STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Kadcyla (ado-trastuzumab emtansine)
PAM–007

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	08/15/2013
Revision Number:	8	**Last Rev Date:**	10/20/2023
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	10/18/2024
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	08/23/2019

Overview

Medication:[1]	ado-trastuzumab emtansine
Brand Name:	Kadcyla®
Pharmacologic Category:	Human epidermal growth factor receptor 2 *(HER2)*-targeted antibody and microtubule inhibitor conjugate
FDA-Approved Indication(s):	• Breast cancer, metastatic (MBC) ≠: as a single agent, indicated 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 6 months of completing adjuvant therapy. • Early breast cancer (EBC) ≠: as a single agent, indicated for the treatment of patients with HER2-positive EBC cancer who have residual invasive disease following neoadjuvant taxane and trastuzumab-based treatment. ≠ Select patients for therapy based on an FDA-approved companion diagnostic test.
How Supplied:	Single-dose vial: 100 mg or 160 mg
Dosage and Administration:	IV infusion: 3.6 mg/kg every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity, or a total of 14 cycles for patients with early breast cancer.
Benefit Category:	Medical

BOXED WARNING: Hepatotoxicity, cardiac toxicity, embryo-fetal toxicity

Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with Kadcyla®. Monitor serum transaminases and bilirubin prior to initiation of Kadcyla® treatment and prior to each dose. Reduce dose or discontinue Kadcyla® as appropriate in cases of increased serum transaminases or total bilirubin.

Cardiac Toxicity: Kadcyla® administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment. Withhold treatment for clinically significant decrease in left ventricular function.

Embryo-Fetal Toxicity: Exposure to Kadcyla® during pregnancy can result in embryo-fetal harm. Advise patients of these risks and the need for effective contraception.

Descriptive Narrative

Breast cancer is a heterogenous, phenotypically diverse disease composed of several biologic subtypes that have distinct behavior. Amplification or overexpression of the human epidermal growth factor receptor 2 *(HER2)* oncogene* is present in approximately 15 percent of primary invasive breast cancers. Women with both early-stage and metastatic** breast cancer that meet criteria for HER2 positivity are treated with regimens including HER2-directed therapy.[2]

* HER2 is a growth-promoting protein on the outside of all breast cells. Breast cancer cells with higher-than normal levels of HER2 are referred to as HER2-positive.

** Metastatic breast cancer (MBC). Also called stage IV, MBC is breast cancer that has spread to another part of the body, most commonly the liver, brain, bones, or lungs.

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[3]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines for Breast Cancer (Version 4.2023 – March 23, 2023)[4]

NCCN Guidelines® Recommendation(s) for ado-trastuzumab emtansine (Kadcyla®)[a] in invasive breast cancer
(1) Preoperative/adjuvant therapy regimens [b] A. HER2-Positive: Preferred regimens i. If residual disease after preoperative therapy: ado-trastuzumab emtansine as monotherapy: Category 1 B. HER2-Positive: Useful in certain circumstances i. Ado-trastuzumab emtansine (TDM-1) (adjuvant setting only): Category 2A (2) Systemic therapy regimens for recurrent unresectable (local or regional) or stage IV (M1) disease [c] A. HR-Positive or -Negative and HER2-Positive (third-line) [c] i. Ado-trastuzumab emtansine (TDM-1): Category 2A [d]

[a] Additional Considerations: Trastuzumab and hyaluronidase-oysk injection for subcutaneous use may be substituted for trastuzumab. It has different dosage and administration instructions compared to intravenous trastuzumab. Do not substitute trastuzumab and hyaluronidase-oysk for or with ado-trastuzumab emtansine or fam-trastuzumab deruxtecan-nxki.

[b] Alternative taxanes (i.e., docetaxel, paclitaxel, albumin-bound paclitaxel) may be substituted for select patients due to medical necessity (i.e., hypersensitivity reaction). If substituted for weekly paclitaxel or docetaxel, then the weekly dose of albumin-bound paclitaxel should not exceed 125 mg/m^2.

[c] Assess for germline *BRCA1/2* mutations in all patients with recurrent or metastatic breast cancer to identify candidates for PARP inhibitor therapy. While olaparib and talazoparib are FDA-indicated in HER2-negative disease, the panel supports use in any breast cancer subtype associated with a germline mutation. There is lower-level evidence for HER2-positive tumors, therefore category 2A for this setting.

[d] May be used as an option for third-line and beyond; the optimal sequence for third-line therapy and beyond is not known. If not a candidate fam-trastuzumab T-DM1 could be considered in the second-line.

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Criteria

Prior authorization is required.

