



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.

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Coverage Policy Number 8005

Subject **Lapatinib (Tykerb®)**

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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 lapatinib (Tykerb®) as medically necessary for the treatment of ANY of the following indications:

- **advanced or metastatic Human Epidermal Receptor 2 (HER2) positive breast cancer** when used in combination with trastuzumab (Herceptin®) or capecitabine (Xeloda®) for trastuzumab-exposed disease
- **advanced or metastatic hormone receptor positive, HER2 positive breast cancer when** used in combination with an aromatase inhibitor [i.e. letrozole (Femara®)] in a postmenopausal woman
- **advanced or metastatic hormone receptor positive, HER2 positive breast cancer when** used in combination with an aromatase inhibitor [i.e. letrozole (Femara)] in men receiving concomitant suppression of testicular steroidogenesis [i.e. leuprolide (Lupron®), goserelin (Zoladex®)]

FDA Approved Indications

Tykerb is indicated in combination with:

- capecitabine for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress HER2 and who have received prior therapy including an anthracycline, a taxane, and trastuzumab.
- letrozole for the treatment of postmenopausal women with hormone receptor positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated.

Tykerb in combination with an aromatase inhibitor has not been compared to a trastuzumab-containing chemotherapy regimen for the treatment of metastatic breast cancer.

FDA Recommended Dosing

HER2 Positive Metastatic Breast Cancer

The recommended dose of Tykerb is 1,250 mg given orally once daily on Days 1-21 continuously in combination with capecitabine 2,000 mg/m²/day (administered orally in 2 doses approximately 12 hours apart) on Days 1-14 in a repeating 21 day cycle. Tykerb should be taken at least one hour before or one hour after a meal. The dose of Tykerb should be once daily (5 tablets administered all at once); dividing the daily dose is not recommended. Treatment should be continued until disease progression or unacceptable toxicity occurs.

Hormone Receptor Positive, HER2 Positive Metastatic Breast Cancer

The recommended dose is 1,500 mg given orally once daily continuously in combination with letrozole. When co-administered with Tykerb, the recommended dose of letrozole is 2.5 mg once daily. Tykerb should be taken at least one hour before or one hour after a meal. The dose of Tykerb should be once daily (6 tablets administered all at once); dividing the daily dose is not recommended.

Block Box Warning

Hepatotoxicity has been observed in clinical trials and post-marketing experience. The hepatotoxicity may be severe and deaths have been reported. Causality of the deaths is uncertain.

Drug Availability

The 250 mg tablets of Tykerb are oval, biconvex, orange, and film-coated with GS XJG debossed on one side and are available in bottles of 150 tablets.

General Background

Pharmacology/Disease Overview

Breast cancer is staged according to the primary tumor size, lymph node involvement, and presence of metastases. A pathological report of excised cancer tissue can determine hormone receptor and HER2 status. Receptor profile status, tumor size, and lymph node involvement are used in determining the cancer prognosis. The presence of Epidermal Growth Factor Receptor (EGFR) and HER2, which promote tumor cell growth and survival, are predictors of poor clinical outcomes. These receptors are targets for chemotherapy.

Lapatinib inhibits the tyrosine kinase domain of the EGFR and HER2 receptors. Cell proliferation is blocked through inhibition of these receptors. Peak concentrations are reached approximately 4 hours after administration. Lapatinib is metabolized primarily by CYP3A4 and CYP3A5. Minimal renal excretion occurs. Hepatic impairment increases drug exposure. Pharmacokinetic properties of lapatinib have not been studied in patients with renal impairment or on dialysis.

Guidelines

The National Comprehensive Cancer Network (NCCN) recommends lapatinib as follows:

Breast Cancer

Grade 2A

Used in combination with aromatase inhibition for the treatment of recurrent or stage IV estrogen receptor-positive, human epidermal growth factor receptor 2 (HER2)-positive disease in postmenopausal women who have received no prior endocrine therapy within one year. Men with breast cancer should be treated similarly to postmenopausal women, except that use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis.

Preferred agent for patients with human epidermal growth factor receptor 2 (HER2)-positive recurrent or metastatic disease in combination with trastuzumab (without cytotoxic therapy) or capecitabine for trastuzumab-exposed disease.

Adverse Reactions

In addition to the Black Box Warning, common adverse reactions include diarrhea, nausea, vomiting, palmar-plantar erythrodysesthesia, rash, and fatigue. Severe diarrhea is the most common adverse drug reaction leading to discontinuation of lapatinib. Lapatinib is a substrate of CYP3A4. Strong inhibitors and inducers of CYP3A4 may influence serum concentrations of lapatinib. Lapatinib inhibits CYP3A4 and CYP2C8 in vitro.

Coding/Billing Information

Note: This section is not in use.

References

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	6/15/2008	8005	Lapatinib (Tykerb®)
Great-West Healthcare	6/2007	P07.101	Tykerb

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