09-J1000-90

Original Effective Date: 05/15/13

Reviewed: 03/11/26

Revised: 04/15/26

Subject: Ado-trastuzumab emtansine (Kadcyla™)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Ado-trastuzumab emtansine (Kadcyla™) is an anti-body-drug conjugate comprising trastuzumab and emtansine. In February 2013, ado-trastuzumab emtansine was approved by the US Food and Drug Administration (FDA) for the treatment of persons with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Emtansine is a sulfur-containing derivative of the potent microtubule inhibitor, maytansine. Emtansine is conjugated to trastuzumab by lysine side chains, forming a stable thioether linker. Ado-trastuzumab emtansine binds HER2 with an affinity comparable to that of trastuzumab (Herceptin) and is the fourth anti-HER2 therapy currently approved by the FDA for the treatment of HER2-positive breast cancer.

The HER tyrosine kinase receptor family includes four transmembrane receptors (HER1/epidermal growth factor receptor [EGFR], HER2, HER3, and HER4) that mediate cell growth, survival, and differentiation. HER receptors activate intracellular signaling pathways. In 20% to 30% of breast tumors, the HER2 gene is amplified and overexpressed, leading to altered regulation of tumor cell growth, proliferation, and survival. The approval of ado-trastuzumab emtansine was based primarily on the results of a phase III, randomized, multicenter, active-controlled study, EMILIA. The study included 991 subjects with unresectable locally advanced or metastatic HER2-positive breast cancer previously treated with trastuzumab and a taxane.

Subjects were randomized to one of two groups:

- Ado-trastuzumab emtansine 3.6 mg/kg every 21 days
- Oral lapatinib 1250 mg daily + capecitabine 1000 mg/m2 every 12 hours for the first 14 days of each 21 day treatment cycle

The primary efficacy endpoints were progression-free survival (PFS) and overall survival (OS). The PFS in the ado-trastuzumab emtansine-treated group was extended by 3.2 months when compared to that of the comparator arm (9.6 months vs. 6.4 months, respectively; HR=0.65, 95% CI 0.55-0.77, p<0.001). The median OS was also significantly greater in subjects randomized to the ado-trastuzumab group compared to that of the comparator arm (30.9 months vs. 25.1 months, respectively; HR=0.68, 95% CI 0.55-0.85, p<0.001).

Ado-trastuzumab is included in the National Comprehensive Cancer Network (NCCN) Breast Cancer Guidelines (Version 1.2024), Head and Neck Cancer (Version 3.2024), Non-Small Cell Lung Cancer (Version 2.2024), and Non-Small Cell Lung Cancer Guidelines (Version 2.2024).

POSITION STATEMENT:

Initiation of ado-trastuzumab emtansine (Kadcyla™) **meets the definition of medical necessity** for members diagnosed with **ANY** of the following conditions when **ALL** associated criteria are met:

1. Breast cancer
    a. Member has been diagnosed with **ONE** of the following:
        i. Locally advanced, inflammatory, or early stage breast cancer
        ii. Metastatic breast cancer
        iii. Recurrent breast
    b. Member has HER2-positive disease
    c. Ado-trastuzumab emtansine is used as **monotherapy**
    d. Member **has not** received ado-trastuzumab emtansine as part of another line of therapy (i.e., previously exposed to ado-trastuzumab emtansine, disease progressed, and drug was discontinued)
    e. Dose does not exceed 3.6 mg/kg every 21 days
2. Central Nervous System Cancers
    a. Member has limited or extensive brain metastases
    b. Member has HER2-positive breast cancer
    c. Use will be as a single agent OR in combination with neratinib (Nerlynx)
    d. Dose does not exceed 3.6 mg/kg every 21 days
3. Non-Small Cell Lung Cancer
    a. Member has recurrent, advanced, or metastatic disease
    b. Member has ERBB2 (HER2) mutation positive disease
    c. Use will be as subsequent therapy
    d. Use will be as a single agent
    e. Dose does not exceed 3.6 mg/kg every 21 days
4. Salivary Gland Tumor
    a. Member has recurrent disease
    b. Member has HER2-positive disease
    c. Use will be as a single agent
    d. Dose does not exceed 3.6 mg/kg every 21 days
5. Other FDA-approved or NCCN supported diagnosis (not previously listed above)
    a. Member meets **ONE** of the following:
        i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND**

member meets any additional requirements listed in the “Indications and Usage” section of the FDA-approved prescribing information (or package insert)

ii. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation

b. Dose does not exceed 3.6 mg/kg every 21 days

Approval duration: 6 months

Continuation of ado-trastuzumab emtansine (Kadcyla™) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of breast cancer, non-small cell lung cancer, salivary gland tumor, or other FDA-approved or NCCN supported diagnosis, OR the member has previously met all indication-specific initiation criteria
2. Member’s disease has not progressed during treatment with ado-trastuzumab emtansine
3. Dose does not exceed 3.6 mg/kg every 21 days

Approval duration: 6 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER’S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved: ado-trastuzumab emtansine is indicated as monotherapy for the treatment of persons with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Individuals should have either 1) received prior therapy for metastatic disease 2) developed disease recurrence during or within six months of completing adjuvant therapy. The recommended dose is 3.6 mg/kg given as in intravenous (IV) infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity occurs.

