Effective Date..... 4/1/2023
Next Review Date..... 4/1/2024

Prior Authorization
Oncology – Tykerb® (lapatinib ditosylate tablets, generic)

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Product Identifier(s)

02918

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National Formulary Medical Necessity

Cigna covers lapatinib ditosylate (Tykerb®) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

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.

FDA Indication(s)

1. **Breast Cancer.** Approve for 1 year if the individual meets the following criteria (A, B, C, and D):
   - **A)** Individual is ≥ 18 years of age; AND
   - **B)** Individual has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
   - **C)** Individual has recurrent or metastatic breast cancer; AND
   - **D)** Individual meets one of the following criteria (i or ii):

i. Individual meets both of the following criteria (a and b):
- **a)** The medication will be used in combination with capecitabine or trastuzumab; AND
- **b)** Individual 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 tablet) + trastuzumab + capecitabine.

ii. The medication will be used in combination with an aromatase inhibitor (that is, letrozole, anastrozole, or exemestane) AND individual meets the following criteria (a and b):
- **a)** Individual 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.** Individual is a postmenopausal woman*; OR
  - **2.** Individual 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.** Individual 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 individual meets the following criteria (A, B, and C):
- **A)** Individual is ≥ 18 years of age; AND
- **B)** Individual has recurrent chordoma; AND
- **C)** Individual has epidermal growth-factor receptor (*EGFR*)-positive disease.

3. Colon or Rectal Cancer. Approve for 1 year if the individual meets the following criteria (A, B, C, D, E, F, and G)
- **A)** Individual is ≥ 18 years of age; AND
- **B)** Individual has unresectable, advanced, or metastatic disease; AND
- **C)** Individual has human epidermal receptor 2 (HER2)-amplified disease; AND
- **D)** Individual has wild-type *RAS* and *BRAF* disease; AND
- **E)** Individual meets ONE of the following (i or ii):
  - **i.** Individual 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.** Individual is not a candidate for intensive therapy, according to the prescriber; AND
- **F)** The medication is used in combination with trastuzumab; AND
- **G)** Individual 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

Lapatinib ditosylate (Tykerb®) is considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

1. **Head and Neck, Squamous Cell Carcinoma.** In one Phase III study in 688 individuals 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 individuals 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.

Background

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 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 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 2.2023 – February 7, 2023) 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). The NCCN clinical practice guidelines on central nervous system cancers (version 2.2022 – September 28, 2022) 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 2.2023 – September 28, 2022) 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, *RAS* and *BRAF* wild-type disease, in combination with trastuzumab, if not previously treated with a HER2 inhibitor.[3]

References

1. Tykerb® tablets [prescribing information]. East Hanover, NJ: Novartis; February 2021.
2. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 2.2023 – February 7, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 20, 2023.
3. The NCCN Drugs & Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 20, 2023. Search term: lapatinib.
4. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 2.2022 – September 28, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 20, 2023.
5. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 2.2023 – September 28, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 20, 2023.

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.

Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	**Breast Cancer:** The requirement of trial of at least two prior anti-HER2 based regimens was changed to trial of at least three prior anti-HER2 based regimens. **Conditions Not Recommended for Approval:** The following were removed: cervical carcinoma and renal cell carcinoma.	02/22/2023

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