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Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Antineoplastic Drugs	**Original Policy Date:**	January 29, 2021
Subject:	Margenza	**Page:**	1 of 4

Last Review Date: March 7, 2025

Margenza

Description

Margenza (margetuximab-cmkb)

Background
Margenza (margetuximab-cmkb) is a HER2/neu receptor antagonist 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. Margenza binds to the extracellular domain of the human epidermal growth factor receptor 2 protein (HER2). Upon binding to HER2-expressing tumor cells, Margenza inhibits tumor cell proliferation, reduces shedding of the HER2 extracellular domain and mediates antibody-dependent cellular cytotoxicity (ADCC) (1).

Regulatory Status
FDA-approved indication: Margenza is a HER2/neu receptor antagonist 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 (1).

Margenza has boxed warnings regarding left ventricular dysfunction and embryo-fetal toxicity. Margenza may lead to reductions in left ventricular ejection fraction (LVEF). Cardiac function should be evaluated prior to and during treatment. Margenza treatment should be discontinued for a confirmed clinically significant decrease in left ventricular function (1).

Female patients of reproductive potential should be advised to use effective contraception during treatment with Margenza and for 4 months following the last dose (1).

The safety and effectiveness of Margenza in pediatric patients have not been established (1).

Related policies
Enhertu, Herceptin Hylecta, Kadcyla, Nerlynx, Perjeta, Phesgo, Trastuzumab, Tukysa, Tykerb

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Margenza may be considered **medically necessary** if the conditions indicated below are met.

Margenza may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

Metastatic HER2-positive breast cancer

AND ALL of the following:

1. Patient has received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease
2. Prescriber agrees to evaluate cardiac function prior to and during treatment
3. Prescriber agrees to discontinue Margenza for confirmed clinically significant decrease in left ventricular function
4. Prescriber will not exceed the FDA labeled dose of 15 mg per kg every 3 weeks
5. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Margenza and for 4 months after the final dose

Prior–Approval *Renewal* Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

Metastatic HER2-positive breast cancer

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to evaluate cardiac function during treatment
3. Prescriber agrees to discontinue Margenza for confirmed clinically significant decrease in left ventricular function
4. Prescriber will not exceed the FDA labeled dose of 15 mg per kg every 3 weeks
5. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Margenza and for 4 months after the final dose

Policy Guidelines

Pre–PA Allowance

None

Prior–Approval Limits

Duration 12 months

Prior–Approval *Renewal* Limits

Same as above

Rationale

Summary
Margenza (margetuximab-cmkb) is a HER2/neu receptor antagonist 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. Margenza has boxed warnings regarding left ventricular dysfunction and embryo-fetal toxicity. The safety and effectiveness of Margenza in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Margenza while maintaining optimal therapeutic outcomes.

References

1. Margenza [package insert]. Rockville, MD: MacroGenics, Inc.; May 2023.
2. NCCN Drugs & Biologics Compendium® Margetuximab-cmkb 2025. National Comprehensive Cancer Network, Inc. Accessed on January 8, 2025.

Policy History

Date	Action
January 2021	Addition to PA
March 2021	Annual review
June 2021	Annual editorial review and reference update
June 2022	Annual review and reference update
September 2022	Annual review and reference update
June 2023	Annual review and reference update
March 2024	Annual review and reference update
June 2024	Annual review and reference update
March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.