09-J1000-44

Original Effective Date: 01/01/12

Reviewed: 09/11/19

Revised: 02/15/20

Subject: Erlotinib (Tarceva®) Tablets

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Erlotinib (Tarceva®) is an oral, selective epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI). EGFR is expressed, overexpressed or dysregulated in a variety of cancers including breast cancer, non-small cell lung cancer (NSCLC), and ovarian cancer. Erlotinib was initially approved by the US Food and Drug Administration for the treatment of NSCLC in 2004. In 2005, the approval was expanded to include treatment of pancreatic cancer. Current National Comprehensive Cancer Network guidelines support the use of erlotinib in the treatment of NSCLC, pancreatic, and chordoma.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of erlotinib (Tarceva®) **meets the definition of medical necessity** for members diagnosed with **ANY** of the following conditions when **ALL** associated criteria are met:

1. **Bone Cancer-Chordoma**

a. Member has recurrent disease

b. Erlotinib is used as monotherapy

c. For brand Tarceva only: Member has tried and had intolerable adverse effects to generic erlotinib – specific intolerance to generic erlotinib and rationale for use of brand Tarceva must be provided in addition to **BOTH** of the following:

   i. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda

   ii. Completed Naranjo Adverse Drug reaction probablility scale - https://livertox.nih.gov/Naranjoassessment.pdf

d. Dose does not exceed 150 mg daily (dosage will be achieved using the fewest number of tablets per day) with the following exceptions:

   i. Dose does not exceed 450 mg daily (dosage will be achieved using the fewest number of tablets per day) **AND** member is receiving a concomitant strong CYP3A4 inducer (e.g., phenytoin, rifampin, carbamazepine, St. John's Wort)

   ii. Dose does not exceed 300 mg daily (dosage will be achieved using the fewest number of tablets per day) **AND** member is a current cigarette smoker

2. Non-Small Cell Lung Cancer AND known sensitizing epidermal growth factor receptor mutation

a. Member has a documented epidermal growth factor receptor (EGFR) mutation – laboratory documentation must be provided

b. Member has advanced, recurrent, or metastatic disease

c. **ONE** of the following:

   i. Used as monotherapy

   ii. Used in combination with ramucirumab (Cyramza)

   iii. Used in combination with bevacizumab (Avastin) – nonsquamous cell histology only

d. For brand Tarceva only: Member has tried and had intolerable adverse effects to generic erlotinib – specific intolerance to generic erlotinib and rationale for use of brand Tarceva must be provided in addition to **BOTH** of the following:

   i. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda

   ii. Completed Naranjo Adverse Drug reaction probablility scale - https://livertox.nih.gov/Naranjoassessment.pdf

e. Dose does not exceed 150 mg daily (dosage will be achieved using the fewest number of tablets per day) with the following exceptions:

   i. Dose does not exceed 450 mg daily (dosage will be achieved using the fewest number of tablets per day) **AND** member is receiving a concomitant strong CYP3A4 inducer (e.g., phenytoin, rifampin, carbamazepine, St. John's Wort)

   ii. Dose does not exceed 300 mg daily (dosage will be achieved using the fewest number of tablets per day) **AND** member is a current cigarette smoker

3. Pancreatic Adenocarcinoma

a. Member has locally advanced, unresectable, or metastatic disease

b. Erlotinib will be used in combination with gemcitabine (Gemzar®)

c. For brand Tarceva only: Member has tried and had intolerable adverse effects to generic erlotinib – specific intolerance to generic erlotinib and rationale for use of brand Tarceva must be provided in addition to BOTH of the following:

   i. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda

   ii. Completed Naranjo Adverse Drug reaction probablility scale - https://livertox.nih.gov/Naranjoassessment.pdf

d. Dose does not exceed 100 mg daily (dosage will be achieved using the fewest number of tablets per day) with the following exceptions:

   i. Dose does not exceed 450 mg daily (dosage will be achieved using the fewest number of tablets per day) **AND** member is receiving a concomitant strong CYP3A4 inducer (e.g., phenytoin, rifampin, carbamazepine, St. John's Wort)

   ii. Dose does not exceed 300 mg daily (dosage will be achieved using the fewest number of tablets per day) **AND** member is a current cigarette smoker

4. Kidney Cancer

a. Member meets one of the following:

   i. Member's disease is relapsed

   ii. Member's disease is stage IV **AND** medically or surgically unresectable

b. Erlotinib will be used as either of the following:

   i. Monotherapy for non-clear cell histology

   ii. In combination with bevacizumab (Avastin) in patients with advanced papillary renal cell carcinoma, including hereditary leiomyomatosis and renal cell cancer (HLRCC)

c. For brand Tarceva only: Member has tried and had intolerable adverse effects to generic erlotinib – specific intolerance to generic erlotinib and rationale for use of brand Tarceva must be provided in addition to **BOTH** of the following:

   i. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda

   ii. Completed Naranjo Adverse Drug reaction probablility scale - https://livertox.nih.gov/Naranjoassessment.pdf

d. Dose does not exceed 150 mg daily (dosage will be achieved using the fewest number of tablets per day) with the following exceptions:

   i. Dose does not exceed 450 mg daily (dosage will be achieved using the fewest number of tablets per day) **AND** member is receiving a concomitant strong CYP3A4 inducer (e.g., phenytoin, rifampin, carbamazepine, St. John's Wort)

   ii. Dose does not exceed 300 mg daily (dosage will be achieved using the fewest number of tablets per day) **AND** member is a current cigarette smoker

