ROCKY MOUNTAIN HEALTH PLANS®
We understand Colorado. We understand you.

# UNIFORM PHARMACY PRIOR AUTHORIZATION REQUEST FORM

**CONTAINS CONFIDENTIAL PATIENT INFORMATION**

**Complete this form in its entirety and send to Rocky Mountain Health Plans at 858-357-2538**

☐ **Urgent**[1] ☐ **Non-Urgent**

**Requested Drug Name: Tykerb® (lapatinib)**

| **Patient Information:** | **Prescribing Provider Information:** |
|---|---|
| Patient Name: | Prescriber Name: |
| Member/Subscriber Number: | Prescriber Fax: |
| Policy/Group Number: | Prescriber Phone: |
| Patient Date of Birth (MM/DD/YYYY): | Prescriber Pager: |
| Patient Address: | Prescriber Address: |
| Patient Phone: | Prescriber Office Contact: |
| Patient Email Address: | Prescriber NPI: |
| | Prescriber DEA: |
| Prescription Date: | Prescriber Tax ID: |
| | Specialty/Facility Name (If applicable): |
| | Prescriber Email Address: |

**Prior Authorization Request for Drug Benefit:** ☐ New Request ☐ Reauthorization

Patient Diagnosis and ICD Diagnostic Code(s):

Drug(s) Requested (with J-Code, if applicable):

Strength/Route/Frequency:

Unit/Volume of Named Drug(s):

Start Date and Length of Therapy:

Location of Treatment: (e.g. provider office, facility, home health, etc.) including name, Type 2 NPI (if applicable), address and tax ID:

Clinical Criteria for Approval, Including other Pertinent Information to Support the Request, other Medications Tried, Their Name(s), Duration, and Patient Response:

## Tykerb® (lapatinib)

**Diagnosis (documentation supportive of diagnosis is required)**

☐ Locally advanced or metastatic HER2+ Breast Cancer
☐ Other (please state): _____

**Clinical Consideration (for approval, please indicate and provide documentation of the following):**

☐ Patient refractory to first-line treatment (may include PCH, TCH, anthracycline, taxane, or trastuzumab)
☐ Tykerb used in combination capecitabine treatment
☐ Patient is post-menopausal with hormone receptor positive cancer for which hormonal therapy is indicated
☐ Tykerb to be used in combination with an aromatase inhibitor
☐ Patient and physician have been registered with the TYKERB CARES Program: 1-866-4-TYKERB or www.tykerb.com

**Physician Specialty**

☐ Oncology
☐ Other (please state): _____

☐ For use in clinical trial? (If yes, provide trial name and registration number):

Drug Name (Brand Name and Scientific Name)/Strength:

| Dose: | Route: | Frequency: |
|---|---|---|
| Quantity: | Number of Refills: | |

Product will be delivered to: ☐ Patient's Home ☐ Physician Office Other:

**Prescriber or Authorized Signature:** Date:

Dispensing Pharmacy Name and Phone Number:

☐ **Approved** ☐ **Denied**

If denied, provide reason for denial, and include other potential alternative medications, if applicable, that are found in the formulary of the carrier:

1. A request for prior authorization that if determined in the time allowed for non-urgent requests could seriously jeopardize the life or health of the covered person or the ability of the covered person to regain maximum function, or subject the person to severe pain that cannot be adequately managed without the drug benefit contained in the prior authorization request

