PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Lapatinib (Tykerb) Prior Authorization Policy
- Tykerb® (lapatinib ditosylate tablets – Novartis Pharmaceuticals; generics)

REVIEW DATE: 01/13/2021

OVERVIEW

Lapatinib, a tyrosine kinase inhibitor, is indicated for the following uses:[1]

- **Breast cancer**, in combination with capecitabine tablets for the treatment of patients with **advanced or metastatic disease** whose tumors overexpress human epidermal growth factor receptor 2 (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 lapatinib in combination with capecitabine tablets.
- **Breast cancer**, in combination with letrozole tablets for the treatment of postmenopausal women with **hormone receptor-positive (HR+) metastatic disease** that overexpresses HER2 for whom hormonal therapy is indicated. Lapatinib in combination with an aromatase inhibitor (AI) has not been compared to a trastuzumab-containing chemotherapy regimen for the treatment of metastatic breast cancer.

Guidelines

- **Breast Cancer:** The National Comprehensive Cancer Network (NCCN) clinical practice guidelines on breast cancer (version 6.2020 – September 8, 2020) recommend laptinib in combination with trastuzumab (without cytotoxic therapy) or capecitabine for HER2-positive (HER2+) recurrent or metastatic trastuzumab-exposed disease with symptomatic visceral disease or visceral crisis OR that is hormone receptor-negative or HR+ and endocrine therapy refractory (category 2A).[2] Lapatinib is also recommended in combination with an AI with or without trastuzumab for the treatment of recurrent or Stage IV HR+, HER2+ disease in postmenopausal women.[2] Premenopausal women with HR+ disease should have ovarian ablation/suppression and follow the guidelines for postmenopausal patients. Men with breast cancer should be treated similarly to postmenopausal women except that using an AI is ineffective without suppression of testicular steroidogenesis (category 2A). The NCCN clinical practice guidelines on central nervous system (CNS) cancers (version 3.2020 – September 11, 2020) recommend treatments for patients with brain metastases from breast cancer.[3,4] Capecitabine with or without lapatinib is recommended for recurrent disease in patients with limited (one to three) metastatic lesions or treatment for recurrent stable systemic disease in patients with multiple (> three) metastatic lesions if lapatinib is active against the primary tumor (breast).
- **Bone Cancer:** The NCCN guidelines for bone cancer (version 1.2021 – November 20, 2020) and the compendium recommends the use of lapatinib for epidermal growth factor receptor (*EGFR)*-positive recurrent disease.[3,5]
- **Colon or Rectal Cancer:** The NCCN Compendium supports the use of lapatinib in colon or rectal cancer for HER2-amplified, RAS and BRAF wild-type disease, in combination with trastuzumab.

POLICY STATEMENT
Prior Authorization is recommended for prescription benefit coverage of Tykerb. All approvals are provided for 3 years in duration unless otherwise noted below. In the clinical criteria, as appropriate, an asterisk (*) is noted next to the specified gender. In this context, the specified gender is defined as follows: a woman is defined as an individual with the biological traits of a woman, regardless of the individual's gender identity or gender expression; a man is defined as an individual with the biological traits of a man, regardless of the individual's gender identity or expression.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of lapatinib is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Breast Cancer, Human Epidermal Growth Factor Receptor 2 Positive (HER2+).** Approve for 3 years if the patient meets one of the following criteria (A or B):
   - **A)** Patient has advanced or metastatic breast cancer and the following criteria are met (i or ii):
     - **i.** Patient has received prior therapy with trastuzumab AND the medication will be used in combination with capecitabine; OR
     - **ii.** The medication will be used in combination with trastuzumab; OR
   - **B)** Patient has hormone receptor-positive (that is, estrogen- and/or progesterone-positive) metastatic breast cancer and the following criteria are met (i and ii):
     - **i.** One of the following (a, b, or c) applies:
       - **a)** Patient is a postmenopausal woman*; OR
       - **b)** Patient is a premenopausal or perimenopausal woman* and is receiving ovarian suppression/ablation with a gonadotropin-releasing hormone (GnRH) agonist, surgical bilateral oophorectomy, or ovarian irradiation; OR
         Note: Examples are Lupron® [leuprolide], Trelstar® [triptorelin], Zoladex® (goserelin].
       - **c)** Patient is a man* and is receiving a gonadotropin-releasing hormone (GnRH) agonist; AND
         Note: Examples are Lupron [leuprolide, Trelstar [triptorelin], Zoladex (goserelin].
     - **ii.** The medication will be used in combination with an aromatase inhibitor (that is, letrozole, anastrozole, or exemestane).

   ***** Refer to the Policy Statement.

Other Uses with Supportive Evidence

2. **Bone Cancer – Chordoma.** Approve for 3 years if the patient has epidermal growth-factor receptor (*EGFR*)-positive recurrent disease.

