

## Tykerb® (lapatinib)

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### I. Length of Authorization

Coverage is provided for six months and may be renewed.

### II. Dosing Limits

#### A. Quantity Limit (max daily dose) [NDC Unit]:

- Tykerb 250 mg tablet: 6 tablets per day

#### B. Max Units (per dose and over time) [HCPCS Unit]:

- 1,500 mg per day

### III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is at least 18 years old; **AND**

#### Universal Criteria

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals during treatment; **AND**
- Patient's disease is human epidermal growth factor receptor positive (HER2+)\*; **AND**

#### Breast Cancer † 1,2,5,6,12

- Patient's disease is advanced, metastatic or recurrent; **AND**
  - Used as subsequent therapy in combination with trastuzumab or capecitabine; **AND**
    - Patient's disease is hormone receptor negative; **OR**
    - Patient's disease is hormone receptor positive and used with or without endocrine therapy; **OR**
  - Used in combination with an aromatase inhibitor (e.g., letrozole); **AND**
    - Patient's disease must be hormone receptor-positive; **AND**
      - Patient is a male receiving concomitant androgen deprivation therapy; **OR**
      - Patient is a postmenopausal female; **OR**

- Patient is a premenopausal female treated with ovarian ablation/suppression

### **Bone Cancer – Chordoma ‡<sup>2,3</sup>**

- Used as a single agent therapy; **AND**
- Patient has EGFR-positive recurrent disease

### **Central Nervous System Cancers – Brain Metastases ‡<sup>2,9-11</sup>**

- Patient has brain has brain metastases from HER2-positive breast cancer; **AND**
- Used in combination with capecitabine; **AND**
  - Used as initial treatment of with small, asymptomatic brain lesions; **OR**
  - Used for relapsed disease in patients with limited brain metastases and stable systemic disease or reasonable systemic treatment options; **OR**
  - Patient has recurrent limited brain metastases; **OR**
  - Used for recurrent disease in patients with extensive brain metastases and stable systemic disease or reasonable systemic treatment options

### **Colorectal Adenocarcinoma ‡<sup>2,7,8</sup>**

- Used in combination with trastuzumab; **AND**
- Patient has RAS and BRAF wild-type disease; **AND**
  - Patient has not previously received HER2-targeted therapy; **AND**
    - Used as primary treatment in patients with unresectable advanced or metastatic disease who are not appropriate for intensive therapy; **OR**
    - Used for unresectable metastases that remain unresectable after primary treatment in patients who are not appropriate for intensive therapy; **OR**
    - Used as subsequent therapy for progression of advanced or metastatic disease; **AND**
      - Patient has previously been treated with oxaliplatin-based therapy without irinotecan, irinotecan-based therapy without oxaliplatin, oxaliplatin and irinotecan, or fluoropyrimidine-based therapy without irinotecan or oxaliplatin; **OR**
  - Used as adjuvant therapy in patients who are not appropriate for intensive therapy; **AND**
    - Used for unresectable metastases that converted to resectable disease after primary treatment; **OR**
    - Used following resection and/or local therapy for resectable metastases in patients who have received previous chemotherapy

**\*HER2 overexpression must be confirmed as follows: <sup>4</sup>**

- Immunohistochemistry (IHC) assay 3+; **OR**
- Dual-probe in situ hybridization (ISH) assay HER2/CEP17 ratio  $\geq 2.0$  AND average HER2 copy number  $\geq 4.0$  signals/cell; **OR**
- Dual-probe in situ hybridization (ISH) assay AND concurrent IHC indicating one of the following:
  - HER2/CEP17 ratio  $\geq 2.0$  AND average HER2 copy number  $< 4.0$  signals/cell AND concurrent IHC 3+; **OR**
  - HER2/CEP17 ratio  $< 2.0$  AND average HER2 copy number  $\geq 6.0$  signals/cell AND concurrent IHC 2+ or 3+; **OR**
  - HER2/CEP17 ratio  $< 2.0$  AND average HER2 copy number  $\geq 4.0$  and  $< 6.0$  signals/cell AND concurrent IHC 3+

† FDA Approved Indication(s); ‡ Compendia recommended indication(s)

#### IV. Renewal Criteria <sup>1,2</sup>

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in Section III; **AND**
- Left ventricular ejection fraction (LVEF) has not had an absolute decrease of  $>20\%$  from pre-treatment baseline and is within normal limits; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: hepatotoxicity (severe changes in liver function tests); cardiac toxicity (QT prolongation, decreased LVEF), interstitial lung disease/pneumonitis, severe cutaneous reactions, severe diarrhea, etc.

