



# CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Effective Date ..... 8/15/2011  
Next Review Date.....8/15/2012  
Coverage Policy Number ..... 4002

Subject **Gefitinib (Iressa®)**

## Table of Contents

Coverage Policy .....	1
General Background .....	2
Coding/Billing Information .....	3
References .....	3
Policy History.....	4

## Hyperlink to Related Coverage Policies

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of CIGNA. Copyright ©2011 CIGNA

## Coverage Policy

**CIGNA covers gefitinib (Iressa®) as medically necessary as monotherapy for locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of both platinum-based and docetaxel chemotherapies in an individual who is benefiting or has benefited from gefitinib.**

### Manufacturer Update

AstraZeneca, Iressa's manufacturer, has informed U.S. patients taking Iressa and their prescribing physicians that patients currently benefitting from Iressa therapy will be able to continue to receive treatment through a clinical study. This action was announced after AstraZeneca informed the FDA that it will be withdrawing the Accelerated Approval New Drug Application (NDA) for Iressa, effective 9/30/2011. AstraZeneca does not plan to pursue approval for Iressa in the U.S.

After 9/30/2011, the Iressa Access program will be taken over by United Biosource Corporation (UBC), a clinical resource organization (CRO), and the program will be known as the AstraZeneca Iressa Clinical Access Program (CAP). Iressa will no longer be commercially available after 9/30/2011. The new CAP program will be instituted for those already taking and receiving benefit from Iressa so they may continue on the drug. No new patients will be able to receive Iressa after 9/30/2011.

## **FDA Approved Indications**

Iressa is indicated as monotherapy for the continued treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of both platinum-based and docetaxel chemotherapies who are benefiting or have benefited from Iressa. In light of positive survival data with other agents including another oral EGFR inhibitor, physicians should use other treatment options in advanced NSCLC patient populations who have received one or two prior chemotherapy regimens and are refractory or intolerant to their most recent regimen.

## **FDA Recommended Dosing**

The recommended daily dose of gefitinib is 250 mg given orally without regard to meals. Higher doses did not show increased efficacy in clinical trials and may result in a higher incidence of adverse drug events. No dosage adjustments are necessary based on age, body weight, gender, ethnicity, renal function, or moderate-to-severe hepatic impairment due to liver metastases.

## **Drug Availability**

Iressa tablets are supplied as round, biconvex, brown film-coated tablets intagliated with "IRESSA 250" on one side and plain on the other side, each containing 250 mg of gefitinib in bottles of 30 tablets.

## **Iressa Access Program**

As of September 15, 2005, gefitinib is available only to patients registered in AstraZeneca's restrictive distribution program, the Iressa Access Program. Prescribers must register patients with the program before prescribing gefitinib. To qualify for the program, patients must meet the following criteria:

- patient has been treated with gefitinib prior to September 15, 2005,
- patient previously benefited from gefitinib, or the patient's physician believes the patient will benefit from further gefitinib therapy, or
- patient is enrolled in a clinical trial that was approved by an Institutional Review Board prior to June 17, 2005

## **General Background**

### **Disease Overview**

The growth, differentiation, angiogenesis, and inhibition of apoptosis of cells are controlled by transmembrane proteins called receptor tyrosine kinases. A family of receptor tyrosine kinases is the epidermal growth factor receptor tyrosine kinases (EGFR-TK). Solid human tumors, NSCLC, prostate cancer, breast cancer, gastric cancer, colorectal cancer, head and neck cancer, bladder cancer and ovarian cancer are associated with EGFR expression or overexpression. High levels of EGFR are also associated with advanced disease, development of metastases, and poor prognosis.

### **Pharmacology**

Gefitinib is an oral medication that inhibits the intracellular phosphorylation of numerous tyrosine kinases associated with transmembrane cell surface receptors, including EGFR-TK. Oral absorption of gefitinib is slow, with peak plasma levels occurring three to seven hours after dosing, and a mean bioavailability of 60%. The package labeling states that gefitinib is unaffected by food; however, a study of healthy volunteers found that food reduced gefitinib maximum concentrations. Gefitinib is hepatically metabolized via cytochrome P450 isoenzyme 3A4 (CYP3A4).

### **Guidelines**

To date there are no available guidelines for gefitinib from the National Comprehensive Cancer Network (NCCN) for the FDA indication or other uses.

The FDA is not currently considering withdrawal of Iressa. When the number of patients receiving Iressa under the limited access program becomes small, Iressa may either be removed from the market or, depending on any additional clinical data, the indication may be modified. If Iressa is eventually withdrawn from the market, the FDA will consider authorizing continued Iressa access under an IND protocol for patients who are benefiting or have benefited from Iressa.

The reason for market removal consideration is based upon a placebo-controlled phase III study investigated the effect on survival of gefitinib as second-line or third-line treatment for patients with locally advanced or

metastatic NSCLC. 1692 patients were included in the study. The primary endpoint was survival in the overall population of patients and those with adenocarcinoma. 1129 patients were assigned gefitinib and 563 placebo. At median follow-up of 7.2 months, median survival did not differ significantly between the groups in the overall population (5.6 months for gefitinib and 5.1 months for placebo; hazard ratio 0.89 [95% CI 0.77-1.02], p=0.087) or among the 812 patients with adenocarcinoma (6.3 months vs 5.4 months; 0.84 [0.68-1.03], p=0.089). Gefitinib was well tolerated, as in previous studies. Treatment with gefitinib was not associated with significant improvement in survival in either co-primary population.

### **Ongoing Studies**

Gefitinib is being studied for use in gliomas and advanced head and neck cancer. At this time, however, there is insufficient published data in terms of safety and efficacy to support the use of gefitinib for these indications.

### **Gliomas**

To date there is a completed phase 1 trial and an ongoing phase 2 trial for the use of gefitinib in combination with radiation for treatment of brain stem gliomas.

### **Advanced Head and Neck Cancer**

A completed phase 2 prospective trial for the use of gefitinib in combination with radiation shows promising results. However, since the trial only consisted of 15 patients and was not a controlled, randomized study, further larger, randomized studies need completed to evaluate the safety and efficacy for the use of gefitinib in advanced head and neck cancer.

### **Adverse Reactions**

The most common adverse drug reactions associated with gefitinib are diarrhea, rash, acne, dry skin, nausea, and vomiting. Gefitinib is generally well-tolerated but has the potential to cause serious adverse effects, such as liver dysfunction, interstitial lung disease, corneal erosions, and QT prolongation. Higher doses of gefitinib are associated with an increased rate of adverse effects (i.e., doses above 250 mg).

In terms of drug interactions, gefitinib is hepatically metabolized by the CYP3A4 isoenzyme. Medications that induce or inhibit CYP3A4 may reduce or increase gefitinib serum concentrations, respectively. Gefitinib dosage should be increased to 500 mg per day in the absence of severe adverse drug reactions, if CYP3A4 inducers (e.g., rifampin, phenytoin) are used concomitantly.

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## **Coding/Billing Information**

**Note:** This section is not in use

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## Policy History

<u>Pre-Merger Organizations</u>	<u>Last Review Date</u>	<u>Policy Number</u>	<u>Title</u>
CIGNA HealthCare	8/15/2008	4002	Gefitinib (Iressa®)

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