Pharmacy Policy Bulletin: J-0896 EGFR-Targeting Kinase Inhibitors - Commercial and Healthcare Reform	
Number: J-0896	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes with Prior Authorization **Quantity Limits (1., 2., 3., or 4.):** **1.** Rx Mgmt Quantity Limits = Safety/ Specialty **2.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt **3.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt + Watchful **4.** Rx Mgmt Performance = MRxC = Yes **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0896-014	**Original Date:** 06/04/2003
Effective Date: 10/08/2025	**Review Date:** 09/17/2025

Drugs Product(s):	• Gilotrif (afatinib) • Iressa (gefitinib) • Lazcluze (lazertinib) • Tagrisso (osimertinib) • Tarceva (erlotinib) • Vizimpro (dacomitinib)

FDA-Approved Indication(s):	• Gilotrif (afatinib)
	  ○ First-line treatment of metastatic NSCLC in patients whose tumors have non-resistant *EGFR* mutations (i.e., exon 19 deletions, exon 21 (L858R) substitution mutations, S768I, L861Q, G719X) as detected by an FDA-approved test.
	  ○ Treatment of metastatic squamous NSCLC in patients who have progressed on platinum-based chemotherapy (e.g. carboplatin, oxaliplatin, etc.)
	• Iressa (gefitinib)
	  ○ First-line treatment of metastatic NSCLC in adults whose tumors have *EGFR* exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

	• Lazcluze (lazertinib)
	  ○ In combination with Rybrevant (amivantamab) for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.
	• Tagrisso (osimertinib)
	  ○ Adjuvant therapy after tumor resection in adult patients with NSCLC whose tumors have *EGFR* exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
	  ○ Treatment of adult patients with locally advanced, unresectable (stage III) NSCLC whose disease has not progressed during or following concurrent or sequential platinum-based chemoradiation therapy and whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
	  ○ First-line treatment of adult patients with metastatic NSCLC whose tumors have *EGFR* exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
	  ○ In combination with pemetrexed and platinum-based chemotherapy for the first-line treatment of adult patients with locally advanced or metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
	  ○ Treatment of adult patients with metastatic *EGFR* T790M mutation-positive NSCLC, as detected by an FDA-approved test, who have progressed on or after EGFR TKI therapy.
	• Tarceva (erlotinib)
	  ○ Treatment of patients with metastatic NSCLC whose tumors have *EGFR* exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen.
	  ○ First-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine.
	• Vizimpro (dacomitinib)
	  ○ First-line treatment of metastatic NSCLC with *EGFR* exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test

Background:	• Gilotrif inhibits the autophosphorylation and in vitro proliferation of cell lines expressing wild-type EGFR or those expressing selected EGFR exon 19 deletion mutations or exon 21 L858R mutations. Gilotrif 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. • Iressa is a tyrosine-kinase inhibitor of activating mutations of EGFR, prevents the autophosphorylation, thereby inhibiting downstream signally and blocking EGFR-dependent proliferation. Its affinity for EGFR exon 19 deletion or exon 21 point mutation L858R mutations is higher than affinity for wild-type EGFR. • Lazcluze (lazertinib) is a self-administered, oral, third-generation TKI of EGFR that works by irreversibly inhibiting *EGFR*; this results in inhibition of EGFR phosphorylation and downstream signaling pathways and inhibition of cancer cell proliferation as well as increased tumor cell apoptosis. ○ Lazcluze in combination with Rybrevant is the first chemotherapy-free combination regimen for first-line treatment of patients with *EGFR*-mutated NSCLC. This targeted approach reserves chemotherapy for later stages of treatment when resistance becomes more complex.

