Clinical Policy Title:	afatinib
Policy Number:	RxA.151
Drug(s) Applied:	Gilotrif®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Afatinib (Gilotrif®) is a kinase inhibitor. It is indicated for:

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

Limitation(s) of Use: The safety and efficacy of Gilotrif® have not been established in patients whose tumors have resistant EGFR mutations.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
afatinib (Gilotrif®)	NSCLC	40 mg PO once daily Renal impairment: 30 mg orally once daily in patients with severe renal impairment	40 mg/day

Dosage Forms

- Tablets: 20 mg, 30 mg, 40 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of recurrent, advanced or metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
    a. Disease is positive for a sensitizing EGFR mutation (e.g., exon 19 deletion or L858R)

b. Squamous cell carcinoma histology with progression after platinum-based chemotherapy (e.g., cisplatin, carboplatin);

5. Request meets one of the following (a or b):
   a. Dose does not exceed 40 mg (1 tablet) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for the covered indications and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 40 mg (1 tablet) per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
EGFR: epidermal growth factor receptor
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
NSCLC: non-small cell lung cancer

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Platinum-based chemotherapy (e.g., cisplatin, carboplatin)	Varies	Varies

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None.

- Boxed Warning(s):

- None.

APPENDIX D: General Information

- 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. Certain mutations in EGFR, including non-resistant mutations in its kinase domain, can result in increased autophosphorylation of the receptor, leading to receptor activation, sometimes in the absence of ligand binding, and can support cell proliferation in NSCLC. Non-resistant mutations are defined as those occurring in exons constituting the kinase domain of EGFR that lead to increased receptor activation and where efficacy is predicted by:
  a. Clinically meaningful tumor shrinkage with the recommended dose of afatinib;
  b. Inhibition of cellular proliferation or EGFR tyrosine kinase phosphorylation at concentrations of afatinib sustainable at the recommended dosage according to validated methods. The most commonly found of these mutations are exon 21 L858R substitutions and exon 19 deletions.
- Afatinib demonstrated inhibition of autophosphorylation and/or in vitro proliferation of cell lines expressing wild-type EGFR and in those expressing selected EGFR exon 19 deletion mutations, exon 21 L858R mutations, or other less common non-resistant mutations, at afatinib concentrations achieved 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.

References

1. Gilotrif Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; October 2019. Available at: https://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Gilotrif/Gilotrif.pdf?DMW_FORMAT=pdf Accessed February 18, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 19, 2021.
3. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer Version 3.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/nscl_blocks.pdf. Accessed February 19, 2021.
4. National Comprehensive Cancer Network Guidelines. Central Nervous System Cancers Version 3.2020 Available at https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed February 19, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Continued Therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 2. Dosing information was updated to add renal impairment dosing. 3. I.A.4.a was updated to remove, “insertion; exon 21 point mutation L8618……S7681.” 4. Appendix B was rephrased to “Below are suggested therapeutic alternatives based on clinical…”.	02/19/2021	09/14/2021

5. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 6. Appendix D: Updated general information. 7. References were reviewed and updated.		