Clinical Policy: Afatinib (Gilotrif)

Reference Number: CP.PHAR.298
Effective Date: 01/17
Last Review Date: 11/16

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for afatinib (Gilotrif®) tablets for oral use.

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Gilotrif is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Small Cell Lung Cancer (must meet all):

1. Diagnosis of non-small cell lung cancer (NSCLC);
2. Meets a or b:
   a) FDA recommended use (meets i, ii and iii):
      i. Disease is recurrent or metastatic;
      ii. Disease is positive for a sensitizing epidermal growth factor receptor (EGFR) mutation (exon 19 deletion or exon 21 [L858R] substitution) as detected by an FDA approved test;
      iii. Gilotrif is prescribed as first-line therapy;
   b) Off-label NCCN recommended use (i or ii):
      i. Disease is positive for a human epidermal growth factor receptor 2 (HER2) mutation as detected by an FDA approved test;
      ii. Disease is positive for a sensitizing EGFR mutation (exon 19 deletion or exon 21 [L858R] substitution) as detected by an FDA approved test AND meets all of the following:
         a) Disease is metastatic;
         b) Gilotrif is prescribed in combination with cetuximab (Erbitux);
         c) EGFR mutation is T790M negative;
         d) Disease has progressed on EGFR tyrosine kinase inhibitor therapy;
         e) Disease is positive for multiple symptomatic systemic lesions.

Approval duration: 3 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

1. The following NCCN recommended uses for Gilotrif, meeting NCCN categories 1, 2a or 2b, are approved per the CP.PHAR.57 Global Biopharm Policy:
   a. Head and neck cancers - very advanced and recurrent/persistent head and neck cancer meeting both of the following (i and ii):
      i. Squamous cell carcinoma with mixed subtypes;

ii. Second-line systemic therapy as a single agent for non-nasopharyngeal cancer in patients with performance status 0-1.

II. Continued Approval

A. Non-Small Cell Lung Cancer (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. If Gilotrif is requested after disease progression on Gilotrif, NSCLC is positive for a sensitizing EGFR mutation (exon 19 deletion or exon 21 [L858R] substitution) and is characterized by any of the following *(off-label NCCN recommended use):*
   a. Asymptomatic disease (without rapid radiologic progression or threatened organ function);
   b. Symptomatic brain lesions;
   c. Isolated symptomatic systemic lesions;
3. Member has none of the following reasons to discontinue:
   a. Life-threatening bullous, blistering, or exfoliative skin lesions;
   b. Confirmed interstitial lung disease;
   c. Severe drug-induced hepatic impairment (Child-Pugh C);
   d. Persistent ulcerative keratitis;
   e. Symptomatic left ventricular dysfunction;
   f. Severe or intolerable adverse reaction occurring at a dose of 20 mg per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:
Gilotrif tablets contain afatinib, a tyrosine kinase inhibitor which is a 4-anilinoquinazoline. 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. Afatinib demonstrated inhibition of autophosphorylation and in vitro proliferation of cell lines expressing wildtype EGFR or those expressing selected EGFR exon 19 deletion mutations or exon 21 L858R mutations, including some with a secondary T790M mutation, at afatinib concentrations achieved, at least transiently, in patients. In addition, afatinib inhibited in vitro proliferation of cell lines overexpressing HER2. Treatment with afatinib resulted in inhibition of tumor growth in nude mice implanted with tumors either overexpressing wild type EGFR or HER2 or in an EGFR L858R/T790M double mutant model.

Formulations:
Gilotrif tablets for oral administration are available in 40 mg, 30 mg, or 20 mg of afatinib (equivalent to 59.12 mg, 44.34 mg, or 29.56 mg afatinib dimaleate, respectively).

FDA Approved Indications:
Gilotrif is a tyrosine kinase inhibitor/oral tablet formulation indicated for:

- First-line treatment of patients with 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.
  - Limitation of use: The safety and efficacy of GILOTRIF have not been established in patients whose tumors have other EGFR mutations.
- Treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy.

Appendices
Appendix A: Abbreviation Key
EGFR: epidermal growth factor receptor
HER2: human epidermal growth factor receptor 2
NSCLC: non-small cell lung cancer

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
New policy.	11/16	01/17

References
1. Gilotrif Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; October 2016. Available at: http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Gilotrif/Gilotrif.pdf?DMW_FORMAT=pdf. Accessed November 21, 2016.
2. Afatinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed November 21, 2016.
3. Non-small cell lung cancer (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed November 21, 2016.

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional

organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.