**RMHP Formulary Coverage Policy**

THIS INFORMATION IS NOT ALL-INCLUSIVE AND IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY

# Tykerb (lapatinib ditosylate)

## CLASSIFICATION

- Antineoplastic, tyrosine kinase inhibitor

## DESCRIPTION

- Lapatinib is a dual tyrosine kinase inhibitor against epidermal growth factor receptors (EGFR) HER1 and HER2. HER1 and HER2 are overexpressed in over 20% of breast tumors, and is a key component in regulating tumor cell growth, proliferation, metastasis, and transformation. Lapatinib reversibly binds to the intracellular cytoplasmic site of tyrosine kinase at the ATP-binding site, inhibits receptor phosphorylation and activation of HER1 and HER2 homodimers and heterodimers, thereby blocking the downstream signaling pathway involved in cell proliferation, survival and invasion. As a dual inhibitor, lapatinib offers a *theoretical* advantage over monoclonal antibodies that target extracellular HER2 only (e.g. trastuzumab).
- In vitro studies suggest that lapatinib is not cross-resistant with trastuzumab, as lapatinib retained activity in trastuzumab-conditioned cell lines.
- 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.
  - **Limitation of Use:** Patients should have disease progression on trastuzumab prior to initiation of treatment with TYKERB in combination with capecitabine.
- In the final analysis of a phase 3, open-label, randomized trial (EGR100151; n=408), the combination use of lapatinib and capecitabine resulted in a 25% improvement in overall survival (OS) compared with capecitabine alone in patients with human epidermal growth factor receptor (HER2)-positive locally advanced or metastatic breast cancer refractory to prior treatment . Patients were randomized to receive either lapatinib 1250 mg once daily continuously on days 1 to 21 in combination with capecitabine 2000 mg/m(2) per day in 2 divided doses on days 1 to 14 every 21 days (n=207; mean age, 54 years), or capecitabine 2500 mg/m(2) per day in 2 divided doses on days 1 to 14 during each 21-day cycle (n=201; mean age, 51 years) until disease progression or intolerable toxic effects. Based on an interim analysis, the use of combination therapy compared with monotherapy prolonged time to progression (primary endpoint) (HR, 0.57 (95% CI, 0.43 to 0.77; $p < 0.001$) and enrollment was terminated early. Thirty-six patients receiving monotherapy crossed over to combination therapy. In the intent-to-treat population, the median OS in the lapatinib and capecitabine group was 75 weeks compared with 64.7 weeks in the capecitabine-alone group (HR, 0.87, 95% CI, 0.7 to 1.08; p=0.206). However, in an analysis controlling for the effect of prognostic factors and the effect of crossover, a survival benefit in the lapatinib and capecitabine group was suggested (HR, 0.75; 95% CI, 0.6 to 0.94; p=0.013).
- In an analysis conducted 4 months after the interim analysis, significant improvements (HR, 0.57; 95% CI, 0.43 to 0.77; p=0.00013) in median time to progression were still observed in the lapatinib plus capecitabine arm (27.1 weeks; 25th to 75th percentile, 17.4 to 49.4 weeks) compared with the capecitabine monotherapy arm (18.6 weeks; 25th to 75th percentile, 9.1 to 36.9 weeks). Response rates were 23.7% (95% CI, 18% to 30.3%) and 13.9% (95% CI, 9.5% to 19.5%) in the lapatinib/capecitabine and capecitabine arms, respectively.

- Tykerb is indicated **in combination with 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.
- In a randomized, double-blind, controlled, parallel-group, multicenter, phase 3 study, treatment with letrozole and lapatinib significantly increased median progression-free survival (PFS) compared with letrozole and placebo in patients with estrogen and/or progesterone receptor (ER/PR) and human epidermal growth factor receptor 2 (HER2) positive invasive breast cancer. Patients (n=1286) with stage IIIB/IIIC or IV ER/PR positive invasive breast cancer received oral letrozole (2.5 mg) and lapatinib (1500 mg) or letrozole (2.5 mg) and placebo daily until disease progression or withdrawal from study. Prior therapy for advanced or metastatic disease was not permitted; adjuvant antiestrogen, aromatase inhibitor, and trastuzumab were allowed if therapy was completed at least 1 year prior to study enrollment. After a median of 1.8 yr and adjustment for baseline prognostic factors, the median PFS (evaluated using RECIST) in the HER2 positive group (primary endpoint) was significantly prolonged in the letrozole-lapatinib arm compared with letrozole-placebo (8.2 months vs 3 months, respectively; HR, 0.65; 95% CI, 0.47 to 0.89; p=0.008). Additionally, the overall response rate (ORR) was significantly improved in the HER2 positive population who received letrozole-lapatinib (15% to 28%; OR, 0.4; 95% CI, 0.2 to 0.9; p=0.021). After a median of 2 year in the overall population of ER and/or PR positive patients, an intent-to-treat analysis showed a significantly increased PFS in the letrozole-lapatinib group compared with letrozole-placebo group (11.9 months vs 10.8 months, respectively; HR=0.86; 95% CI, 0.76 to 0.98; p=0.026), but there was no statistically significant difference in ORR between the treatment groups.
- The benefits of lapatinib in the treatment of brain metastasis are being studied due to the small molecular size which makes lapatinib more penetrable through the blood-brain barrier than larger molecules, such as trastuzumab, allowing lapatinib to reach adequate pharmacologic concentrations.

