Clinical Policy: Margetuximab-cmkb (Margenza)

Reference Number: PA.CP.PHAR.522
Effective Date: 01/2022
Last Review Date: 01/2026

Description
Margetuximab-cmkb (Margenza™) is a human epidermal growth factor receptor 2 (HER2)/neu receptor antagonist.

FDA Approved Indication(s)
Margenza is 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Margenza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Breast Cancer (must meet all)**:**

1. Diagnosis of metastatic or recurrent unresectable (local or regional) HER2-positive breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. For metastatic disease: failure of at least two anti-HER2-based regimens (*see Appendix B*), at least one of which was for metastatic disease, unless contraindicated or clinically significant adverse effects are experienced;
   b. For recurrent unresectable (local or regional) disease or for patients with no response to preoperative systemic therapy: failure of three anti-HER2-based regimens (*see Appendix B*), unless contraindicated or clinically significant adverse effects are experienced;

   **Prior authorization may be required for anti-HER2-based regimens*
5. Prescribed in combination with chemotherapy (e.g., capecitabine, eribulin, gemcitabine, vinorelbine);
6. Request meets one of the following (a or b):
   a. Dose does not exceed 15 mg/kg every 3 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Breast Cancer (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 15 mg/kg every 3 weeks;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Herceptin® (trastuzumab) ± any of the following: • Aromatase inhibitor • Aromatase inhibitor ± Tykerb® (lapatinib) • Fulvestrant (Faslodex®)	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
• Tamoxifen		
Aromatase inhibitor ± Tykerb (lapatinib)		
Perjeta® (pertuzumab) + Herceptin (trastuzumab) + either of the following: • Docetaxel • Paclitaxel		
Kadcyla® (ado-trastuzumab emtansine)	3.6 mg/kg IV every 3 weeks (21-day cycle)	3.6 mg/kg
Enhertu® (fam-trastruzumab-nxki)	5.4 mg/kg IV every 3 weeks	5.4 mg/kg
Herceptin (trastuzumab) + any of the following: • Paclitaxel ± carboplatin • Docetaxel • Vinorelbine • Xeloda® (capecitabine) • Tykerb (lapatinib)	Varies	Varies
Tykerb (lapatinib) + Xeloda (capecitabine)	Tykerb 1,250 mg PO QD days 1-21 + Xeloda 1,000 mg/m^2 PO BID days 1-14 (21-day cycle)	Tykerb 1,250 mg/day Xeloda 2,000 mg/m^2/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): left ventricular dysfunction; embryo-fetal toxicity

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Breast cancer	15 mg/kg IV every 3 weeks	15 mg/kg

VI. Product Availability

Single-dose vial: 250 mg/10 mL

VII. References

1. Margenza Prescribing Information. Rockville, MD: MacroGenics, Inc.; February 2025. Available at: www.margenza.com. Accessed November 6, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at http://www.nccn.org/professionals/drug_compendium. Accessed December 5, 2025.
3. National Comprehensive Cancer Network. Breast Cancer Version 5.2025. Available at:http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed December 5, 2025.

4. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed November 28, 2023.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9353	Injection, margetuximab-cmkb, 5 mg

Reviews, Revisions, and Approvals	Date
Policy created	01/2022
1Q 2023 annual review: no significant changes; references reviewed and updated.	01/2023
1Q 2024 annual review: updated HCPCS codes; references reviewed and updated.	01/2024
1Q 2025 annual review: added criteria for fourth-line use for recurrent unresectable disease and for patients with no response to preoperative systemic therapy to align with NCCN 2A recommendations; references reviewed and updated.	01/2025
1Q 2026 annual review: no significant changes; changed initial auth duration from 6 months to 12 months; references reviewed and updated.	01/2026