CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Ado -Trastuzumab Emtansine (Kadcyla®)

Version: 1.0

EFFECTIVE DATE: 10/1/2024

NantHealth® | Eviti®

Please note the following:

Ado -Trastuzumab Emtansine (Kadcyla®)

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Ado -Trastuzumab Emtansine (Kadcyla): Discussion

Ado-trastuzumab emtansine is an antibody–drug conjugate that combines an anti-human epidermal growth factor receptor 2 (HER2) antibody, trastuzumab, with the cytotoxic microtubule inhibitor, DM1. Ado-trastuzumab emtansine targets and binds to the HER2 protein on the surface of cancer cells, the conjugate is internalized via receptor-mediated endocytosis, and DM1 is subsequently released and binds to tubulin. This disrupts the microtubule assembly/disassembly dynamics and inhibits cell division and the proliferation of cancer cells that overexpress HER2.[1]

Ado-trastuzumab emtansine is approved by the Food and Drug Administration (FDA) as a single agent for the treatment for the treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and taxane, separately or in combination, AND received prior therapy for metastatic disease or developed disease recurrence during or within six months of completing adjuvant therapy. It is also approved for adjuvant treatment of patients with HER2-positive early breast cancer who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment.[2]

Adverse side effects include serious hepatotoxicity including liver failure and death as well as cardiac toxicity and embryo-fetal toxicity. Reduce the dose or discontinue ado-trastuzumab as appropriate in cases of increased serum transaminases, increased total bilirubin, and decreased left ventricular function. Left ventricular function should be evaluated prior to treatment. Effective contraception must be utilized prior to and during treatment. The most common adverse reactions (≥ 25%) with Ado-trastuzumab emtansine were fatigue, nausea, musculoskeletal pain, hemorrhage, thrombocytopenia, headache, increased transaminases, constipation and epistaxis.[2]

The National Comprehensive Cancer Network (NCCN) endorses ado-trastuzumab emtansine in the following cancer types: breast, central nervous system (CNS), head and neck, and non-small cell lung cancer (NSCLC).[3,4,5,6]

Ado -Trastuzumab Emtansine : Definitions

- **Antibody-drug conjugate** - A class of biopharmaceuticals which deliver small-molecule cytotoxic drug to antigen-expressing tumor cells.
- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
- **Microtubule inhibitor** - A class of compounds that stop the function of cellular microtubules.
- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than thirty leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.

Ado -Trastuzumab emtansine: Policy

Note: Coverage of Ado-Trastuzumab Emtansine will be provided for an FDA-approved indication or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation OR when all criteria are met.

Ado-trastuzumab emtansine will be considered for coverage when the following criteria are met:

Breast Cancer - Inflammatory

1. Age 18 years or older; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** criteria coverage:

3. As a single agent for the treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease or developed disease recurrence during or within six months of completing the therapy[2]; OR

For **NCCN** criteria coverage:

4. As a single agent adjuvant therapy for one of the following:
   a) Patients who had a response to preoperative systemic therapy, followed by surgery, and need to complete planned chemotherapy, with HER2-positive tumors
   b) Residual disease following preoperative therapy for HER2-positive tumors; OR
5. Third-line and beyond (or second-line if not a candidate for fam-trastuzumab deruxtecan) single agent therapy for patients with no response to preoperative systemic therapy, or for

recurrent unresectable (local or regional) or stage IV (M1) HER2-positive disease that is hormone receptor-negative or hormone receptor-positive with or without endocrine therapy[4]; OR

Breast Cancer – Invasive

1. Age 18 years or older; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** criteria coverage:

3. As a single agent for the treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease or developed disease recurrence during or within six months of completing the therapy[2]; OR

For **NCCN** criteria coverage:

4. As a single agent adjuvant therapy for one of the following:
   a) HER2-positive tumors and locally advanced c≥T2 or cN+ and M0 disease, or cT1c, cN0 disease following completion of planned chemotherapy and following mastectomy or breast-conserving surgery (BCS) with surgical axillary staging if ypT1-4N0 or ypN≥1
   b) HER2-positive tumors and cT1c-3, cN0 or N+, M0 (pT1-3 and pN0 or pN+ tumors) disease; OR
5. Third-line and beyond (or second-line if not a candidate for fam-trastuzumab deruxtecan) single agent therapy for recurrent unresectable (local or regional) or stage IV (M1) HER2-positive disease that is hormone receptor-negative or hormone receptor-positive with or without endocrine therapy.[4]

Central Nervous System (CNS) Cancer

1. Age 18 years or older; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. As a single agent treatment for limited brain metastases in HER2 positive breast cancer in one of the following:
   a) Initial treatment in select cases (e.g., small asymptomatic brain metastases).
   b) Recurrent brain metastases.
   c) Relapsed disease with either stable systemic disease or reasonable systemic treatment options; OR
4. As a single agent treatment for extensive brain metastases in HER2 positive breast cancer in one of the following:
   a) Primary treatment in select cases (e.g., small asymptomatic brain metastases).

b) Treatment for recurrent disease with stable systemic disease or reasonable systemic treatment options.[5]

Head and Neck Cancer - Salivary Gland

1. Age 18 years or older; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Single agent therapy for HER2-positive recurrent disease for one of the following:
   a) Distant metastases in patients with a performance status (PS) of 0-3
   b) Unresectable locoregional recurrence or second primary with prior radiation therapy.[6]

Non-Small Cell Lung Cancer (NSCLC)

1. Age 18 years or older; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Subsequent single agent therapy for ERBB2 (HER2) mutation positive recurrent, advanced, or metastatic disease.[3]

Note: Do not substitute ado-trastuzumab emtansine for or with trastuzumab.

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Ado -Trastuzumab Emtansine: References

1. National Cancer Institute (NCI) Drug Dictionary. https://www.cancer.gov/publications/dictionaries/cancer-drug. Accessed October 14, 2024.
2. Ado-Trastuzumab Emtansine Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125427s111lbl.pdf. Accessed October 14, 2024.
3. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed October 14, 2024.
4. National Comprehensive Cancer Network. Breast Cancer. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed October 14, 2024.

5. National Comprehensive Cancer Network. Central Nervous System Cancers. https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed October 14, 2024.
6. National Comprehensive Cancer Network. Head and Neck Cancers. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed October 14, 2024.

Ado -Trastuzumab Emtansine: Coding (CPT®, ICD 10 and HCPCS)*

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

CODE	DESCRIPTION
C08.9	Salivary Gland Cancer
C34.90	Non-Small Cell Lung Cancer
C50.911, C50.912	Invasive Breast Cancer
C50.919	Inflammatory Breast Cancer
C72.9	Central Nervous System Cancer
J9354	Ado-Trastuzumab Emtansine

Ado-Trastuzumab Emtansine: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	10/1/2024
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	11/20/2024
6	Revision Changes:	