Margenza (margetuximab-cmkb)
PAM – 056

Iowa Medicaid Program	Prior Authorization	**Effective Date**	07/01/2021
Revision Number	2	**Last Reviewed**	10/18/2024
Reviewed By	Medicaid Medical Director	**Next Review**	10/17/2025
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	07/21/2023

Overview

Medication: [1]	margetuximab-cmkb
Brand Name:	Margenza®
Pharmacologic Category:	Antineoplastic; human epidermal growth factor 2 (HER2/neu) receptor antagonist
FDA-Approved Indication(s):	Indicated, in combination with chemotherapy, for the treatment of adult patients with metastatic HER2- positive breast cancer who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease.
How Supplied:	• Single-dose vial, 250 mg/10 mL (25 mg/mL) • Supplied in a carton containing either 1 or 4 single-dose vials
Dosage and Administration:	Intravenous (IV) infusion: 15 mg/kg every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity
Benefit Category:	Medical

BOXED WARNING: LEFT VENTRICULAR DYSFUNCTION AND EMBRYO-FETAL TOXICITY

Left Ventricular Dysfunction: Margenza® may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate cardiac function prior to and during treatment. Discontinue treatment for a confirmed clinically significant decrease in left ventricular function.

Embryo-Fetal Toxicity: Exposure to Margenza® during pregnancy can cause embryo-fetal harm. Advise patients of the risk and need for effective contraception.

Descriptive Narrative

Globally, breast cancer is the most frequently diagnosed malignancy, accounting for over two million cases each year. It is also the leading cause of cancer death in women worldwide. In the United States, breast cancer is the most common female cancer, and the second most common cause of cancer death in women.[2] An estimated 3,010 new cases of breast cancer in females will be diagnosed in Iowa in 2024, making it the second most commonly diagnosed cancer in the state (second only to prostate cancer), and with an estimated 370 deaths, it is the fourth highest cause of cancer deaths in Iowa in 2024.[3]

Up to 5 percent of women diagnosed with breast cancer in the U.S. have metastatic disease at the time of first presentation, despite the gains in early detection, and up to 30 percent of women with early-stage non-metastatic breast cancer at diagnosis will develop distant metastatic disease.

Available treatment options vary based on whether the tumor is hormone receptor positive (estrogen and/or progesterone receptor positive) and whether human epidermal growth factor receptor 2 (HER2) is overexpressed (i.e., HER2-positive). Approximately 20 percent of breast cancers overexpress HER2, a transmembrane glycoprotein epidermal growth factor receptor (EGFR) with tyrosine kinase activity. Historically, overexpression of this receptor was associated with an increased risk of disease recurrence and an overall worse prognosis. However, therapies that target HER2 have become important agents in the treatment of metastatic breast cancer and have altered the natural course of HER2-positive breast cancer.[4]

Guidelines

The National Comprehensive Cancer Network (NCCN) publishes guidelines for the prevention, diagnosis, and management of malignancies across the continuum of care. The NCCN Guidelines® are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the United States. The guidelines are developed and updated by 61 individual panels, comprising over 1,700 clinicians and oncology researchers from the 33 NCCN Member Institutions.

Guidelines are reviewed and updated on a continual basis to ensure that the recommendations take into account the most current evidence. 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.[5,6]

The information referenced at the time of this policy writing/revision is from the NCCN Guidelines® for (note version number and effective date):[7]

- Breast Cancer (v.4.2024 – July 3, 2024)

NCCN Guidelines® Recommendation(s) – Systemic Therapy Regimens for Recurrent Unresectable (Local or Regional) Stage IV (M1) Disease [a]
(1) HR-Positive or -Negative and HER2-positive [a] a. Fourth Line and Beyond (optimal sequence not known) [b] i. Margetuximab-cmkb + chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine: Category 2A
[a] 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.

NCCN Guidelines® Recommendation(s) – Systemic Therapy Regimens for Recurrent Unresectable (Local or Regional) Stage IV (M1) Disease [a]
[b] Multiple lines of concurrent chemotherapy with anti-HER2 therapy (trastuzumab or a TKI) offer clinical benefit for recurrent unresectable HER2+ metastatic breast cancer and have been studied in phase 2 or 3 trials. Clinical experience suggests frequent clinical benefit for such treatment. However, there are no meaningful data for use of any of these regimens among patients previously treated with pertuzumab-based chemotherapy, ado-trastuzumab emtansine, fam-trastuzumab deruxtecan-nxki, or trastuzumab/capecitabine/tucatinib regimens. Thus, the optimal sequence or true benefit of therapy is not known.

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.

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

1. Diagnosis of metastatic breast cancer that is HER2-positive (HER2+); **AND**
2. Member has received two (2) or more prior lines of anti-HER2-directed therapy, at least one of which was in the metastatic setting; **AND**
3. Member is 18 years of age or older; **AND**
4. Margenza® is prescribed in combination with chemotherapy (e.g., capecitabine, eribulin, gemcitabine, or vinorelbine); **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 15 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.

Margenza® 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. Prescribed by, or in consultation with, an oncologist; **AND**
4. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 15 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.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months
Quantity Limits	15 mg/kg every 3 weeks (21-day cycle)	

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
J9353	Injection, margetuximab-cmkb, 5 mg

ICD-10	Description
C50.011 – C50.929	Malignant neoplasm of breast
C79.81	Secondary malignant neoplasm of breast
D05.00 – D05.92	Lobular carcinoma in situ of breast
Z17.0	Estrogen receptor positive status (ER+)

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
74527-0022-02 (250 mg/10 mL, 1 vial)	MacroGenics, Inc. (74527)	5 mg	1	EA	50
74527-0022-03 (250 mg/10 mL, 4 vials)	MacroGenics, Inc. (74527)	5 mg	4	EA	200

Compliance

1. Should conflict exist between the 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] Margenza® prescribing information (05/2023). MacroGenics, Inc.: Rockville, MD. Available online: www.margenzahcp.com. Accessed July 3, 2024.

[2] Joe BN. Clinical features, diagnosis, and staging of newly diagnosed breast cancer. Vora SR, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed July 29, 2024.

[3] American Cancer Society: Cancer Statistics Center. State of Iowa. Available online at cancerstatisticscenter.cancer.org/states/iowa. Accessed July 29, 2024.

[4] Schott AF. Systemic treatment for HER2-positive metastatic breast cancer. Vora SR, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed July 29, 2024.

[5] National Comprehensive Cancer Network (NCCN). Guidelines Process: About Clinical Practice Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[6] National Comprehensive Cancer Network (NCCN). Guidelines Process: Development and Update of Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[7] NCCN Clinical Practice Guidelines in Oncology. 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, go online to NCCN.org. NCCN Guidelines® referenced (note version number and effective date):

- Breast Cancer (v.4.2024 – July 3, 2024)

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
[mm/dd/yyyy]	CAC		[#]
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		[#]
Signature			

Change Date	Changed By	Description of Change	Version
10/18/2024	CAC	Annual review (moved from July to October review period to align with other policies with breast cancer indication). Added dosing information into criteria. Updated description of the National Comprehensive Cancer Network (NCCN). Reviewed NCCN Guidelines (no changes).	2
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
07/21/2023	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee