STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

# Margenza (margetuximab-cmkb)
## PAM-056

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| **Iowa Medicaid Program:** | Prior Authorization | **Effective Date:** | 07/01/2021 |
| **Revision Number:** | 1 | **Last Rev Date:** | 07/21/2023 |
| **Reviewed By:** | Medicaid Medical Director | **Next Rev Date:** | 07/19/2024 |
| **Approved By:** | Medicaid Clinical Advisory Committee | **Approved Date:** | 07/21/2023 |

## Overview

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| Medication:[1] | margetuximab-cmkb |
| Brand Name: | Margenza® |
| Pharmacologic Category: | Oncology; 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: | • Carton containing either one or four single-dose vials<br>• Each vial contains 250 mg/10 mL (25 mg/mL) |
| Dosage and Administration: | 15 mg/kg, administered as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity |
| Benefit Category: | Medical |

**Boxed Warnings:** 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 Margenza treatment for a confirmed clinically significant decrease in left ventricular function.
- Embryo-Fetal Toxicity: Exposure to Margenza during pregnancy can cause embryofetal 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 2,770 new cases of breast cancer in females will be diagnosed in Iowa in 2022, making it the most commonly diagnosed cancer in the state, and with an estimated 380 deaths, it is the fifth highest cause of cancer deaths in Iowa in 2022.[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

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.[5]

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).[6]

Recommendation(s):
Margetuximab-cmkb (Margenza®) in combination with chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine) is recommended by NCCN as a Category 2A, "fourth line and beyond" systemic therapy regimen for recurrent unresectable (local or regional) or stage IV (M1) disease (HR-Positive or -Negative and HER2-Positive).

| **NCCN Categories of Evidence and Consensus**<br>(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. Margenza® is prescribed in combination with chemotherapy (e.g., capecitabine, eribulin, gemcitabine, or vinorelbine); **AND**
4. Member is 18 years of age or older; **AND**
5. Prescribed by, or in consultation with, an oncologist; **AND**
6. The regimen prescribed is within the FDA-approved labeling. If dose or schedule exceeds the FDA-approved labeling, therapy regimen (including dosage) must be supported by clinical practice guidelines (i.e., must be recommended in the NCCN Clinical Practice Guidelines®). Supporting clinical documentation must be provided with any request for which the regimen or dosage 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. The regimen prescribed is within the FDA-approved labeling. If dose or schedule exceeds the FDA-approved labeling, therapy regimen (including dosage) must be supported by clinical practice guidelines (i.e., must be recommended in the NCCN Clinical Practice Guidelines®). Supporting clinical documentation must be provided with any request for which the regimen or dosage 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) 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 |
|---|---|
| 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 | Labeler | Dosage | Pkg Size | Pkg Qty | Units/Pkg |
|---|---|---|---|---|---|
| 74527-0022-02 | MacroGenics, Inc. (74527) | 5 mg | 1 | EA | 50 |
| 74527-0022-03 | MacroGenics, Inc. (74527) | 5 mg | 4 | EA | 200 |

## 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] Margenza prescribing information (05/2023). MacroGenics, Inc.: Rockville, MD. Available online at www.margenzahcp.com. Accessed June 15, 2023.

[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 December 29, 2022.

[3] American Cancer Society: Cancer Statistics Center. State of Iowa. Available online at cancerstatisticscenter.cancer.org/#!/state/Iowa. Accessed December 29, 2022.

[4] Schott AF. Systemic treatment for HER2-positive metastatic breast cancer. Vora SR, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed December 29, 2022.

[5] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed January 19, 2023.

[6] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer (v.4.2023 – March 23, 2023). Accessed June 15, 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 guidelines, 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 |
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| | CAC | | |
| **Signature** | | | |

| Change Date | Changed By | Description of Change | Version |
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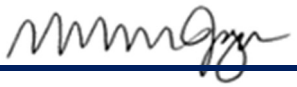
| **Signature** | | | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 07/21/2023 | CAC | Criteria implementation. | 1 |
| **Signature**<br>William (Bill) Jagiello, DO | |  | |

CAC = Medicaid Clinical Advisory Committee