

Medication Policy Manual

Policy No: dru145

Topic: Tykerb[®], lapatinib

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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

Lapatinib (Tykerb[®]) is an oral cancer medication indicated for the treatment of a specific type of advanced or metastatic breast cancer.

Policy/Criteria

- I.** Most contracts require prior authorization approval of lapatinib (Tykerb) prior to coverage. Lapatinib may be considered medically necessary for the treatment of HER2 positive breast cancer.

II. Administration, Quantity Limitations and Authorization Period

- A.** Regence considers lapatinib to be a self-administered medication.
- B.** When prior authorization is approved, up to 150 lapatinib 250 mg tablets may be authorized per month. Quantities exceeding 150 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.** Lapatinib is considered investigational when used for all other conditions, including, but not limited to:

- A.** Advanced solid tumors.
- B.** High-risk head and neck cancer.
- C.** Ovarian cancer.
- D.** Glioblastoma multiforme
- E.** Refractory malignant glioma.
- F.** Refractory prostate cancer.
- G.** Transitional Cell Carcinoma
- H.** Unresectable liver or biliary tract cancer.

Position Statement

- Lapatinib is a tyrosine kinase inhibitor. It prevents tumor growth by blocking activity at both Epidermal Growth Factor Receptor (EGFR) and Human Epidermal Receptor Type 2 (HER2) receptors. ^[1]
- Lapatinib, in combination with capecitabine, is used for treatment of patients with advanced or metastatic breast cancer whose tumors are positive for HER2 (also referred to as overexpression of HER2) and who have received prior therapy with an anthracycline, a taxane, and trastuzumab (Herceptin[®]). ^[1]
 - * Anthracyclines include:
 - doxorubicin (Adriamycin[®], Doxil[®])
 - daunorubicin (Cerubidine[®], DaunoXome[®])
 - epirubicin (Ellence[®])
 - idarubicin (Idamycin[®])
 - * Taxanes include:
 - paclitaxel (Taxol[®])
 - docetaxel (Taxotere[®])
- The usual dose is five lapatinib 250 mg tablets (1,250 mg) orally once per day. Lapatinib should be administered: ^[1]
 - * In combination with capecitabine (Xeloda[®]).
 - * As a single once-daily dose.
 - * At least one hour before or one hour after a meal (food decreases absorption).
- The dose of lapatinib should be decreased with: ^[1]
 - * Decreased left ventricular ejection fraction.
 - * Hepatic impairment.
- There is no information that supports continuation of therapy with lapatinib once disease progression occurs. ^[1]

- There is currently no published clinical information to support lapatinib doses exceeding 1,250 mg once daily (the FDA-approved dose).
- National Comprehensive Cancer Network (NCCN) guidelines for treatment of breast cancer recognize lapatinib as a potential option in women with advanced or metastatic disease who were previously treated with an anthracycline, a taxane, and trastuzumab. ^[2]
- There is currently no useful evidence for use of lapatinib as monotherapy, or as first-line treatment of breast cancer.
 - * Lapatinib has only been studied in combination with capecitabine (Xeloda) in women who failed to respond to treatment with an anthracycline, a taxane, and trastuzumab. ^[1, 4]
- There is no evidence that lapatinib is effective for the treatment of patients who have developed central nervous system metastases due to their breast cancer, though there are several ongoing clinical trials. ^[6]

Clinical Efficacy

Advanced and Metastatic HER-2 Overexpressing (HER-2 positive) Breast Cancer

- There is a single, unreliable, published trial that studied the use of lapatinib in advanced and metastatic breast cancer. ^[1, 4, 9]
 - * The trial was an open-label design.
 - * The women in the trial had HER2 positive tumors and had received prior therapy with an anthracycline, a taxane, and trastuzumab.
 - * The trial studied capecitabine (Xeloda) alone versus capecitabine (Xeloda) plus lapatinib (Tykerb).
 - * The primary endpoint was time to progression (TTP) of disease.
- Results: ^[1]
 - * The difference in median TTP between the two treatment groups was 1.9 months (Tykerb + Xeloda, 6.2 months; Xeloda alone, 4.3 months). ^[1,9]

