Gilotrif (afatinib)

Background
Gilotrif is a tyrosine kinase inhibitor that blocks proteins that promote the development of cancerous cells in patients with metastatic non-small cell lung cancer (NSCLC). It is intended for first line treatment in patients who have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test. The most commonly found of these mutations are exon 21 L858R substitutions and exon 19 deletions, however, patients with non-resistant, less common mutations of EGFR may also receive benefit from this agent. Gilotrif is also indicated for patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy (1).

Regulatory Status
FDA-approved indication: Gilotrif is a kinase inhibitor indicated for: (1)

1. 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
2. Treatment of patients with metastatic, squamous NSCLC progressing after platinum-based chemotherapy

Limitation of Use
Safety and efficacy of Gilotrif have not been established in patients whose tumors have resistant EGFR mutations (1).
Off Label Uses: (2)

1. Very advanced and recurrent/persistent head and neck cancers, therapy as a single agent for non-nasopharyngeal cancer if disease progression on or after platinum containing chemotherapy
2. Treatment for recurrent stable systemic disease as a single agent for brain metastases if active against primary tumor (EGFR sensitizing mutation-positive non-small cell lung cancer)

Diarrhea has resulted in dehydration and renal failure; some of these cases were fatal. Withhold Gilotrif for diarrhea that is severe (Grade 2 or higher) and persisting for 2 or more consecutive days while taking antidiarrheal agents. Gilotrif treatment should be withheld if renal function is Grade 2 or higher. Treatment can be resumed when the adverse reaction fully resolves, returns to baseline, or improves to Grade 1 (1).

Discontinue Gilotrif in patients who develop life-threatening bullous, blistering, or exfoliating lesions. For patients who develop prolonged Grade 2 cutaneous adverse reactions lasting more than 7 days, intolerable Grade 2, or Grade 3 cutaneous reactions, withhold Gilotrif until the adverse reaction resolves to Grade 1 or less, and resume Gilotrif with appropriate dose reduction (1).

Gilotrif may cause interstitial lung disease (ILD) or ILD-like adverse reactions (e.g., lung infiltration, pneumonitis, acute respiratory distress syndrome, or alveolitis allergic). Withhold Gilotrif during evaluation of patients with suspected ILD, and discontinue Gilotrif in patients with confirmed ILD (1).

Gilotrif may cause hepatic impairment; some cases were fatal. Periodic liver testing should be conducted in patients during treatment with Gilotrif. Withhold Gilotrif in patients who develop worsening of liver function. In patients who develop severe hepatic impairment while taking Gilotrif, treatment should be discontinued (1).

Gilotrif may cause keratitis, characterized as acute or worsening eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain, and/or red eye. Gilotrif can cause fetal harm when administered to a pregnant woman. Gilotrif is a pregnancy category D (1).

Safety and effectiveness of Gilotrif in pediatric patients have not been established (1).

**Related policies**
Alecensa, Iressa, Mekinist, Tafinlar, Tagrisso, Tarceva, Xalkori, Zykadia
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Gilotrif may be considered medically necessary in patients that are 18 years of age and older with metastatic non-small cell lung cancer, metastatic squamous non-small cell lung cancer (NSCLC); advanced, recurrent, persistent head and neck cancers; or recurrent brain metastases; and if the conditions indicated below are met.

Gilotrif is considered investigational in patients that are less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age
18 years of age or older

Diagnoses

Patient must have ONE of the following:

1. Metastatic non-small cell lung cancer (NSCLC)
   a. Confirmed non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test

2. Metastatic squamous non-small cell lung cancer
   a. Confirmed non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test
   b. Progressing after platinum-based chemotherapy

3. Advanced, recurrent, or persistent head and neck cancers
   a. Used as single agent therapy
   b. NOT used for nasopharyngeal cancer
   c. Progression on or after platinum containing chemotherapy

4. Recurrent brain metastases
   a. Confirmed non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test
   b. Used as single agent therapy
Prior – Approval Renewal Requirements

Age
18 years of age or older

Diagnoses

Patient must have ONE of the following:

1. Metastatic non-small cell lung cancer (NSCLC)
2. Metastatic squamous non-small cell lung cancer
3. Advanced, recurrent, or persistent head and neck cancers
4. Recurrent brain metastases

AND NONE of the following:

1. Development of life-threatening bullous, blistering, or exfoliating lesions
2. Confirmed interstitial lung disease (ILD)
3. Severe hepatic impairment

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits

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<tr>
<th>Quantity</th>
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<th>Duration</th>
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<tr>
<td>20 mg</td>
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<td>12 months</td>
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<tr>
<td>30 mg</td>
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<tr>
<td>40 mg</td>
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Rationale

Summary
Gilotrif is a tyrosine kinase inhibitor indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) who have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test, in patients with metastatic squamous non-small cell lung cancer (NSCLC); advanced, recurrent, persistent head and neck cancers; or recurrent brain metastases. Safety and efficacy of Gilotrif have not been established in patients whose tumors have resistant EGFR mutations. Gilotrif therapy may cause diarrhea, bullous and exfoliative skin disorders, interstitial lung disease, hepatic toxicity, keratitis, and embryofetal toxicity. Safety and effectiveness of Gilotrif in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Gilotrif while maintaining optimal therapeutic outcomes.

References


Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>July 2013</td>
<td>New Addition to PA</td>
</tr>
<tr>
<td>September 2014</td>
<td>Annual criteria review and reference update</td>
</tr>
<tr>
<td>December 2015</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>June 2016</td>
<td>Annual review and reference update</td>
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<td>Addition of indication: metastatic squamous non-small cell lung cancer (NSCLC) who have progressed after platinum-based chemotherapy Policy code changed from 5.04.39 to 5.21.39</td>
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<tr>
<td>June 2017</td>
<td>Annual editorial review and reference update</td>
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<td>Addition of indication: advanced, recurrent, or persistent head and neck cancers, when used as single agent therapy for non- nasopharyngeal cancer if disease progression on or after platinum containing chemotherapy</td>
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<tr>
<td>September 2017</td>
<td>Annual review</td>
</tr>
<tr>
<td></td>
<td>Added quantity limits</td>
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</table>
January 2018  Update in initiation criteria from metastatic NSCLC with EGFR exon 19 deletions or exon 21 substitution mutations to metastatic NSCLC with non-resistant epidermal growth factor receptor (EGFR) mutations
March 2018  Annual review
March 2019  Annual review

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 15, 2019 and is effective on April 1, 2019.