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5.21.039

Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	September 13, 2013
Subject:	Gilotrif	**Page:**	1 of 6

Last Review Date: March 8, 2024

Gilotrif

Description

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 indications: 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

Limitations 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, Erlotinib, Exkivity, Iressa, Mekinist, Tafinlar, Tagrisso, Vizimpro, Xalkori, Zykadia

Policy

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** if the conditions indicated below are met.

Gilotrif may be considered **investigational** 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

Quantity	20 mg	90 tablets per 90 days **OR**
	30 mg	90 tablets per 90 days **OR**
	40 mg	90 tablets per 90 days
Duration	12 months	

Prior – Approval *Renewal* Limits

Same as above

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

1. Gilotrif [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc; April 2022.
2. NCCN Drugs & Biologics Compendium® Afatinib 2024. National Comprehensive Cancer Network, Inc. Accessed on January 16, 2024.

Policy History

Date	Action
July 2013	New Addition to PA
September 2014	Annual criteria review and reference update
December 2015	Annual editorial review and reference update
June 2016	Annual review and reference update 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
June 2017	Annual editorial review and reference update 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
September 2017	Annual review Added quantity limits
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 Addition of recurrent brain metastases
March 2018	Annual review
March 2019	Annual review
June 2020	Annual review and reference update
June 2021	Annual review and reference update
March 2022	Annual review and reference update

June 2023	Annual review and reference update. Changed policy number to 5.21.039
March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.