- * There was no improvement in overall survival observed with the preliminary data cut.
- * Future reports of overall survival from this trial will not be valid because crossover to lapatinib (Tykerb) + capecitabine (Xeloda) was allowed after the preliminary results were tabulated.
- Chemotherapy regimens combining anthracyclines, taxanes, and fluorouracil have demonstrated overall survival benefit in the treatment of breast cancer. ^[2]
- A non-comparative, open-label, dose-ranging trial evaluated two lapatinib regimens used as first-line treatment in 138 patients with locally advanced or metastatic, HER-2 positive breast cancer. While a modest effect on overall response was noted, larger comparative trials with clinically relevant endpoints are needed to establish a role for lapatinib in this setting. ^[7]
- In a phase-II, open-label study, patients with previously treated, metastatic, HER-2 negative and positive breast cancer were treated with once daily lapatinib as monotherapy. Patients who were HER-2 positive experienced a modest effect while HER-2 negative patients experienced no effect. Larger comparative trials with clinically relevant endpoints are needed to establish a role for lapatinib as monotherapy in this setting. ^[8]
- In a randomized, controlled trial of 579 women with metastatic breast cancer (HER-2-positive and HER-2-negative), lapatinib plus paclitaxel was compared to paclitaxel alone as first line therapy. Patients with HER-2-negative or untested status did not benefit from the addition of lapatinib, but patients with HER-2-positive status exhibited improved time to progression of their tumors. ^[10]
- Lapatinib demonstrated a modest benefit in patients with brain metastases from HER-2-positive breast cancer, both as a single agent and combined with capecitabine. Further, better controlled studies are needed to establish the optimum regimen for the management of brain metastases in HER-2-positive breast cancer. ^[11]

Other Uses

- There are plans to study lapatinib in the treatment of several other types of cancers, including solid tumors, refractory malignant glioma, refractory prostate cancer, and unresectable liver or biliary tract cancer. There are currently no published data that support any benefit of lapatinib in these conditions. ^[3]

In two small, preliminary trials, lapatinib did not demonstrate significant clinical response for the treatment of either glioblastoma multiforme or ovarian carcinoma. ^[12-13]

Preliminary trials of lapatinib in advanced/metastatic transitional-cell carcinoma and in squamous-cell carcinoma of the head and neck are suggestive of a useful response, but larger, better designed trials are needed to establish safety and efficacy. ^[14-15]

Safety

- The most common adverse events reported with lapatinib include diarrhea, nausea, vomiting, and rash. Diarrhea can be severe and proactive management is recommended. ^[1]
- Prolongation of the QTc interval was also reported in lapatinib clinical trials. Baseline and on treatment electrocardiograms are recommended. ^[1]
- Use of lapatinib with strong CYP3A4 inhibitors or inducers should be avoided. ^[1]
- Lapatinib has been associated with interstitial lung disease and pneumonitis in monotherapy or in combination with other chemotherapies. Patients should be monitored for pulmonary symptoms indicative of interstitial lung disease or pneumonitis. Lapatinib should be discontinued in patients who experience pulmonary symptoms indicative of interstitial lung disease/pneumonitis which are \geq Grade 3. ^[1]

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

POTENT INHIBITORS:	INDUCERS:
amiodarone (Cordarone [®] , Pacerone [®])	carbamazepine (Tegretol [®] , Eptol [®])
atazanavir (Reyataz [®])	efavirenz (Sustiva [®])
cisapride (Propulsid [®])	nevirapine (Viramune [®])
clarithromycin (Biaxin [®])	phenytoin (Dilantin [®])
indinavir (Crixivan [®])	phenobarbital
itraconazole (Sporanox [®])	rifabutin (Mycobutin [®])
ketoconazole (Nizoral [®])	rifapentine (Priftin [®])
nefazodone (Serzone [®])	rifampin (Rifadin [®])
nelfinavir (Viracept [®])	St. John's Wort
ritonavir (Norvir [®])	
telithromycin (Ketek [®])	
troleandomycin (TAO [®])	
voriconazole (Vfend [®])	

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Cross References
N/A

Codes	Number	Description
HCPCS	J8999	Oral chemotherapy drug, not otherwise classified