 8, 2017. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.