

**Regence BlueCross BlueShield of Oregon • Regence BlueShield
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Medication Policy Manual

Policy No: dru118

Topic: Tarceva[®], erlotinib

Date of Origin: July 22, 2005

Revised/Effective Date: July 17, 2009

Next Review Date: July 2010

IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Erlotinib (Tarceva[®]) is an oral cancer medication used as a single agent in the second- or third-line treatment of non-small cell lung cancer (NSCLC) and in combination with gemcitabine for the first-line treatment of locally advanced, unresectable or metastatic pancreatic cancer.

Policy/Criteria

- I.** Most contracts require prior authorization approval of erlotinib prior to coverage. Erlotinib may be considered medically necessary when prescribed by an oncologist and any of the following criteria are met:
 - A.** A diagnosis of either locally advanced or metastatic non-small cell lung cancer when at least one prior chemotherapy regimen prescribed for non-small cell lung cancer was not effective (documented disease progression either during or after treatment).

OR

 - B.** Palliative treatment for the indication of non-small cell lung cancer in a terminally-ill patient at the end of life.

OR

 - C.** A diagnosis of locally advanced, unresectable or metastatic pancreatic cancer when given in combination with gemcitabine.

- II.** Administration, Quantity Limitations, and Authorization Period
 - A.** Regence considers erlotinib to be a self-administered medication.
 - B.** When prior authorization is approved, erlotinib may be authorized in quantities of up to thirty 150 mg doses per month. Quantities exceeding thirty tablets per month are considered not medically necessary.
 - C.** Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

- III.** Erlotinib is considered investigational when used for all other conditions, including, but not limited to:
 - A.** Advanced hepatocellular carcinoma.
 - B.** Advanced ovarian carcinoma.
 - C.** Advanced solid tumors.
 - D.** Gastric adenocarcinomas.

- E.** Glioblastoma multiforme.
- F.** Head and neck cancer, recurrent and/or metastatic.
- G.** Malignant pleural mesothelioma
- H.** Metastatic colorectal cancer.
- I.** Metastatic renal cell carcinoma.
- J.** Recurrent malignant gliomas.

Position Statement

Summary

- Erlotinib is used for: ^[1]
 - * Treatment of locally advanced or metastatic non-small cell lung cancer after failure of at least one prior chemotherapy regimen.
 - * First-line treatment of locally advanced, unresectable, or metastatic pancreatic cancer in combination with gemcitabine.
- In each of these populations, large randomized controlled trials showed that erlotinib improved overall survival over the current standard of care. ^[11, 16]
- Erlotinib is currently being studied in many other types of cancers; however, evidence to support use in other cancers is still preliminary.
- There is no evidence that continued treatment with erlotinib after disease progression is beneficial. ^[1]

Clinical Efficacy

NON-SMALL CELL LUNG CANCER (NSCLC)

- Cisplatin or carboplatin in combination with paclitaxel, docetaxel, gemcitabine, vinorelbine, irinotecan, etoposide or vinblastine have all been proven effective as first-line therapies in the treatment of advanced NSCLC. ^[2]
- In the second- or third- line treatment of advanced or metastatic NSCLC, erlotinib improved survival in a reliable randomized controlled trial when compared to placebo (best supportive care). Median overall survival was 6.7 months versus 4.7 months for erlotinib and placebo, respectively. ^[1, 11]
- Results from two large controlled, randomized trials in which erlotinib was added to a regimen of carboplatin plus paclitaxel ^[6] or to a regimen of cisplatin plus gemcitabine as first-line therapy in the treatment of locally advanced or metastatic NSCLC demonstrated no additional benefit with erlotinib based on a primary endpoint of overall survival. ^[1, 3, 13]
- Erlotinib was given to elderly patients with advanced non-small cell lung cancer in a first-line setting in a small (n=80), open-label trial. Because this trial only had a single arm, it is unknown whether erlotinib provides any benefit in this setting. ^[15]
- Clinical practice guidelines from the National Comprehensive Cancer Network (NCCN, version 2.2009) position single agent erlotinib as second- or third-line therapy for the treatment of advanced non-small cell lung cancer (patients whose disease has progressed either during or after first-line chemotherapy). ^[2]

PANCREATIC CANCER

- A reliable phase III, randomized trial (n=569) comparing gemcitabine plus erlotinib versus gemcitabine plus placebo in patients with locally advanced metastatic or unresectable pancreatic cancer reported a statistically significant improvement in overall survival (23.5%) in the gemcitabine plus erlotinib treatment arm. The median survival in the erlotinib arm was 6.4 months (versus 5.9 months with placebo) and the 1-year survival was 25.6% (versus 19.7% with placebo). ^[1, 4, 7, 16]
- The National Comprehensive Cancer Network (NCCN) guideline lists erlotinib as a potential first-line treatment of pancreatic adenocarcinoma when used in combination with gemcitabine based on evidence that it may improve overall survival. ^[21]

OTHER CANCERS

- There are published clinical studies in advanced hepatocellular carcinoma ^[8], advanced ovarian carcinoma ^[9], gastric adenocarcinomas ^[14], advanced head and neck cancer ^[17], metastatic colorectal cancer ^[12, 18], and metastatic renal cell carcinoma ^[10, 19]. Additional trials in larger numbers of patients are necessary to confirm the preliminary results.
- In a single small trial, erlotinib did not demonstrate any benefit in the treatment of malignant pleural mesothelioma ^[20] or recurrent glioblastomas ^[22].
- There are ongoing studies of erlotinib in glioblastoma multiforme, advanced solid tumors, and recurrent malignant gliomas; ^[3] however, it is too early to draw conclusions regarding its potential benefit and safety in these populations.

Safety

- The most common adverse events reported with erlotinib at 150 mg daily were rash (75%) and diarrhea (54%). ^[1] Cases of interstitial lung disease (ILD) have been reported in patients receiving erlotinib. The erlotinib prescribing information states that in the event of acute onset of worsening of pulmonary symptoms (cough, dyspnea, fever), erlotinib therapy should be interrupted and the symptoms investigated.
- Several additional warnings have been added to the erlotinib prescribing information based on post marketing experience. These warnings include increased risk of gastrointestinal perforation, bullous skin disorders, ocular disorders, renal failure, and hepatotoxicity. ^[1]

Dosing and administration

- The usual dose of erlotinib varies by indication: ^[1]
 - * **Non-small cell lung cancer:** 150 mg orally once per day.
 - * **Pancreatic cancer:** 100 mg orally once per day.
- Erlotinib should be dosed 1 to 2 hours after a meal to improve absorption. ^[1]
- Dose reductions should be considered if erlotinib is administered along with a potent CYP3A4 inhibitor (see *Appendix 1*). ^[1]

Appendix 1: Potent Inhibitors of CYP3A. ^[5]

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|--|-------------------------------------|
| amiodarone (Cordarone [®] , Pacerone [®]) | nefazodone (Serzone [®]) |
| atazanavir (Reyataz [®]) | nelfinavir (Viracept [®]) |
| cisapride (Propulsid [®]) | ritonavir (Norvir [®]) |
| clarithromycin (Biaxin [®]) | telithromycin (Ketek [®]) |
| indinavir (Crixivan [®]) | troleandomycin (TAO [®]) |
| itraconazole (Sporanox [®]) | voriconazole (Vfend [®]) |
| ketoconazole (Nizoral [®]) | |

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| Cross References |
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| None |

| Codes | Number | Description |
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| HCPCS | J8999 | Oral chemotherapeutic drug, not otherwise classified |