Clinical Policy: Margetuximab-cmkb (Margenza)

Reference Number: CP.PHAR.522
Effective Date: 03.01.21
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 health plans affiliated with Centene Corporation® 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 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 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*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Breast Cancer (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Margenza for a covered indication and has received this medication for at least 30 days;
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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

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 for all relevant lines of business 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®) • Tamoxifen	Varies	Varies
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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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.; May 2023. Available at: www.margenza.com. Accessed October 21, 2024.
2. National Comprehensive Cancer Network. Breast Cancer Version 6.2024. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed December 2, 2024.
3. 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	P&T Approval Date
Policy created	01.07.21	02.21
1Q 2022 annual review: added requirement for use in combination with chemotherapy per FDA label and NCCN recommendations; updated HCPCS codes; references reviewed and updated	11.20.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.03.22	
1Q 2023 annual review: no significant changes; references reviewed and updated.	11.15.22	02.23
1Q 2024 annual review: no significant changes; references reviewed and updated.	10.13.23	02.24
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.	12.02.24	02.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.