Approved Revision: Do Not Implement Until 6/2/21

Ado-Trastuzumab Emtansine (Kadcyla®)

NDC CODE(S) 50242-0088-XX KADCYLA 100MG Solution Reconstituted (GENENTECH)
50242-0087-XX KADCYLA 160MG Solution Reconstituted (GENENTECH)

DESCRIPTION

Ado-trastuzumab emtansine is an antibody-drug conjugate. It consists of the anti-HER2 IgG1 antibody trastuzumab covalently linked to the drug DM1 via the stable thioether linker MCC. DM1 is a maytansine derivative.

Maytansine, an ansamycin antibiotic, is a potent microtubule inhibitor which has not been found to have a clinical use due to severe side effects and lack of tumor specificity. The term emtansine references both the source drug and the covalent linker of the small molecule complex MCC-DM1.

In the body, ado-trastuzumab emtansine binds to the HER2 receptor on cancer cells. It is then internalized into the cell where it causes lysosomal degradation resulting in the intracellular release of DM1-containing cytotoxic catabolites. These bind to tubulin causing disruption of the cellular microtubule network resulting in cell cycle arrest and apoptotic cell death. Ado-trastuzumab emtansine additionally appears to inhibit HER2 receptor signaling, mediate antibody-dependent cell-mediated cytotoxicity and inhibit shedding of the HER2 extracellular domain in human breast cancer cells that overexpress HER2, as is found with trastuzumab.

POLICY

- Ado-trastuzumab emtansine for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Breast Cancer
  - Non-Small Cell Lung Cancer
  - Head and Neck Cancer
- Ado-trastuzumab emtansine for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

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

Universal Criteria:
- 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
- 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 ~~and was previously treated with trastuzumab and a taxane (separately or in combination)~~

Non-Small Cell Lung Cancer

Head and Neck Cancer
- Further diagnosed as Salivary Gland Tumors; **AND**
- Disease is recurrent; **AND**
  - Patient has distant metastases with a performance status (PS) of 0-3; **OR**
  - Unresectable locoregional recurrence or second primary with prior radiation therapy

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

***HER2 positive overexpression criteria: ~~defined as ANY ONE of the following:~~**
• 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+

RENEWAL 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 initial approval criteria; **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 ≥ 50% OR LVEF is ≥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)

DOSAGE/ADMINISTRATION

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

LENGTH OF AUTHORIZATION

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

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

DOSAGE LIMITS

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

- 480 billable units every 21 days

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice

Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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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.
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7. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer 56.2020. 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.
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11. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer 68.2020. 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.
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EFFECTIVE DATE 6/2/2021

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Policy

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