PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Lapatinib Prior Authorization Policy
- Tykerb® (lapatinib ditosylate tablets – Novartis, generic)

REVIEW DATE: 02/02/2022; selected revision 06/22/2022

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 (HR)-positive 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

Lapatinib is discussed in guidelines from National Comprehensive Cancer Network (NCCN):

- **Breast Cancer:** NCCN guidelines (version 2.2022 – December 20, 2021) recommend lapatinib in combination with trastuzumab (without cytotoxic therapy) or capecitabine for HER2-positive recurrent unresectable (local or regional) or stage IV disease that is HR-negative or HR+ with or without endocrine therapy as third-line therapy or beyond (category 2A).[2] Lapatinib is also recommended in combination with an AI with or without trastuzumab for the treatment of recurrent unresectable (local or regional) or Stage IV HR+, HER2+ disease in postmenopausal women or premenopausal women receiving ovarian ablation or suppression (category 2A).[2] 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 cancers (version 2.2021 – September 8, 2021) recommend treatments for patients with brain metastases from breast cancer.[3,4] Capecitabine with lapatinib is recommended as primary treatment in select patients (e.g. patients with small asymptomatic brain metastases), as treatment for recurrent disease or relapsed disease with stable systemic disease or reasonable systemic treatment options.
- **Bone Cancer:** NCCN guidelines (version 1.2021 – November 20, 2020) and the compendium recommends the use of lapatinib for epidermal growth factor receptor (*EGFR)*-positive recurrent conventional or chondroid chordoma as useful in certain circumstances (category 2A).[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, if not previously treated with a HER2 inhibitor.[3]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of lapatinib. All approvals are provided for the duration 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 one of the following criteria:

FDA-Approved Indications

1. **Breast Cancer.** Approve for 1 year if the patient meets the following criteria (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
   - **C)** Patient has recurrent or metastatic breast cancer; AND
   - **D)** Patient meets one of the following criteria (i or ii):
     - **i.** The patient meets both of the following criteria (a and b):
       - **a)** The medication will be used in combination with capecitabine or trastuzumab; AND
       - **b)** Patient has tried at least two prior anti-HER2 based regimens; OR
         Note: Examples of anti-HER2 regimens include: Perjeta (pertuzumab intravenous infusion) + trastuzumab + docetaxel, Perjeta + trastuzumab + paclitaxel; Enhertu (fam-trastuzumab deruxtecan-nxki intravenous infusion); Kadcyla (ado-trastuzumab emtansine intravenous infusion).
     - **ii.** The medication will be used in combination with an aromatase inhibitor (that is, letrozole, anastrozole, or exemestane) AND patient meets the following criteria (a and b):
       - **a)** Patient has hormone receptor-positive (HR+) [i.e., estrogen receptor positive {ER+}- and/or progesterone receptor positive {PR+}]disease; AND
       - **b)** One of the following ([1] [2] or [3]) applies:
         - **1.** Patient is a postmenopausal woman*; OR
         - **2.** 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 of a GnRH agonist include leuprolide acetate, Lupron Depot (leuprolide acetate intramuscular injection), Trelstar (triptorelin pamoate intramuscular injection), Zoladex (goserelin acetate subcutaneous injection).
         - **3.** Patient is a man* and is receiving a gonadotropin-releasing hormone (GnRH) analog.
           Note: Examples of a GnRH analog include leuprolide acetate, Lupron Depot (leuprolide acetate intramuscular injection), Trelstar (triptorelin pamoate intramuscular injection), Zoladex (goserelin acetate subcutaneous implant), Firmagon (degarelix acetate subcutaneous injection), Orgovyx (relugolix tablet).

***** Refer to the Policy Statement.

Other Uses with Supportive Evidence

2. **Bone Cancer.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has recurrent chordoma; AND
   C) Patient has epidermal growth-factor receptor (*EGFR*)-positive disease.

3. **Colon or Rectal Cancer.** Approve for 1 year if the patient meets the following criteria (A, B, C, D, E, F, and G)
   A) Patient is ≥ 18 years of age; AND
   B) Patient has unresectable, advanced, or metastatic disease; AND
   C) Patient has human epidermal receptor2 (HER2)-amplified disease; AND
   D) Patient has wild-type *RAS* and *BRAF* disease; AND
   E) Patient meets ONE of the following (i or ii):
      i. Patient has tried at least one chemotherapy regimen; OR
      Note: Examples of chemotherapy are fluoropyrimidine such as 5-fluorouracil (5-FU), capecitabine; oxaliplatin, irinotecan, or an adjunctive chemotherapy regimen such as FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin).
      ii. Patient is not a candidate for intensive therapy, according to the prescriber; AND
   F) The medication is used in combination with trastuzumab; AND
   G) 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 intravenous infusion) Perjeta (pertuzumab intravenous infusion).

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 combination 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. **Head and Neck, Squamous Cell Carcinoma.** In one Phase III study in 688 patients with squamous cell carcinoma of the head and neck, adding lapatinib to chemoradiotherapy and as maintenance monotherapy was not more effective than placebo in improving disease-free survival or OS.[7]

3. **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).[8] The median OS was 46.9 weeks and 43.1 weeks for lapatinib and hormone therapy, respectively (HR 0.88; P = 0.29).

4. **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.[9] 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).

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

REFERENCES

1. Tykerb® tablets [prescribing information]. East Hanover, NJ: Novartis; February 2021
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3. The NCCN Drugs & Biologics Compendium. © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 5, 2022. Search terms: lapatinib.
4. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 2.2021 – September 8, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. . Accessed on January 31, 2022.
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9. Powles T, Huddart RA, Elliott T, et al. Phase III, double-blind, randomized trial that compared maintenance lapatinib versus placebo after first-line chemotherapy in patients with human epidermal growth factor receptor 1/2-positive metastatic bladder cancer. *J Clin Oncol*. 2017;35(1):48-55.