



Kadcyla[®] (ado-trastuzumab emtansine) (Intravenous)

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I. Length of Authorization ¹

Coverage will be provided for six months and may be renewed unless otherwise specified.

- Use as adjuvant treatment of HER2-positive disease in patients with locally advanced or early breast cancer with residual disease is limited to 14 cycles (42 weeks total).

II. Dosing Limits

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

- Kadcyla 100 mg vial – 1 vial every 21 days
- Kadcyla 160 mg vial – 3 vials every 21 days

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

- 480 billable units every 21 days

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient at least 18 years of age; **AND**

Universal Criteria ¹

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
- Patient has human epidermal growth factor receptor 2 (HER2)-positive* disease as determined by an FDA-approved or CLIA-compliant test[❖]; **AND**
- Used as single agent therapy; **AND**
- Therapy will not be substituted with or for any trastuzumab-based formulation (i.e., trastuzumab [or trastuzumab biosimilar product], fam-trastuzumab deruxtecan-nxki, trastuzumab-hyaluronidase, pertuzumab/trastuzumab and hyaluronidase-zzxf, etc.); **AND**

Breast Cancer † ^{1,2,3,4,7}

- Used as adjuvant therapy in patients with:

- Locally advanced residual or node positive disease following completion of planned chemotherapy and mastectomy or lumpectomy ‡; **OR**
- Early breast cancer with residual invasive disease after neoadjuvant taxane and trastuzumab-based therapy; **OR**
- Patient has metastatic or recurrent disease

Non-Small Cell Lung Cancer ‡^{2,5,11}

❖ *If confirmed using an immunotherapy assay* <http://www.fda.gov/companiondiagnostics>

† FDA approved indication(s); ‡ Compendia Recommended Indication(s)

*HER2-positive overexpression criteria:^{7,8}

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

IV. Renewal Criteria^{1,5}

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**
- 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, left ventricular dysfunction, pulmonary toxicity (i.e., interstitial lung disease, pneumonitis), thrombocytopenia, neurotoxicity, infusion-related and hypersensitivity reactions, hemorrhage, extravasation at infusion site, etc.; **AND**

Non-Small Cell Lung Cancer:

- Left ventricular ejection fraction (LVEF) is $\geq 50\%$ OR LVEF is $\geq 45\%$ and absolute decrease is $< 10\%$ from baseline (LVEF results must be within the previous 3 months)

Metastatic or Recurrent Breast Cancer:

- Left ventricular ejection fraction (LVEF) is >45% OR LVEF is ≥40% and absolute decrease is <10% from baseline (LVEF results must be within the previous 3 months)

Adjuvant Therapy of Locally Advanced or Early Stage Breast Cancer:

- Left ventricular ejection fraction (LVEF) is >50% OR LVEF is ≥45% and absolute decrease is <10% from baseline (LVEF results must be within the previous 3 months); **AND**
- Use for adjuvant treatment of breast cancer is limited to 14 cycles (42 weeks total)

V. Dosage/Administration ^{1,5}

| Indication | Dose |
|-------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|
| Adjuvant therapy of locally advanced or early stage breast cancer | 3.6 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) for up to 14 cycles unless there is disease recurrence or unmanageable toxicity |
| Metastatic or recurrent breast cancer | 3.6 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity |
| NSCLC | 3.6 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity |

VI. Billing Code/Availability Information

HCPCS Code:

- J9354 - Injection, ado-trastuzumab emtansine, 1 mg; 1 billable unit = 1 mg

NDC:

- Kadcylla 100 mg single-use vial: 50242-0088-xx
- Kadcylla 160 mg single-use vial: 50242-0087-xx

VII. References

1. Kadcylla [package insert]. South San Francisco, CA; Genentech, Inc; September 2020. Accessed October 2020.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium[®]) ado-trastuzumab emtansine. 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 October 2020.
3. Verma S, Miles D, Gianni L, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer. N Engl J Med. 2012 Nov 8; 367(19):1783-91.

4. von Minckwitz G, Huang CS, Mano MS, et al. Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer. *N Engl J Med.* 2019 Feb 14;380(7):617-628.
5. Li BT, Shen R, Buonocore D, et al. Ado-trastuzumab emtansine in patients with HER2 mutant lung cancers: Results from a phase II basket trial. *J Clin Oncol* 2017, 35: Abstract 8510.
6. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. *J Oncol Pract.* 2018 Mar;14(3):e130-e136.
7. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer 6.2020. 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 October 2020.
8. Wolff AC, Hammond EH, 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. *J Clin Oncol* 2018;36:2105-2122.
9. Hematology/Oncology Pharmacy Association (2019). *Intravenous Cancer Drug Waste Issue Brief*. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf
10. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. *BMJ.* 2016 Feb 29;352:i788.
11. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer 8.2020. 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 October 2020.
12. Palmetto GBA. Local Coverage Article: Billing and Coding: Chemotherapy (A56141). Centers for Medicare & Medicaid Services, Inc. Updated on 05/26/2020 with effective date of 04/30/2020. Accessed October 2020.

Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|--------|----------------------------------------------------------------|
| C33 | Malignant neoplasm of trachea |
| C34.00 | Malignant neoplasm of unspecified main bronchus |
| C34.01 | Malignant neoplasm of right main bronchus |
| C34.02 | Malignant neoplasm of left main bronchus |
| C34.10 | Malignant neoplasm of upper lobe, unspecified bronchus or lung |

| | |
|---------|--------------------------------------------------------------------------|
| C34.11 | Malignant neoplasm of upper lobe, right bronchus or lung |
| C34.12 | Malignant neoplasm of upper lobe, left bronchus or lung |
| C34.2 | Malignant neoplasm of middle lobe, bronchus or lung |
| C34.30 | Malignant neoplasm of lower lobe, unspecified bronchus or lung |
| C34.31 | Malignant neoplasm of lower lobe, right bronchus or lung |
| C34.32 | Malignant neoplasm of lower lobe, left bronchus or lung |
| C34.80 | Malignant neoplasm of overlapping sites of unspecified bronchus and lung |
| C34.81 | Malignant neoplasm of overlapping sites of right bronchus and lung |
| C34.82 | Malignant neoplasm of overlapping sites of left bronchus and lung |
| C34.90 | Malignant neoplasm of unspecified part of unspecified bronchus or lung |
| C34.91 | Malignant neoplasm of unspecified part of right bronchus or lung |
| C34.92 | Malignant neoplasm of unspecified part of left bronchus or lung |
| 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 |
| 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 |
| Z85.118 | Personal history of other malignant neoplasm of bronchus and lung |
| 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):

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| Jurisdiction(s): J,M | NCD/LCD/LCA Document (s): A56141 |
| https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56141&bc=gAAAAAAAAAAAA | |

| 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 |