## FORMULARY COVERAGE

Prior authorization: Required
Good Health Formulary: T3
Commercial Formulary: T3
Medicare Part D coverage: T5

## COVERAGE CRITERIA

Tykerb® (lapatinib ditosylate) meets the definition of **medical necessity** for the following:

- Advanced or metastatic HER2 positive breast cancer in combination with capecitabine after prior therapies (i.e. an athracycline, taxane, and trastuzumab). Documentation of diagnosis and prior therapies is required.
- HER2 positive breast cancer in postmenopausal women in combination with letrozole. Documentation of diagnosis required.

Tykerb® (lapatinib ditosylate) is considered **experimental** for the following:

- Any condition or diagnosis not FDA approved or Compendia supported

Required Provider Specialty:

- Approval is limited to Oncology

## DOSAGE/ADMINISTRATION:

Adult Dosing (safety and efficacy in pediatric patients has not been established):
*Normal Dosing:*

**Advanced or metastatic HER2+ Breast cancer in combination with capecitabine after prior therapies:**

- The recommended dose of lapatinib is 1250 mg orally once daily continuously on days 1 through 21, in combination with capecitabine 2000 mg/m(2)/day orally divided into 2 doses (approximately 12 hours apart) on days 1 through 14. Cycles are repeated every 21 days until disease progression or unacceptable toxicity.
- If possible, concomitant use of *strong CYP3A4 inhibitors* and grapefruit juice should be avoided. If the coadministration of a strong CYP3A4 inhibitor is necessary, the dose of lapatinib should be reduced to 500 mg orally once daily. After discontinuation of a strong CYP3A4 inhibitor, a 1-week washout period should be allowed before the dose of lapatinib is increased to the usual dose.
- If possible, concomitant use of *strong CYP3A4 inducers* should be avoided. If the coadministration of a strong CYP3A4 inducer is necessary, the dose of lapatinib should be gradually titrated from 1250 mg daily up to 4500 mg/day, as tolerated. After discontinuation of a strong CYP3A4 inducer, the dose of lapatinib should be reduced to the usual dose.

**HER2+ Breast cancer in postmenopausal women in combination with letrozole:**

- The recommended dose of lapatinib for the treatment of hormone receptor positive, human epidermal receptor-2 (HER2) positive metastatic breast cancer is 1500 mg orally once daily continuously, in combination with letrozole 2.5 mg orally once daily. If possible, concomitant use of strong CYP3A4 inhibitors and grapefruit juice should be avoided.
- If the coadministration of a strong CYP3A4 inhibitor is necessary, the dose of lapatinib should be reduced to 500 mg orally once daily. After discontinuation of a strong CYP3A4 inhibitor, a 1-week washout period should be allowed before the dose of lapatinib is increased to the usual dose.
- If possible, concomitant use of strong CYP3A4 inducers should be avoided. If the coadministration of a strong CYP3A4 inducer is necessary, the dose of lapatinib should be gradually titrated from 1500 mg daily up to 5500 mg/day, as tolerated. After discontinuation of a strong CYP3A4 inducer, the dose of lapatinib should be reduced to the usual dose

Dosing adjustments:

