lapatinib (Tykerb®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO076

Description

Lapatinib (Tykerb) is an orally administered tyrosine kinase inhibitor against epidermal growth factor receptors HER1 and HER2.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit	DDID
lapatinib (Tykerb)	250 mg tablets	Breast cancer, HER2 overexpression, advanced or metastatic in combination with capecitabine after prior therapy	105 tablets/28 days	125759
		Breast cancer, HR-positive, HER2 overexpression, in postmenopausal women, in combination with letrozole	168 tablets/28 days	

Initial Evaluation

I. Lapatinib (Tykerb) may be considered medically necessary when the following criteria below are met:
   A. The member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist; **AND**
   C. Lapatinib (Tykerb) will not be used in combination with any other oncolytic medication with the exception of capecitabine (Xeloda), letrozole, or trastuzumab; **AND**
   D. A diagnosis of **breast cancer** when the following are met:
      1. The tumor is positive for HER2(+) gene expression; **AND**
      2. The breast cancer is advanced (stage III) or metastatic (stage IV); **AND**
      3. The medication will be used in one of the following settings:
         i. Progression following ALL of the following therapies: anthracycline therapy (e.g., doxorubicin), taxane therapy (e.g., paclitaxel, docetaxel), trastuzumab (e.g., Herceptin, Trazimera, Kanjinti, etc.); **AND**
            a. Will be used in combination with capecitabine; **OR**
         ii. Initial therapy in the metastatic setting; **AND**

a. The member is a postmenopausal female (natural or pharmacotherapy induced [e.g., GnRH therapy used concomitantly [e.g., Lupron]); **AND**
b. The disease is hormone receptor (HR)-positive; **AND**
c. Will be used in combination with letrozole or trastuzumab (Herceptin, Trazimera, Kanjinti, etc.).

II. Lapatinib (Tykerb) is considered investigational when used for all other conditions, including but not limited to:
   A. HER2(–) breast cancer
   B. Concurrent use with therapies outside of those listed above
   C. Ovarian, uterine, endometrial cancer
   D. Peritoneal cancer
   E. Pancreatic cancer
   F. Melanoma
   G. Central nervous system cancers
   H. Head and neck cancer
   I. Gastrointestinal cancer
   J. Bladder, urothelial, renal cancer

Renewal Evaluation

I. Member has not been established on therapy by the use of free samples, manufacturer coupons, or otherwise; **AND**
II. Member has received a previous prior authorization approval for this agent; **AND**
III. The medication is prescribed by or in consultation with, an oncologist; **AND**
IV. Lapatinib (Tykerb) will not be used in combination with any other oncolytic medication with the exception of an letrozole, capecitabine or trastuzumab; **AND**
V. Documentation is provided indicating disease response to therapy, as defined by: stabilization of disease, decrease in the size of the tumor, or tumor spread.

Supporting Evidence

I. Lapatinib (Tykerb) was evaluated in in combination with capecitablne for HER2(+), metastatic breast cancer. The trial was a Phase 3, randomized study versus capecitabine monotherapy in subjects that had previous exposure to anthracyclines, taxanes, and trastuzumab. The primary

endpoint was time to progression and the results were statistically significant in favor of lapatinib (Tykerb).

II. Overall survival data was not mature at time of assessment, and future results are likely to be confounded as subjects on placebo were allowed to cross over to active therapy during the trial.

III. In two randomized trials, lapatinib (Tykerb) showed to be less effective than trastuzumab-based chemotherapy regimens. The package label indicates subjects should have disease progression on trastuzumab prior to initiation of lapatinib (Tykerb) when used in combination with capecitabline for those with advanced or metastatic, HER2(+) disease.

IV. Lapainib (Tykerb) in combination with letrozole was evaluated in a double-blind, placebo-controlled study. The trial included women with HR+, HER2(+), metastatic breast cancer who had not received prior therapy for metastatic disease. The primary outcome was progression-free survival (PFS) which was statistically significant in favor of lapatinib (Tykerb).

V. Another trial evaluated lapatinib (Tykerb) in combination with an aromatase inhibitor, again evaluating in HR+, HER2(+), metastatic disease. These subjects had progressed after trastuzumab chemotherapy and endocrine therapies. The treatment arms included lapatinib (Tykerb) + trastuzumab + AI, trastuzumab + AI, or lapatinib (Tykerb) + AI. The results were statistically significant in PFS for the triple therapy, followed by lapatinib (Tykerb) + AI, then trastuzumab + AI. Additionally, lapatinib (Tykerb) has demonstrated a statistically significant improvement in PFS in HER2(+) breast cancer when added to trastuzumab compared to lapatinib (Tykerb) alone.

Investigational or Not Medically Necessary Uses

I. Lapatinib (Tykerb) has not been sufficiently evaluated for safety and efficacy in the following settings:
   - A. HER2(–) breast cancer
   - B. Concurrent use with therapies outside of those listed above
   - C. Ovarian, uterine, endometrial cancer
   - D. Peritoneal cancer
   - E. Pancreatic cancer
   - F. Melanoma
   - G. Central nervous system cancers
   - H. Head and neck cancer
   - I. Gastrointestinal cancer
   - J. Bladder, urothelial, renal cancer

References

1. Tykerb [Prescribing Information[. East Hanover, NJ. Novartis Pharmaceuticals Corporation. December 2018.

2. Diéras V, Miles D, Verma S, et al. Trastuzumab emtansine versus capecitabine plus lapatinib in patients with previously treated HER2-positive advanced breast cancer (EMILIA): a descriptive analysis of final overall survival results from a randomised, open-label, phase 3 trial. Lancet Oncol. 2017;18(6):732-742.
3. Pivot X, Manikhas A, Żurawski B, et al. CEREBEL (EGF111438): A Phase III, Randomized, Open-Label Study of Lapatinib Plus Capecitabine Versus Trastuzumab Plus Capecitabine in Patients With Human Epidermal Growth Factor Receptor 2-Positive Metastatic Breast Cancer. J Clin Oncol. 2015;33(14):1564-73.
4. Johnston S, Pippen J, Pivot X, et al. Lapatinib combined with letrozole versus letrozole and placebo as first-line therapy for postmenopausal hormone receptor-positive metastatic breast cancer. J Clin Oncol. 2009;27(33):5538-46.
5. NCCN Clinical Practice Guideline in Oncology: Breast Cancer. Version 3.2019. National Comprehensive Cancer Network. Available at https://www.nccn.org/professionals/ physician_gls/pdf/breast.pdf. Updated September 6, 2019.
6. Geyer C, Forster J, Lindquist D, et al. Lapatinib plus capecitabine for HER2-positive advanced breast cancer. N Engl J Med 2006;355:2733-2743

Policy Implementation/Update:

Date Created	September 2008
Date Effective	October 2008
Last Updated	October 2019
Last Reviewed	08/2011, 08/2013, 09/2013, 10/2019

Action and Summary of Changes	Date
Criteria transitioned to policy. Policy updated to include the following requirement: specialist prescriber, age, concurrent therapies, specified place in therapy,	10/2019