5. **Other FDA-approved or NCCN supported diagnosis (not previously listed above)**
    a. Member meets one of the following:
        i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) AND member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)
        ii. Indication AND usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
    b. For brand Tarceva only: Member has tried and had intolerable adverse effects to generic erlotinib – specific intolerance to generic erlotinib and rationale for use of brand Tarceva must be provided in addition to **BOTH** of the following:
        i. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda
        ii. Completed Naranjo Adverse Drug reaction probablility scale - https://livertox.nih.gov/Naranjoassessment.pdf
    c. Dose does not exceed 150 mg daily (dosage will be achieved using the fewest number of tablets per day) with the following exceptions:
        i. Dose does not exceed 450 mg daily (dosage will be achieved using the fewest number of tablets per day) **AND** member is receiving a concomitant strong CYP3A4 inducer (e.g., phenytoin, rifampin, carbamazepine, St. John's Wort)
        ii. Dose does not exceed 300 mg daily (dosage will be achieved using the fewest number of tablets per day) **AND** member is a current cigarette smoker

Approval duration: 6 months

Continuation of erlotinib (Tarceva) **meets the definition of medical necessity** when ALL of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of bone cancer, NSCLC with an EGFR mutation, pancreatic adenocarcinoma, or kidney cancer, or other FDA-approved or NCCN supported diagnosis, **OR** the member currently meets all indication-specific initiation criteria.
2. Member has a known EGFR-sensitizing mutation (NSCLC) **OR** member's disease has not progressed during treatment with erlotinib
3. For brand Tarceva only: Member has tried and had intolerable adverse effects to generic erlotinib – specific intolerance to generic erlotinib and rationale for use of brand Tarceva must be provided in addition to **BOTH** of the following:
    a. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda
    b. Completed Naranjo Adverse Drug reaction probablility scale - https://livertox.nih.gov/Naranjoassessment.pdf
4. Dose does not exceed 100 mg daily (Pancreatic Adenocarcinoma) or 150 mg daily (all other indications) using the fewest number of tablets per day with the following exceptions:

a. Dose does not exceed 450 mg daily (dosage will be achieved using the fewest number of tablets per day) **AND** member is receiving a concomitant strong CYP3A4 inducer (e.g., phenytoin, rifampin, carbamazepine, St. John's Wort)

b. Dose does not exceed 300 mg daily (dosage will be achieved using the fewest number of tablets per day) **AND** member is a current cigarette smoker

Approval duration: 1 year

Erlotinib **meets the definition of medical necessity** when used to treat the following designated Orphan Drug indication (and all associated criteria are met) when the dose does not exceed the maximum FDA-approved dose:

1. Malignant gliomas
    a. For brand Tarceva only: Member has tried and had intolerable adverse effects to generic erlotinib – specific intolerance to generic erlotinib and rationale for use of brand Tarceva must be provided in addition to **BOTH** of the following:
        i. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda
        ii. Completed Naranjo Adverse Drug reaction probablility scale - https://livertox.nih.gov/Naranjoassessment.pdf

Approval duration: 6 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved:

- NSCLC: 150 mg orally, on an empty stomach, once daily
- Pancreatic cancer: 100 mg orally, on an empty stomach, once daily

Dose Adjustments:

- Recommendations for dose modifications due to adverse reactions are provided in FDA-approved Prescribing Information
- Strong CYP3A4 inhibitors: Reduce dose by 50 mg
- CYP3A4 inducers: Increase dose by 50 mg increments at two week intervals to a maximum of 450 mg as tolerated
- Concurrent cigarette smoking: Increase dose by 50 mg increments at two week intervals to a maximum of 300 mg

Drug Availability:

- Tablets: 25 mg, 100 mg, and 150 mg

PRECAUTIONS:

- ILD: withhold erlotinib for acute onset of new or progressive unexplained pulmonary symptoms, such as dyspnea, cough and fever. Discontinue erlotinib if ILD is diagnosed
- Renal Failure: monitor renal function and electrolytes, particularly in persons at risk of dehydration. Withhold erlotinib for severe renal toxicity.
- Hepatotoxicity: hepatotoxicity with or without hepatic impairment including hepatic failure and hepatorenal syndrome. Monitor liver function tests and withhold or discontinue erlotinib for severe or worsening liver tests.
- GI perforations: discontinue erlotinib
- Bullous and exfoliative skin disorders: discontinue erlotinib
- Myocardial infarction/ischemia: risk of MI is increased in persons with pancreatic cancer
- Cerebrovascular accident (CVA): the risk of CVA is increased in persons with pancreatic cancer.
- Microangiopathic hemolytic anemia (MAHA): the risk of MAHA is increased in persons with pancreatic cancer.
- Ocular disorders: discontinue erlotinib for corneal perforation, ulceration or persistent severe keratitis.
- Hemorrhage in persons taking warfarin: regularly monitor INR in persons taking warfarin or other coumarin-derivative anticoagulants
- Embryo-fetal toxicity: can cause fetal harm. Advise females of reproductive potential of the potential risk to the fetus and to use highly effective contraception.