	○ This combination can cause serious and fatal venous thromboembolic events (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE). Prophylactic anticoagulation is recommended for the first four months of treatment, • Tagrisso is an EGFR kinase inhibitor which irreversibly binds to mutant forms of EGFR (T790M, L858r, and exon 19 deletion) at approximately 9-fold lower concentrations than wild-type. ○ Tagrisso is indicated in patients with locally advanced, unresectable (stage III) NSCLC whose disease has not progressed during or following concurrent or sequential platinum-based chemoradiation therapy. Sequential chemoradiation therapy is when either chemotherapy or radiation is administered first, and the other follows after the last cycle. Concurrent chemoradiation occurs when radiation therapy is administered during or very close to the chemotherapy treatment. • Tarceva inhibits the intracellular phosphorylation of tyrosine kinase associated with EGFR. Specificity of inhibition with regard to other tyrosine kinase receptors has not been fully characterized. ○ It is recommended to avoid use of concomitant CYP3A4 inducers, such as rifampin, rifabutin, rifapentine, phenytoin, carbamazepine, phenobarbital, or St. John's Wort with Tarceva. If concomitant use cannot be avoided, the dose of Tarceva should be increased by 50 mg increments at 2-week intervals to a maximum of 450 mg, as tolerated. ○ The dose of Tarceva should be increased by 50 mg at 2-week intervals to a maximum of 300 mg for patients who smoke cigarettes. Upon cessation of smoking, the dose of Tarceva should be immediately reduced to the recommended dose (150 mg orally daily or 100 mg orally daily). • Vizimpro is an irreversible inhibitor of the kinase activity of the human EGFR family (EGFR/HER1, HER2, and HER4) and certain EGFR activating mutations (exon 19 deletion or the exon 21 L858R substitution mutation). • The efficacy of Vizimpro was evaluated in a randomized, open-label, active-controlled clinical trial of 452 adult patients with unresectable, metastatic NSCLC with no prior therapy for metastatic disease or recurrent disease. ○ The primary endpoint was progression-free survival (PFS). ○ Median PFS in the Vizimpro group was 14.7 months versus 9.2 months in the gefitinib arm. ○ Vizimpro was associated with a statistically significant improvement in PFS compared with gefitinib ($p < 0.0001$), however no significant improvements in overall response rate (75% for Vizimpro vs 72% for gefitinib; $p = 0.39$) were observed. • Exkivity (mobocertinib) was previously granted accelerated approved in 2021 for the same indication as Zegfrovy; however, in October 2023, the FDA met with Exkivity's manufacturer, Takeda, to discuss voluntary withdrawal of the product due to failure to meet the primary endpoint of progression free survival in the EXCLAIM-2 trial. Approval of Exkivity was then withdrawn in July 2024. • For EGFR kinase inhibitors included in this policy, safety and efficacy of have not been established in pediatric patients. • For information regarding FDA-approved companion diagnostics, please visit: https://www.fda.gov/medical-devices/vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools. • Prescribing Considerations: ○ Kinase inhibitors should be prescribed under the supervision of a hematologist/oncologist

Approval Criteria

I. Initial Authorization

A. Gilotrif (afatinib)

When a benefit, coverage of Gilotrif may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member is 18 years of age or older.
2. The member meets one (1) of the following criteria **(a. or b.)**:
   - **a.** The member has a diagnosis of metastatic NSCLC (ICD-10: C34) and meets one (1) of the following criteria **(i., ii., or iii.)**:
     - **i.** Disease harbors *EGFR* exon 19 deletions.
     - **ii.** Disease harbors *EGFR* exon 21 (L858R) substitution mutations.
     - **iii.** Disease harbors a non-resistant *EGFR* mutation (i.e., S768I, L861Q, G719X)
   - **b.** The member has a diagnosis of squamous metastatic NSCLC and meets the following criterion **(i.)**:
     - **i.** The member has progressed on platinum-based chemotherapy (e.g., carboplatin, oxaliplatin, etc.).