HER2-positive early breast cancer (EBC) with residual disease – Initial Criteria

Kadcyla® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of human epidermal growth factor receptor 2 *(HER2)*-positive early breast cancer (EBC); **AND**
2. Member has residual invasive disease following neoadjuvant taxane (paclitaxel or docetaxel) and trastuzumab-based treatment; **AND**
3. Kadcyla® will be administered as a single agent treatment regimen; **AND**
4. Member is 18 years of age or older; **AND**
5. Prescribed by, or in consultation with, an oncologist; **AND**
6. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 3.6 mg/kg every 3 weeks (21-day cycle) for a maximum of 14 cycles of therapy; or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

HER2-positive metastatic breast cancer (MBC) – Initial Criteria

Kadcyla® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of human epidermal growth factor receptor 2 *(HER2)*-positive metastatic breast cancer (MBC); **AND**
2. Member previously treated with trastuzumab and a taxane (paclitaxel or docetaxel), separately or in combination; **AND**
3. Member meets **ONE** of the following (a or b):
    a. Received prior therapy for metastatic disease; **OR**
    b. Developed disease recurrence during or within 6 months of completing adjuvant therapy; **AND**
4. Kadcyla® will be administered as a single agent treatment regimen; **AND**
5. Member is 18 years of age or older; **AND**
6. Prescribed by, or in consultation with, an oncologist; **AND**
7. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 3.6 mg/kg every 3 weeks (21-day cycle); or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Continuation Criteria – ALL ABOVE INDICATIONS

Kadcyla® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. For early breast cancer (EBC) **ONLY**: Member has not received the maximum of 14 cycles of treatment with Kadcyla®; **AND**
4. Prescribed by, or in consultation with, an oncologist; **AND**
5. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 3.6 mg/kg every 3 weeks (21-day cycle):
        1) for a maximum of 14 cycles of therapy for early breast cancer; or
        2) until disease progression or unacceptable toxicity in metastatic breast cancer; or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	EBC with Residual Invasive Disease	MBC
Initial authorization:	6 months or 8 cycles, whichever comes first	6 months or 8 cycles, whichever comes first
Continuation of therapy:	4 months (6 cycles), or until member has completed the maximum 14 cycles	12 months or 17 cycles, whichever comes first
Quantity limit:	Not to exceed 3.6 mg/kg every 3 weeks (21-day cycle), for a maximum of 14 cycles	Not to exceed 3.6 mg/kg every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9354	Injection, ado-trastuzumab emtansine, 1 mg

ICD-10	Description
C50.11-C50.929	Malignant neoplasm of breast [HER2 positive] [not covered if HER2 negative]
C79.81	Secondary malignant neoplasm of breast
D05.00-D05.92	Carcinoma in situ of breast

NDC	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
50242-0087-01	Genentech, Inc.	1 mg	1	1	160
50242-0088-01	Genentech, Inc.	1 mg	1	1	100

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Kadcyla® prescribing information (02/2022). Genentech, Inc.: South San Francisco, CA. Available online at www.kadcyla-hcp.com. Accessed August 24, 2023.

[2] Yamauchi MD, Bleiweiss MD. HER2 and predicting response to therapy in breast cancer. Vora SR, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed October 8, 2023.

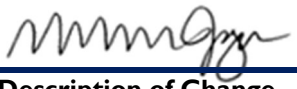
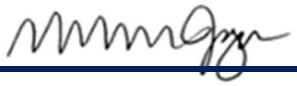
[3] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 11, 2023.

[4] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer (V.4.2023 – March 23, 2023). Accessed October 3, 2023. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guideline, go online to NCCN.org

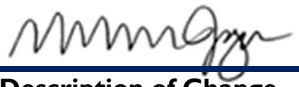
Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
10/20/2023	CAC	Annual review. Added boxed warning to Overview section (hepatotoxicity, cardiac toxicity, embryo-fetal toxicity). Updated NCCN Guidelines. Added dosing regimens into clinical criteria.	8
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
10/21/2022	CAC	• Annual review. Updated NCCN recommendations. Added "Member is 18 years of age or older" to initial coverage criteria. Added standard language to continuation criteria: "1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria." Updated references. • Prior authorization requirement re-implemented effective 6/1/22 to align with current policy.	7
Signature William (Bill) Jagiello, DO			

Criteria Change History *(continued)*

Change Date	Changed By	Description of Change	Version
10/15/2021	CAC	Annual review.	6
Signature			
William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
07/17/2020	CAC	Prior authorization requirement removed.	5
Signature			
William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
07/16/2015	Medical Director	Criterion #1 added "over expression of the HER2 gene". Criterion #2 added "failed treatment or shown inadequate response with".	4
Signature			
Mark E. Randleman, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
07/17/2015	CAC	Added last paragraph in References.	3
Signature			
Change Date	**Changed By**	**Description of Change**	**Version**
07/14/2015	Medical Director	Updated NCCN reference.	2
Signature			
Change Date	**Changed By**	**Description of Change**	**Version**
07/18/2014	CAC	Removed narrative that was a duplication of what is listed under criteria.	1
Signature			

CAC = Medicaid Clinical Advisory Committee