- Severe hepatic impairment (Child-Pugh class C): Consider dose reduction to 750 mg of lapatinib daily (HER2 positive metastatic breast cancer) or 1000 mg of lapatinib daily (hormone receptor positive, HER2 positive breast cancer).
- Decreased Left Ventricular Ejection Fraction: For grade 2 or higher decreased left ventricular ejection fraction (LVEF) or for LVEF that falls below the lower limit of normal, discontinue lapatinib for at least 2 weeks and until the LVEF returns to normal and the patient is asymptomatic. Lapatinib may then be restarted at a reduced dose of 1000 mg daily (in combination with capecitabine) or 1250 mg daily (in combination with letrozole).
- Diarrhea: If grade 3 or grade 1 or 2 diarrhea with complicating features occur, withhold lapatinib until the toxicity improves to grade 1 or less and restart at a dose reduced by 250 mg (reduced from 1250 mg/day to 1000 mg/day or from 1500 mg/day to 1250 mg/day). Pertinent complicating features include moderate to severe abdominal cramping, grade 2 or higher nausea or vomiting, decreased performance status, fever, sepsis, neutropenia, frank bleeding, or dehydration. If grade 4 diarrhea occurs, permanently discontinue lapatinib.
- Interstitial Lung Disease/Pneumonitis: Discontinue use of lapatinib in patients who develop grade 3 or higher pulmonary symptoms that are indicative of interstitial lung disease/pneumonitis.

- Other Toxicity, Grade 2 or Higher: For any other grade 2 or higher toxicity, consider discontinuation or treatment interruption until the toxicity improves to grade 1 or less. When the toxicity improves to grade 1 or less, lapatinib may be restarted at 1250 or 1500 mg/day. If the toxicity recurs after restarting lapatinib, withhold lapatinib again until the toxicity improves to grade 1 or less and then restart at a reduced dose of 1000 mg/day in combination with capecitabine and 1250 mg/day in combination with letrozole.

## PRECAUTIONS:

- **Black Box Warning:** Hepatotoxicity has been observed in clinical trials and postmarketing experience. The hepatotoxicity may be severe and deaths have been reported. Causality of the deaths is uncertain.
- Lapatinib is contraindicated if hypersensitivity, severe (e.g., anaphylaxis) to lapatinib or any component of the product.
- Avoid concomitant use with grapefruit or strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, voriconazole) or inducers (e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifapentin, phenobarbital, St John's wort). Dose adjustments are recommended if concomitant use is clinically warranted.
- Severe hepatic impairment (Child-Pugh Class C): dose adjustment is recommended if pre-existing; discontinue if severe hepatotoxicity develops during therapy and do not retreat.
- Interstitial lung disease has been reported. Discontinue if symptoms greater than or equal to grade 3 develop during therapy.
- Decreases in left ventricular ejection fraction (LVEF) may occur. Monitoring at baseline and during therapy is recommended.
- Pneumonitis has been reported; discontinue if symptoms greater than or equal to grade 3 develop during therapy.
- Diarrhea, which may be severe or fatal, has been reported. Interruption or discontinuation of therapy may be required.
- Category D all trimesters. May cause fetal harm.
- QT prolongation or predisposing factors for QT prolongation (hypokalemia, hypomagnesemia, congenital long QT syndrome, concomitant agents known to prolong the QT interval, or cumulative high-dose anthracycline therapy).

## Billing/Coding information

### Associated CPT Coding:

| | |
|---|---|
| J8999 | Prescription drug, oral chemotherapeutic, not otherwise specified |
| | |

## COST

- AWP (April 2010): Tykerb 250mg tablet (1): $28.40
- AWP (January 2012): Tykerb 250mg tablet (1): $30.10
- AWP (May 2014): Tykerb 250mg tablet (1): $39.80

## COMMITTEE APPROVAL:

- June 2007

## GUIDELINE UPDATE INFORMATION:

| | |
|---|---|
| June 2007 | Policy created |
| January 2010 | New FDA approved indication for hormone positive and HER2-positive advanced breast cancer |
| September 2011 | Coverage policy updated |
| May 2015 | Coverage policy updated |

## REFERENCES:


- DRUGDEX®, accessed 09/19/2011, 1/4/12, 5/10/2014
- Product Information: TYKERB® oral tablets, lapatinib oral tablets. GlaxoSmithKline, Research Triangle Park, NC, 2010, 2013.