3. **Colon or Rectal Cancer.** Approve for 3 years if the patient meets the following criteria (A, B, and C):
   - **A)** Patient has unresectable advanced or metastatic disease that is human epidermal receptor2 (HER2)-amplified and with wild-type RAS; AND
   - **B)** The medication is used as subsequent therapy in combination with trastuzumab; AND
   - **C)** Patient has not been previously treated with a HER2-inhibitor.
     Note: Examples of HER2-inhibitors are trastuzumab products, Nerlynx (neratinib tablets), Kadcyla (ado-trastuzumab emtansine for injection), Perjeta (pertuzumab for injection).

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Coverage of lapatinib is not recommended in the following situations:

1. **Cervical Cancer.** In one Phase II study (n = 228), Tykerb plus Votrient® (pazopanib tablets) was compared with lapatinib monotherapy or Votrient monotherapy in patients with advanced and recurrent cervical cancer.[6] At the interim analysis, the futility boundary was crossed for combination therapy vs. lapatinib monotherapy, and the combinati○on arm was discontinued. The median PFS was shorter among lapatinib-treated patients vs. Votrient-treated patients (17.1 weeks vs. 18.1 weeks, respectively; HR 0.66; 90% CI: 0.48, 0.91; P < 0.013). On the clinical cutoff date, median OS was 11.6 weeks greater with Votrient vs. lapatinib (50.7 weeks vs. 39.1 weeks; HR: 0.67; 90% CI: 0.46, 0.99; P = 0.045). Patients were not preselected on the basis of EGFR or HER2 amplification.

2. **Gastric, Esophageal, or Gastroesophageal Adenocarcinoma Cancer.** In one Phase II study (n = 47), lapatinib demonstrated modest activity in patients with treatment-naïve advanced/metastatic gastric cancer.[7] A total of four patients had a confirmed partial response, one patient had an unconfirmed partial response, and 10 patients had stable disease. An exploratory analysis revealed gene expression of HER2, interleukin (IL)-8 and genomic polymorphisms IL-8, and vascular endothelial growth factor (VEGF) correlated with OS. In one Phase III, open-label trial conducted in China, Japan, South Korea, and Taiwan, Asian patients (n = 261) with HER2+ advanced gastric cancer were randomized to lapatinib 1,500 mg per day plus paclitaxel 80 mg/m^2 on Days 1, 8, and 15 of a 28-day cycle or to paclitaxel alone.[8] Patients had disease progression after prior therapy. The primary endpoint was OS. Median OS was 11.0 months in patients receiving lapatinib plus paclitaxel vs. 8.9 months with paclitaxel alone (P = 0.1044). There was no significant difference between lapatinib plus paclitaxel or paclitaxel alone in median PFS (5.4 vs. 4.4 months) or time to progression (5.5 vs. 4.4 months), respectively. Overall response rate (ORR) was higher with lapatinib plus paclitaxel vs. paclitaxel alone (27% vs. 9%, respectively; 95% CI: 1.80, 8.87; P <0.001). In one Phase III trial in patients (n = 545) with previously untreated HER2+ advanced gastroesophageal adenocarcinoma were randomized to receive CapeOx (capecitabine plus oxaliplatin) with either lapatinib or placebo.[9] Median OS was 12.2 months (95% CI: 10.6, 14.2) and 10.5 months (95% CI: 9.0, 11.3) for lapatinib and placebo, respectively (HR 0.91; 95% CI: 0.73, 1.12). Preplanned exploratory analysis showed OS in the lapatinib was prolonged in Asian and younger patients.

3. **Head and Neck, Squamous Cell Carcinoma.** In one Phase III study in 688 patients with SCCHN, adding lapatinib to chemoradiotherapy and as maintenance monotherapy was not more effective than placebo in improving disease-free survival or OS.[10]

4. **Renal Cell Carcinoma (RCC).** In one Phase III study in patients (n = 416) with advanced RCC who experienced disease progression through first-line cytokine therapy, lapatinib and hormone therapy (megestrol acetate or tamoxifen, selected by the investigator) demonstrated comparable efficacy: the median time to progression was 15.3 weeks and 15.4 weeks for lapatinib and hormone therapy, respectively (HR 0.94; P = 0.60).[11] The median OS was 46.9 weeks and 43.1 weeks for lapatinib and hormone therapy, respectively (HR 0.88; P = 0.29).

5. **Urothelial Carcinoma.** In one Phase III trial, 232 patients with HER1/HER2 metastatic urothelial bladder cancer who did not have progressive disease during chemotherapy were randomized to receive lapatinib or placebo after completing first-line or initial chemotherapy.[12] Median PFS, the primary endpoint, for lapatinib and placebo was 4.5 months (95% CI: 2.8, 5.4) and 5.1 months (95% CI: 3.0, 5.8), respectively (HR 1.07; 95% CI: 0.81, 1.43; P = 0.63).

6. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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