- 1st infusion: Administer over 90 minutes. Observe for signs and symptoms of infusion-related reactions during and for at least 90 minutes following infusion.
- Subsequent infusions: Administer over 30 minutes if prior infusions were well tolerated. Observe for signs and symptoms of infusion-related reactions during and for at least 30 minutes following infusion.

Dose Adjustments

Management of increased serum transaminases, hyperbilirubinemia, left ventricular dysfunction, thrombocytopenia, pulmonary toxicity or peripheral neuropathy may require temporary interruption, dose reduction or treatment discontinuation. Refer to prescribing information for detailed dose adjustments.

Drug Availability: ado-trastuzumab emtansine is supplied as a single-use vial containing 100- or 160 mg per vial.

PRECAUTIONS:

Boxed Warning

- Ado-trastuzumab emtansine should not be substituted for or with trastuzumab

- Hepatotoxicity, liver failure, and death have occurred in ado-trastuzumab emtansine-treated subjects; hepatic function should be monitored prior to therapy initiation and prior to each subsequent doses. Dose adjustment or permanent discontinuation of therapy may be required.
- Therapy may lead to reductions in left ventricular ejection fraction (LVEF). Assess LVEF prior to initiation. Monitor and withhold dosing or discontinue as appropriate.
- Pregnancy Category D: can cause fetal harm. Females should be advised of potential risk to the fetus.

Warnings/Precautions

- Pulmonary toxicity: permanently discontinue ado-trastuzumab emtansine in persons diagnosed with interstitial lung disease or pneumonitis.
- Infusion related reactions: monitor for signs and symptoms during and after infusion. If significant infusion-related reactions or hypersensitivity reactions occur, slow or interrupt the infusion and administer appropriate medical therapies. Permanently discontinue therapy if a life-threatening infusion-related reaction occurs.
- Thrombocytopenia: monitor platelet counts prior to each dose. Institute dose modifications as appropriate.
- Neurotoxicity: monitor for signs and symptoms. Withhold dosing temporarily for persons experiencing Grade 3 or 4 peripheral neuropathy.

BILLING/CODING INFORMATION:

HCPCS Coding

J9354	Injection, ado-trastuzumab emtansine, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

C06.9	Malignant neoplasm of mouth, unspecified
C07	Malignant neoplasm of parotid gland
C08.0-C08.9	Malignant neoplasm of other and unspecified major salivary glands
C50.011 – C50.929	Malignant neoplasm of female and male breast
C33	Malignant neoplasm of trachea
C34.00 – C34.32	Malignant neoplasm of bronchus or lung
C34.80 – C34.92	Malignant neoplasm of bronchus or lung
C79.31	Secondary malignant neoplasm of brain

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time this guideline was drafted.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Adjuvant Treatment: Additional cancer treatment given after the primary treatment to lower the risk that the cancer will return. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, targeted therapy, or biologic therapy. Adjuvant therapy can be used after or in combination with another form of cancer therapy and is commonly used following removal of a cancerous tumor to further help in treatment.

Metastatic cancer: when cancer spreads from the primary site (place where it started) to other places in the body.

RELATED GUIDELINES:

Capecitabine (Xeloda®) Tablets, 09-J1000-42
Carboplatin (Paraplatin®) IV, 09-J0000-93
Docetaxel (Taxotere®) IV, 09-J0000-95
Doxorubicin HCl Liposome (Doxil®) IV, 09-J0000-91
Gemcitabine (Gemzar®), 09-J0000-96
Irinotecan HCl Camptosar®) IV, 09-J0000-99
Lapatinib (Tykerb®) Tablets, 09-J-1000-47
Oxaliplatin (Eloxatin®) IV, 09-J1000-00
Paclitaxel and Nab-Paclitaxel IV, 09-J1000-05
Pertuzumab (Perjeta™) IV, 09-J1000-75
Vinorelbine (Navelbine®) IV, 09-J1000-03

OTHER:

None

REFERENCES:

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7. Verma S, Miles D, Gianni L, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer. NEJM 2012;367(19): 1783-91.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 03/11/26.

GUIDELINE UPDATE INFORMATION:

05/15/13	New Medical Coverage Guideline.
10/15/13	Revision to guideline; consisting of administrative action to update coding
01/01/14	Revision to guideline; consisting of code update.
04/15/14	Review and revision to guideline; consisting of revising and reformatting position statement and updating references.
12/15/14	Revision to guideline; consisting of updating position statement.
04/15/15	Review and revision to guideline; consisting of description, position statement, program exceptions, dosage/administration, references.
04/15/16	Review and revision to guideline; description, position statement, coding, references.
04/15/17	Review and revision to guideline; description, position statement, references.
12/15/17	Revision to guideline to remove HER2 documentation from postion statement.
4/15/18	Review and revision to guideline; updated description, position statement, coding, references.
5/15/19	Review and revision to guideline; updated description, position statement, references.
04/15/20	Review and revision to guideline; updated description, references.
04/15/22	Review and revision to guideline; updated position statement, references.
05/15/22	Updated ICD10 codes.
04/15/23	Review and revision to guideline; updated coding and references.
04/15/24	Review and revision to guideline; updated position statement and references.
04/15/25	Review and revision to guideline; updated references.
04/15/26	Review and revision to guideline; updated position statement and references.