PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Gilotrif™ (afatinib tablets – Boehringer Ingelheim)

TAC APPROVAL DATE: 11/29/2017; selected revision 02/07/2018

OVERVIEW

Gilotrif is a tyrosine kinase inhibitor (TKI) 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 a FDA-approved test.[1] The safety and efficacy of Gilotrif have not been established in patients whose tumors have resistant *EGFR* mutations. Gilotrif is also indicated for the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy. Gilotrif covalently binds to the kinase domains of EGFR (ErbB1), human epidermal growth factor receptor (HER)-2 [ErbB2], and HER4 (ErbB4) and irreversibly inhibits tyrosine kinase autophosphorylation, resulting in down-regulation of ErbB signaling.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for NSCLC (version 2.2018) recommend *EGFR* mutation testing in patients with nonsquamous NSCLC (i.e., adenocarcinoma, large cell) or in NSCLC not otherwise specified (NOS).[2,3] Tarceva® (erlotinib tablets), Iressa® (gefitinib tablets), Gilotrif (all category 1) and Tagrisso™ (osimertinib tablets) [category 2A] are all recommended for the first-line treatment in patients with sensitizing *EGFR*-mutation positive NSCLC discovered before first-line chemotherapy.[3] If *EGFR* mutation is discovered during first-line chemotherapy, complete planned chemotherapy, including maintenance therapy, or interrupt, followed by treatment with Tarceva, Iressa, Gilotrif, or Tagrisso (category 2A). Upon disease progression, T790M testing is recommended in guidelines. Plasma biopsy can be considered if tissue biopsy is not feasible. Patients with asymptomatic progression can consider local therapy; Tagrisso is a category 1 recommended option if T790M mutation-positive. Patients can also continue Tarceva, Gilotrif, or Iressa (category 2A). Patients with symptomatic progression to the brain can consider local therapy, Tagrisso (if T790M mutation-positive) [category 1], or continue on Tarceva, Iressa, or Gilotrif (category 2A). Tagrisso (regardless of T790M status) or pulse Tarceva can be considered for progressive leptomeningeal disease. For symptomatic, systemic isolated lesion, local therapy or continuation of Tarceva, Gilotrif, or Iressa is recommended. For systemic multiple lesions, if T790M mutation-positive, Tagrisso, if not previously given, is the category 1 recommended option. If T790M mutation-negative, , initial cytotoxic therapy options listed for adenocarcinoma, or squamous cell carcinoma (e.g., doublet chemotherapy) can be considered in this setting (category 2A). NCCN added a footnote to this recommendation to also consider Gilotrif and Erbitux® (cetuximab for injection) combination regimen in patients with disease progression (T790M-negative multiple systemic lesions) on EGFR-TKI therapy (category 2A). This is based on data demonstrating similar response rates with this combination therapy in patients with T790M mutation-positive or mutation-negative tumors in pre-treated patients with NSCLC. NCCN notes that data in the second-line setting suggest that immunotherapy is less effective, irrespective of PD-L1 expression, in tumors with an actionable mutation. NCCN notes that for squamous cell carcinoma, Gilotrif is not used in the second-line setting at NCCN institutions for these indications related to the efficacy and safety of these agents compared to the efficacy and safety of other available agents.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Gilotrif. All approvals are provided for 3 years in duration as noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Gilotrif is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Non-Small Cell Lung Cancer (NSCLC) – Epidermal Growth Factor Receptor (EGFR) Mutation-Positive.** Approve for 3 years if the patient meets the following criteria (A and B):
    A) The patient has *metastatic* NSCLC; AND
    B) The patient has non-resistant EGFR mutation-positive NSCLC as detected by an approved test.

2. **Non-Small Cell Lung Cancer (NSCLC) – Squamous Cell Carcinoma.** Approve for 3 years if the patient meets the following criteria (A and B):
    A) The patient has metastatic squamous cell carcinoma; AND
    B) The patient has disease progression after treatment with platinum-based chemotherapy.

    Gilotrif is indicated for the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy.[1] In the Phase III LUX-Lung 8 trial in adults with stage IIIB or IV squamous cell carcinoma, treatment with Gilotrif led to a significant improvement in PFS compared with Tarceva: median PFS 2.6 months vs. 1.9 months for Gilotrif and Tarceva, respectively (HR 0.81; 95% CI: 0.69, 0.96; P = 0.0103).[4] After a median follow-up of 18.4 months, OS was significantly improved with Gilotrif vs. Tarceva with a median OS of 7.9 months vs. 6.8 months, respectively (HR 0.81; 95% CI 0.69, 0.95; P = 0.008).[1,4] In the Gilotrif arm 77% of the patients died (n = 307/398) compared with 82% of patients in the Tarceva arm (n = 325/397).

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Gilotrif has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Gilotrif™ tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; January 2018.
2. The NCCN Drugs & Biologics Compendium. © 2017 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed January 24, 2018. Search terms: afatinib.
3. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (Version 2.2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed January 24, 2018.
4. Soria JC, Felip E, Cobo M, et al. Afatinib versus erlotinib as second-line treatment of patients with advanced squamous cell carcinoma of the lung (LUX-lung 8): an open-label randomized controlled phase 3 trial. *Lancet Oncol.* 2015;16:897-907.

HISTORY

Type of Revision	Summary of Changes*	TAC/DEU Approval Date
Selected revision	Changed approval duration from 1 year to 3 years	09/03/2014
Annual revision	No criteria changes	10/01/2014
Annual revision	Deleted approval for patients already started on Gilotrif without EGFR testing. Added criteria for approval in squamous cell carcinoma and for patients with HER2 mutation.	10/21/2015
DEU revision	Moved approval for Squamous Cell Carcinoma from Other Uses with Supportive Evidence to FDA-approved uses. No criteria changes. Updated NCCN guidelines.	04/18/2016
Annual revision	Minor wording changes to squamous cell carcinoma indication to match FDA-approved indication. Also removed the word "FDA" while referring to the approved test for exon 19 or 21 mutations.	11/09/2016
Annual revision	Deleted approval in HER2 mutation-positive non-small cell lung cancer since NCCN no longer recommends use for this condition.	11/29/2017
Selected revision	Deleted criteria requiring specific EGFR exon 19 or exon 21 mutations with regards to NSCLC. Based on FDA-approval, modified criteria to "non-resistant" EGFR mutation-positive NSCLC.	02/07/2018

TAC – Therapeutic Assessment Committee; DEU – Drug Evaluation Unit; * For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; EGFR – Epidermal growth factor receptor; HER2 – Human epidermal growth factor receptor; NCCN – National Comprehensive Cancer Network.