BILLING/CODING INFORMATION:

HCPCS Coding

C9399	Unclassified drugs or biologicals (This code should only be used for drugs and biologicals that are approved by the FDA on or after January 1, 2004) (Hospital Outpatient Use ONLY)
J8999	Prescription drug, oral, chemotherapeutic, NOS

ICD-10 Diagnosis Codes That Support Medical Necessity

C25.0 – C25.3	Malignant neoplasm of pancreas
C25.7 – C25.9	Malignant neoplasm of pancreas
C33	Malignant neoplasm of trachea
C34.00 – C34.32	Malignant neoplasm of bronchus or lung
C34.80 – C34.92	Malignant neoplasm of bronchus or lung
C64.1-C64.9	Malignant neoplasm of kidney, except renal pelvis
C65.1-C65.9	Malignant neoplasm of renal pelvis
C72.0	Malignant neoplasm of spinal cord
C72.1	Malignant neoplasm of cauda equina
C79.31	Secondary malignant neoplasm of brain

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

DEFINITIONS:

No guideline specific definitions apply.

RELATED GUIDELINES:

Brachytherapy-Oncologic Applications, 04-77260-20

Denosumab (Prolia™; Xgeva™) Injection, 09-J1000-25

Docetaxel (Taxotere®) IV, 09-J0000-95

Gemcitabine (Gemzar®), 09-J0000-96

Gonadotropin Releasing Hormone Analogs and Antagonists, 09-J0000-48

Intensity-Modulated Radiation Therapy (IMRT), 04-77260-22

Irinotecan HCl (Camptosar®) IV, 09-J0000-99

Magnetic Resonance Angiography (MRA), 04-70540-08

Oxaliplatin (Eloxatin®) IV, 09-J1000-00

Pemetrexed Disodium (Alimta®) IV, 09-J1000-01

Positron Emission Tomography (PET Scans) Oncologic Applications, 04-78000-17

Stereotactic Body Radiotherapy, 02-77371-02

Topotecan HCl (Hycamtin®) IV, 09-J1000-02

Vinorelbine Tartrate (Navelbine®) IV, 09-J1000-03

Zoledronic Acid IV (Reclast®; Zometa®), 09-J0000-72

OTHER:

TABLE 1:

ECOG PERFORMANCE STATUS*	
Grade	**ECOG**

0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2019 [cited 8/28/19]. Available from: http://www.clinicalpharmacology.com/.
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3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 8/28/19]. Available from: http://www.thomsonhc.com/.
4. NCCN Drugs & Biologics Compendium [Internet]. Fort Washington (PA): National Comprehensive Cancer Network; 2019 [cited 8/28/19]. Available from: http://www.nccn.org/professionals/drug_compendium/content/contents.asp/.
5. National Comprehensive Cancer Network®. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Bone cancer, v. 1.2020 [cited 8/28/19]. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
6. National Comprehensive Cancer Network®. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Non-small cell lung cancer, v. 7.2019 [cited 8/28/19]. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
7. National Comprehensive Cancer Network®. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Pancreatic cancer, v. 3.2019 [cited 8/28/19]. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
8. National Comprehensive Cancer Network®. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Kidney cancer, v. 2.2020[cited 8/28/19]. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
9. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2018 [cited 8/28/19]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 09/11/19.

GUIDELINE UPDATE INFORMATION:

01/01/12	New Medical Coverage Guideline.
11/15/12	Review and revision to guideline, consisting of updating position statement, added contraindication section, updated program exceptions, added ECOG PS table, and updated references.
09/15/13	Revision to guideline; consisting of administrative action to add treatment of chordoma to

	position statement and update coding.
11/15/13	Review and revision to guideline; consisting of revising description section, dosage/administration, and precautions section, updating references.
12/15/14	Review and revision to guideline; consisting of position statement, coding, references
12/15/15	Review and revision to guideline, consisting of updating position statement, decription, references.
09/15/16	Review and revision to guideline, consisting of updating position statement, coding, references.
12/15/16	Revision to guideline; consisting of updating position statement and references.
10/15/17	Review and revision to guideline, consisting of updating position statement, coding, references.
11/15/17	Revision to guideline to include new NCCN indication.
3/15/18	Revision to guideline to include NCCN update.
10/15/18	Review and revision to guideline, consisting of updating position statement, coding, references.
7/15/19	Revision to guideline; consisting of updating position statement
10/15/19	Review and revision to guideline, consisting of updating references.
02/15/20	Revision to guideline; consisting of updating position statement.