

Kadcyla® (ado-trastuzumab emtansine) (Intravenous)

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I. Length of Authorization ¹

Coverage will be provided for 6 months and may be renewed (unless otherwise specified).

- Adjuvant treatment in breast cancer is limited to 14 cycles (42 weeks total).

II. Dosing Limits

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

- Kadcyla 100 mg single-dose vial: 1 vial every 21 days
- Kadcyla 160 mg single-dose 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 is 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**
- Used as a single agent; **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 † ‡ ^{1-4,7}

- Patient has human epidermal growth factor receptor 2 (HER2)-positive* disease as determined by an FDA-approved or CLIA-compliant test †; **AND**
 - Used as adjuvant therapy; **AND**
 - Patient has early breast cancer with residual invasive disease after neoadjuvant taxane and trastuzumab-based therapy †; **OR**

- Patient has metastatic or recurrent unresectable disease; **AND**
 - Patient previously received trastuzumab and a taxane, separately or in combination; **AND**
 - Used as second-line therapy and beyond; **AND**

- Patient must demonstrate an inadequate response to fam-trastuzumab deruxtecan-nxki, unless there is a contraindication or intolerance, prior to approval of ado-trastuzumab emtansine; **OR**
- Patient has metastatic disease that recurred during or within 6 months of completing adjuvant therapy †; **AND**
 - Patient previously received trastuzumab and a taxane, separately or in combination; **AND**

- Patient must demonstrate an inadequate response to fam-trastuzumab deruxtecan-nxki, unless there is a contraindication or intolerance, prior to approval of ado-trastuzumab emtansine

Central Nervous System (CNS) Cancer ‡ 2,13

- Patient has human epidermal growth factor receptor 2 (HER2)-positive* disease as determined by an FDA-approved or CLIA-compliant test †; **AND**
- Used for the treatment of brain metastases in patients with breast cancer; **AND**
- Prior treatment for breast cancer included both chemotherapy and HER2-directed therapy, either separately or in combination; **AND**
 - Used as initial treatment in patients with small asymptomatic brain metastases; **OR**
 - Used for relapsed limited brain metastases with either stable systemic disease or reasonable systemic treatment options; **OR**
 - Patient has recurrent limited brain metastases; **OR**
 - Used for recurrent extensive brain metastases with stable systemic disease or reasonable systemic treatment options

Non-Small Cell Lung Cancer (NSCLC) ‡ 2,5,11

- Patient has ERBB2 (HER2) mutation positive disease as determined by an FDA-approved or CLIA-complaint test †; **AND**
 - Patient has metastatic disease; **AND**
 - Patient has adenocarcinoma histology; **AND**
 - Used as subsequent therapy; **AND**
- Patient must demonstrate an inadequate response to fam-trastuzumab deruxtecan-nxki, unless there is a contraindication or intolerance, prior to approval of ado-trastuzumab emtansine

***HER2-positive overexpression criteria:**

Breast and CNS Cancer: ^{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+

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

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

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

IV. **Renewal Criteria** ^{1,5}

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the 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: hepatotoxicity, pulmonary toxicity (i.e., interstitial lung disease, pneumonitis), thrombocytopenia, neurotoxicity, infusion-related and hypersensitivity reactions, hemorrhage, extravasation at infusion site, etc.; **AND**
- Left ventricular ejection fraction (LVEF) obtained within the previous 3 months as follows:
 - Metastatic or Recurrent Breast Cancer: LVEF is $>45\%$ OR LVEF is 40% to $\leq 45\%$ and absolute decrease is $<10\%$ from baseline; **OR**
 - All other indications: LVEF is $\geq 50\%$ OR LVEF is 45% to $<50\%$ and absolute decrease is $<10\%$ from baseline; **AND**

Breast Cancer (adjuvant treatment)

- Patient has not exceeded a maximum of 14 cycles of therapy (42 weeks total)

V. Dosage/Administration ^{1,5,12,13}

Indication	Dose
Breast Cancer (adjuvant treatment)	Administer 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.
Breast Cancer (all other treatment settings), CNS Cancer, NSCLC	Administer 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(s):

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

VII. References (STANDARD)

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2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium[®]) ado-trastuzumab emtansine. National Comprehensive Cancer Network, 2022. 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 September 2022.
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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
C79.31	Secondary malignant neoplasm of brain
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: <https://www.cms.gov/medicare-coverage-database/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