B. Iressa (gefitinib)

When a benefit, coverage of Iressa may be approved when all of the following criteria are met **(1., 2., and 3.)**:

1. The member is 18 years of age or older.
2. The member has a diagnosis of metastatic NSCLC (ICD-10: C34) and meets one (1) of the following criteria **(a. or b.)**:
   - **a.** Disease harbors *EGFR* exon 19 deletion.
   - **b.** Disease harbors *EGFR* exon 21 (L858R) substitution mutation.
3. If the request is for brand Iressa, the member has experienced therapeutic failure or intolerance to generic gefitinib.

C. Lazcluze (lazertinib)

When a benefit, coverage of Lazcluze may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 18 years of age or older.
2. The member has a diagnosis of locally advanced or metastatic NSCLC (ICD-10: C34) and meets one (1) of the following criteria determined by an FDA-approved test **(a. or b.)**:
   - **a.** Disease harbors EGFR exon 19 deletion.
   - **b.** Disease harbors EGFR exon 21 (L858R) substitution mutation,
3. The member is treatment naïve for advanced disease.
4. Lazcluze will be administered in combination with Rybrevant.

D. Tagrisso (osimertinib)

1. NSCLC

a. Adjuvant Therapy after Tumor Resection

When a benefit, coverage of Tagrisso may be approved when all of the following criteria are met **(i. through iv.)**:

- **i.** The member is 18 years of age or older.
- **ii.** The member has a diagnosis of NSCLC (ICD-10: C34).
- **iii.** The member is using Tagrisso as adjuvant therapy after tumor resection.
- **iv.** The member meets one (1) of the following, as detected by an FDA-approved test **(A) or B))**:
  - **A)** Disease harbors *EGFR* exon 19 deletions.
  - **B)** Disease harbors *EGFR* exon 21 L858R mutations.

b. Locally Advanced, Unresectable (Stage III) NSCLC

When a benefit, coverage of Tagrisso may be approved when all of the following criteria are met **(i. through iv.)**:

i. The member is 18 years of age or older.
ii. The member has a diagnosis of locally advanced, unresectable (stage III) NSCLC (ICD-10: C34).
iii. Disease has not progressed during or following concurrent or sequential platinum-based chemoradiation therapy.
iv. The member meets one (1) of the following, as detected by an FDA-approved test **(A) or B))**:
  A) Disease harbors *EGFR* exon 19 deletions.
  B) Disease harbors *EGFR* exon 21 L858R mutations.

c. First-Line Treatment of Metastatic NSCLC

When a benefit, coverage of Tagrisso may be approved when all of the following criteria are met **(i. through iv.)**:

i. The member is 18 years of age or older.
ii. The member has a diagnosis of metastatic NSCLC (ICD-10: C34).
iii. The member is using Tagrisso as first-line treatment.
iv. The member meets one (1) of the following, as detected by an FDA-approved test **(A) or B))**:
  A) Disease harbors *EGFR* exon 19 deletions.
  B) Disease harbors *EGFR* exon 21 L858R mutations.

d. In Combination with pemetrexed and Platinum-Based Chemotherapy for First-Line Treatment of Locally Advanced or Metastatic NSCLC

When a benefit, coverage of Tagrisso may be approved when all of the following criteria are met **(i. through v.)**:

i. The member is 18 years of age or older.
ii. The member has a diagnosis of locally advanced or metastatic NSCLC (ICD-10: C34).
iii. The member is using Tagrisso as first-line treatment.
iv. The member is using Tagrisso in combination with pemetrexed and platinum-based chemotherapy.
v. The member meets one (1) of the following, as detected by an FDA-approved test **(A) or B))**:
  A) Disease harbors *EGFR* exon 19 deletions.
  B) Disease harbors *EGFR* exon 21 L858R mutations.

e. Metastatic EGFR T790M Mutation-Positive NSCLC

When a benefit, coverage of Tagrisso may be approved when all of the following criteria are met **(i. through iv.)**:

i. The member is 18 years of age or older.
ii. The member has a diagnosis of metastatic NSCLC (ICD-10: C34).
iii. Disease harbors an *EGFR* T790M mutation, as detected by an FDA-approved test.
iv. The member has experienced disease progression on or after EGFR tyrosine kinase inhibitor therapy (e.g., erlotinib, gefitinib, etc.).