#### V. Dosage/Administration <sup>1,3,7,8,10-12</sup>

Indication	Dose
Breast Cancer in combination with capecitabine	1,250 mg (5 tablets) by mouth once daily continuously until disease progression or unacceptable toxicity
Breast Cancer in combination with trastuzumab	1000 mg (4 tablets) by mouth once daily continuously
Breast Cancer in combination with aromatase inhibitor (letrozole)	1,500 mg (6 tablets) by mouth once daily continuously
Central Nervous System Cancers – Brain Metastases	1,250 mg (5 tablets) by mouth once daily continuously
Bone Cancer-Chordoma	1,500 mg (6 tablets) by mouth once daily continuously until disease progression or unacceptable toxicity
Colorectal Adenocarcinoma	1000 mg (4 tablets) by mouth once daily continuously

## VI. Billing Code/Availability Information

### HCP/PCS Code:

- J8999 - Prescription drug, oral, chemotherapeutic, nos

### NDC:

- Tykerb 250 mg tablet – 00078-0671- xx

## VII. References

1. Tykerb [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corp; December 2018. Accessed April 2020.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for lapatinib. National Comprehensive Cancer Network, 2020. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2020.
3. Stacchiotti S, Tamborini E, Lo Vullo S, et al. Phase II study on lapatinib in advanced EGFR-positive chordoma, *Annals of Oncology*. 2013 July;24(7):1931-1936.
4. Wolff AC, Hammond MEH, Allison KH, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. *Arch Pathol Lab Med*. 2018 Nov;142(11):1364-1382. doi: 10.5858/arpa.2018-0902-SA. Epub 2018 May 30. *Arch Pathol Lab Med*. 2018. PMID: 29846104.
5. Cameron D, Casey M, Press M, et al. A Phase III Randomized Comparison of Lapatinib Plus Capecitabine Versus Capecitabine Alone in Women With Advanced Breast Cancer That Has Progressed on Trastuzumab: Updated Efficacy and Biomarker Analyses. *Breast Cancer Res Treat*, 112 (3),533-43; Dec 2008. PMID: 18188694. DOI: [10.1007/s10549-007-9885-0](https://doi.org/10.1007/s10549-007-9885-0).
6. Schwartzberg LS, Franco SX, Florance A, et al. Lapatinib Plus Letrozole as First-Line Therapy for HER-2+ Hormone Receptor-Positive Metastatic Breast Cancer. *Oncologist*, 15 (2), 122-9; 2010. PMID: 20156908; PMCID: PMC3227947. DOI: [10.1634/theoncologist.2009-0240](https://doi.org/10.1634/theoncologist.2009-0240).
7. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer 2.2020. National Comprehensive Cancer Network, 2020. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2020.

8. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Rectal Cancer 2.2020. National Comprehensive Cancer Network, 2020. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2020.
9. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers 1.2020. National Comprehensive Cancer Network, 2020. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2020.
10. Petrelli F, Ghidini M, Lonati V, et al. The Efficacy of Lapatinib and Capecitabine in HER-2 Positive Breast Cancer With Brain Metastases: A Systematic Review and Pooled Analysis. *Eur J Cancer*, 84, 141-148; Oct 2017. PMID: 28810186. DOI: [10.1016/j.ejca.2017.07.024](https://doi.org/10.1016/j.ejca.2017.07.024).
11. Bachelot T, Romieu G, Campone M, et al. Lapatinib Plus Capecitabine in Patients With Previously Untreated Brain Metastases From HER2-positive Metastatic Breast Cancer (LANDSCAPE): A Single-Group Phase 2 Study. *Lancet Oncol*, 14 (1), 64-71; Jan 2013. PMID: 23122784. DOI: [10.1016/S1470-2045\(12\)70432-1](https://doi.org/10.1016/S1470-2045(12)70432-1).
12. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer 3.2020. National Comprehensive Cancer Network, 2020. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2020.

## Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C17.0	Malignant neoplasm of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum
C17.8	Malignant neoplasm of overlapping sites of small intestine
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure

### TYKERB® (lapatinib) Prior Auth Criteria

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ICD-10	ICD-10 Description
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast



ICD-10	ICD-10 Description
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C72.0	Malignant neoplasm of spinal cord
C72.1	Malignant neoplasm of cauda equina
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct

ICD-10	ICD-10 Description
C79.31	Secondary malignant neoplasm of brain
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.3	Personal history of malignant neoplasm of breast

## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC