PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 02/18/2026

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

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.
- **Breast cancer**, in combination with letrozole for the treatment of postmenopausal women with **hormone receptor (HR)-positive metastatic disease** that overexpresses the HER2 receptor for whom hormonal therapy is indicated.

Lapatinib in combination with an aromatase inhibitor (AI) has not been compared with 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 1.2026 – January 16, 2026) 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-positive with or without endocrine therapy as fourth-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). NCCN central nervous system cancers guidelines (version 3.2025 – December 5, 2025) recommend treatments for patients with brain metastases from HER2-positive breast cancer.[3,4] Capecitabine with lapatinib is recommended as initial treatment in select patients (e.g. patients with small asymptomatic brain metastases), or in select patients with newly diagnosed or stable systemic disease, or as treatment for recurrent disease (category 2A). .
- **Bone Cancer:** NCCN guidelines (version 2.2026 – December 19, 2025) recommend 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 and *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.

Tykerb® (lapatinib ditosylate tablets – Novartis, generic) is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Breast Cancer.** Approve for 1 year if the patient meets ALL of the following (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 (i, ii, or iii):
     - **i.** Patient meets BOTH of the following (a and b):
       - **a)** The medication will be used in combination with capecitabine; AND
       - **b)** Patient has brain metastases; OR
     - **ii.** Patient meets BOTH of the following (a and b):
       - **a)** The medication will be used in combination with capecitabine or trastuzumab; AND
       - **b)** Patient has tried at least three 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); Tukysa (tucatinib tablets) + trastuzumab + capecitabine.
     - **iii.** The medication will be used in combination with an aromatase inhibitor (that is, letrozole, anastrozole, or exemestane) AND patient meets the following (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)** Patient meets ONE of the following [(1) (2) or (3)]:
         - **(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 tablets).

***** Refer to the Policy Statement.

Other Uses with Supportive Evidence

2. **Bone Cancer.** Approve for 1 year if the patient meets ALL of the following (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 ALL of the following (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 receptor 2 (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), Enhertu (fam-trastuzumab deruxtecan-nxki intravenous infusion).

CONDITIONS NOT COVERED

Tykerb® (lapatinib ditosylate tablets – Novartis, generic) is(are) considered not medically necessary for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **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 overall survival.[6]

2. **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.[7] Median progression-free survival

was the primary endpoint, for lapatinib and placebo was 4.5 months and 5.1 months respectively; no statistically significant difference was detected between the two group.

REFERENCES

1. Tykerb® tablets [prescribing information]. East Hanover, NJ: Novartis; December 2024.
2. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 1.2026 – January 16, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 13, 2026.
3. The NCCN Drugs & Biologics Compendium. © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 13, 2026. Search term: lapatinib.
4. The NCCN Central Nervous System Clinical Practice Guidelines in Oncology (version 3.2025 – December 5, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 13, 2026.
5. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 2.2026 – December 19, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 13, 2026.
6 Harrington K, Temam S, Mehanna H, et al. Postoperative adjuvant lapatinib and concurrent chemoradiotherapy followed by maintenance lapatinib monotherapy in high-risk patients with resected squamous cell carcinoma of the head and neck: a phase III, randomized, double-blind, placebo-controlled study. *J Clin Oncol*. 2015;33:4202-4209
7. 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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	02/28/2024
Annual Revision	No criteria changes.	02/19/2025
Annual Revision	**Breast Cancer:** An option for approval was added for a patient with brain metastases when used in combination with capecitabine.	02/18/2026