E. Tarceva (erlotinib)

1. NSCLC

When a benefit, coverage of Tarceva (erlotinib) may be approved when all of the following criteria are met **(a., b., and c.)**:

a. The member is 18 years of age or older.
b. The member has a diagnosis of metastatic NSCLC (ICD-10: C34) and meets one (1) of the following criteria **(i. or ii.)**:
  i. Disease harbors *EGFR* exon 19 deletions.
  ii. Disease harbors *EGFR* exon 21 (L858R) substitution mutations

c. If the request is for brand Tarceva, the member has experienced therapeutic failure or intolerance to generic erlotinib.

2. Pancreatic Cancer
When a benefit, coverage of Tarceva (erlotinib) may be approved when all of the following criteria are met **(a. through d.):**
- **a.** The member has a diagnosis of pancreatic cancer (ICD-10 C25) and meets one (1) of the following criteria **(i. or ii.):**
  - **i.** Disease is classified as locally advanced, unresectable.
  - **ii.** Disease is classified as metastatic.
- **b.** The member is using Tarceva as first-line therapy.
- **c.** The member is using Tarceva in combination with gemcitabine.
- **d.** If the request is for brand Tarceva, the member has experienced therapeutic failure or intolerance to generic erlotinib.

Quantity Limits
When a benefit, additional quantities of Tarceva 150 mg, up to 2 tablets per day, may be approved when one of the following criteria are met **(1. or 2.)**:
1. The member is taking a strong CYP3A inducer.
2. The member is smoking cigarettes.

F. Vizimpro (dacomitinib)
When a benefit, coverage of Vizimpro may be approved when all of the following criteria are met **(1. and 2.)**:
1. The member is 18 years of age or older.
2. The member has a diagnosis of metastatic NSCLC and meets one (1) of the following criteria **(a. or b.)**:
   - **a.** Disease harbors *EGFR* exon 19 deletions.
   - **b.** Disease harbors *EGFR* exon 21 L858R substitution mutations.

II. Reauthorization
When a benefit, reauthorization of an EGFR kinase inhibitor may be approved when all of the following criteria are met **(A. and B.)**:
- **A.** The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as either one of the following **(1. or 2.)**:
  1. Disease improvement
  2. Delayed disease progression
- **B.** If the request is for brand Tarceva or brand Iressa, documentation that the AB-rated generic is ineffective or not tolerated.
- **C.** If the request is for Lazcluze, the prescriber attests that combination therapy with Rybrevant will continue.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology medications listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drugs addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

I. Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

Refer to J-699 and J-824 for previous versions.

References:

1. Gilotrif [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; October 2022.
2. Iressa [package insert]. Wilmington, DE: AstraZeneca; May 2021.
3. Lazcluze [package insert]. Horsham, PA: Janssen Biotech, Inc.; August 2024.
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5. Tarceva [package insert]. South San Francisco, CA: Genentech, Inc.; October 2016.
6. Vizimpro [package insert]. New York, NY: Pfizer; September 2018.NCCN Guidelines. Non-Small Cell Lung Cancer v.5.2021. National Comprehensive Cancer Network. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed June 19, 2023.
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9. Cancer Center. Chemoradiation. Available at: https://www.cancercenter.com/treatment-options/chemoradiation. Accessed October 17, 2024.
10. Federal Register. Takeda Pharmaceuticals U.S.A., Inc.; Withdrawal of Approval of New Drug Application for EXKIVITY (Mobocertinib Succinate) Capsule, Equivalent to 40 Milligrams Base. Available at: https://www.federalregister.gov/documents/2024/07/15/2024-15371/takeda-pharmaceuticals-usa-inc-withdrawal-of-approval-of-new-drug-application-for-exkivity. Accessed July 14, 2025.