



Margenza™ (margetuximab-cmkb) (Intravenous)

-E-

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Margenza 250 mg single-dose vial: 7 vials every 21 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 350 billable units (1,750 mg) every 21 days

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria ¹

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
- Patient has human epidermal growth factor receptor 2 (HER2)-positive* disease; **AND**
- Used in combination with capecitabine, eribulin, gemcitabine, or vinorelbine; **AND**

Breast Cancer † ^{1,2,4,8}

- Patient has recurrent unresectable or metastatic disease; **AND**
- Used as fourth-line therapy and beyond; **AND**
- Patient has previously been treated with at least two (2) prior HER2-targeted regimens, at least one of which was used for metastatic disease

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA approved indication(s); ‡ Compendia Recommended Indication(s); ◊ Orphan Drug

***HER2-positive overexpression criteria: ^{4,5}**

- Immunohistochemistry (IHC) assay 3+; **OR**
- Dual-probe in situ hybridization (ISH) assay HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number ≥ 4.0 signals/cell; **OR**
- Dual-probe in situ hybridization (ISH) assay AND concurrent IHC indicating one of the following:
 - HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number < 4.0 signals/cell AND concurrent IHC 3+; **OR**
 - HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 6.0 signals/cell AND concurrent IHC 2+ or 3+; **OR**
 - HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 4.0 and < 6.0 signals/cell AND concurrent IHC 3+

IV. Renewal Criteria ¹

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: left ventricular dysfunction, infusion related reactions, etc.; **AND**
- Left ventricular ejection fraction (LVEF) obtained within the previous 3 months as follows:
 - LVEF is within the institutional normal limits, and has not had an absolute decrease of $\geq 16\%$ from pre-treatment baseline; **OR**
 - LVEF is below the institutional lower limits of normal (or $< 50\%$ if no limits are available), and has not had an absolute decrease of $\geq 10\%$ from pre-treatment baseline

V. Dosage/Administration ¹

| Indication | Dose |
|---------------|--|
| Breast Cancer | Administer 15 mg/kg as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity |

VI. Billing Code/Availability Information

HCP/PCS Code:

- J9353 – Injection, margetuximab-cmkb, 5 mg; 1 billable unit = 5 mg

NDC:

- Margenza 250 mg/10 mL single-dose vial: 74527-0022-xx

VII. References (STANDARD)

1. Margenza [package insert]. Rockville, MD; MacroGenics, Inc; December 2020. Accessed March 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) margetuximab. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2023.
3. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. *J Oncol Pract.* 2018 Mar;14(3):e130-e136.
4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer 3.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed March 2023.
5. Wolff AC, Hammond EH, Allison KH, et al. Human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. *J Clin Oncol* 2018;36:2105-2122.
6. Hematology/Oncology Pharmacy Association (2019). *Intravenous Cancer Drug Waste Issue Brief*. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf
7. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. *BMJ.* 2016 Feb 29;352:i788. No changes to the clinical criteria.
8. Rugo HS, Im SA, Shaw-Wright GL, et al. SOPHIA primary analysis: A phase 3 (P3) study of margetuximab (M) + chemotherapy (C) versus trastuzumab (T) + C in patients (pts) with HER2+ metastatic (met) breast cancer (MBC) after prior anti-HER2 therapies (Tx). *Journal of Clinical Oncology* 2019 37:15_suppl, 1000-1000.

VIII. References (ENHANCED)

- 1e. Modi S, Saura C, Yamashita T, et al. Trastuzumab Deruxtecan in Previously Treated HER2-Positive Breast Cancer. *N Engl J Med*. 2020 Feb 13;382(7):610-621. doi: 10.1056/NEJMoa1914510. Epub 2019 Dec 11.
- 2e. Murthy RK, Loi S, Okines A, et al. Tucatinib, Trastuzumab, and Capecitabine for HER2-Positive Metastatic Breast Cancer. *N Engl J Med*. 2020 Feb 13;382(7):597-609. doi: 10.1056/NEJMoa1914609. Epub 2019 Dec 11.
- 3e. Saura C, Oliveira M, Feng YH, et al. NALA Investigators. Neratinib Plus Capecitabine Versus Lapatinib Plus Capecitabine in HER2-Positive Metastatic Breast Cancer Previously Treated With ≥ 2 HER2-Directed Regimens: Phase III NALA Trial. *J Clin Oncol*. 2020 Sep 20;38(27):3138-3149. doi: 10.1200/JCO.20.00147. Epub 2020 Jul 17.
- 4e. Cameron D, Casey M, Oliva C, Newstat B, Imwalle B, Geyer CE. Lapatinib plus capecitabine in women with HER-2-positive advanced breast cancer: final survival analysis of a phase III randomized trial. *Oncologist*. 2010;15(9):924-934. doi:10.1634/theoncologist.2009-0181.
- 5e. Blackwell KL, Burstein HJ, Storniolo AM, et al. Overall survival benefit with lapatinib in combination with trastuzumab for patients with human epidermal growth factor receptor 2-positive metastatic breast cancer: final results from the EGF104900 Study. *J Clin Oncol*. 2012 Jul 20;30(21):2585-92.
- 6e. Magellan Health, Magellan Rx Management. Margenza Clinical Literature Review Analysis. Last updated March 2023. Accessed March 2023.

Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|---------|---|
| C50.011 | Malignant neoplasm of nipple and areola, right female breast |
| C50.012 | Malignant neoplasm of nipple and areola, left female breast |
| C50.019 | Malignant neoplasm of nipple and areola, unspecified female breast |
| C50.021 | Malignant neoplasm of nipple and areola, right male breast |
| C50.022 | Malignant neoplasm of nipple and areola, left male breast |
| C50.029 | Malignant neoplasm of nipple and areola, unspecified male breast |
| C50.111 | Malignant neoplasm of central portion of right female breast |
| C50.112 | Malignant neoplasm of central portion of left female breast |
| C50.119 | Malignant neoplasm of central portion of unspecified female breast |
| C50.121 | Malignant neoplasm of central portion of right male breast |
| C50.122 | Malignant neoplasm of central portion of left male breast |
| C50.129 | Malignant neoplasm of central portion of unspecified male breast |
| C50.211 | Malignant neoplasm of upper-inner quadrant of right female breast |
| C50.212 | Malignant neoplasm of upper-inner quadrant of left female breast |
| C50.219 | Malignant neoplasm of upper-inner quadrant of unspecified female breast |

MARGENZA™ -E- (margetuximab-cmkb) Prior Auth Criteria

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|---------|---|
| C50.221 | Malignant neoplasm of upper-inner quadrant of right male breast |
| C50.222 | Malignant neoplasm of upper-inner quadrant of left male breast |
| C50.229 | Malignant neoplasm of upper-inner quadrant of unspecified male breast |
| C50.311 | Malignant neoplasm of lower-inner quadrant of right female breast |
| C50.312 | Malignant neoplasm of lower-inner quadrant of left female breast |
| C50.319 | Malignant neoplasm of lower-inner quadrant of unspecified female breast |
| C50.321 | Malignant neoplasm of lower-inner quadrant of right male breast |
| C50.322 | Malignant neoplasm of lower-inner quadrant of left male breast |
| C50.329 | Malignant neoplasm of lower-inner quadrant of unspecified male breast |
| C50.411 | Malignant neoplasm of upper-outer quadrant of right female breast |
| C50.412 | Malignant neoplasm of upper-outer quadrant of left female breast |
| C50.419 | Malignant neoplasm of upper-outer quadrant of unspecified female breast |
| C50.421 | Malignant neoplasm of upper-outer quadrant of right male breast |
| C50.422 | Malignant neoplasm of upper-outer quadrant of left male breast |
| C50.429 | Malignant neoplasm of upper-outer quadrant of unspecified male breast |
| C50.511 | Malignant neoplasm of lower-outer quadrant of right female breast |
| C50.512 | Malignant neoplasm of lower-outer quadrant of left female breast |
| C50.519 | Malignant neoplasm of lower-outer quadrant of unspecified female breast |
| C50.521 | Malignant neoplasm of lower-outer quadrant of right male breast |
| C50.522 | Malignant neoplasm of lower-outer quadrant of left male breast |
| C50.529 | Malignant neoplasm of lower-outer quadrant of unspecified male breast |
| C50.611 | Malignant neoplasm of axillary tail of right female breast |
| C50.612 | Malignant neoplasm of axillary tail of left female breast |
| C50.619 | Malignant neoplasm of axillary tail of unspecified female breast |
| C50.621 | Malignant neoplasm of axillary tail of right male breast |
| C50.622 | Malignant neoplasm of axillary tail of left male breast |
| C50.629 | Malignant neoplasm of axillary tail of unspecified male breast |
| C50.811 | Malignant neoplasm of overlapping sites of right female breast |
| C50.812 | Malignant neoplasm of overlapping sites of left female breast |
| C50.819 | Malignant neoplasm of overlapping sites of unspecified female breast |
| C50.821 | Malignant neoplasm of overlapping sites of right male breast |
| C50.822 | Malignant neoplasm of overlapping sites of left male breast |
| C50.829 | Malignant neoplasm of overlapping sites of unspecified male breast |
| C50.911 | Malignant neoplasm of unspecified site of right female breast |
| C50.912 | Malignant neoplasm of unspecified site of left female breast |

| | |
|---------|---|
| C50.919 | Malignant neoplasm of unspecified site of unspecified female breast |
| C50.921 | Malignant neoplasm of unspecified site of right male breast |
| C50.922 | Malignant neoplasm of unspecified site of left male breast |
| C50.929 | Malignant neoplasm of unspecified site of unspecified male breast |

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|---|---|---|
| Jurisdiction | Applicable State/US Territory | Contractor |
| E (1) | CA, HI, NV, AS, GU, CNMI | Noridian Healthcare Solutions, LLC |
| F (2 & 3) | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC |
| 5 | KS, NE, IA, MO | Wisconsin Physicians Service Insurance Corp (WPS) |
| 6 | MN, WI, IL | National Government Services, Inc. (NGS) |
| H (4 & 7) | LA, AR, MS, TX, OK, CO, NM | Novitas Solutions, Inc. |
| 8 | MI, IN | Wisconsin Physicians Service Insurance Corp (WPS) |
| N (9) | FL, PR, VI | First Coast Service Options, Inc. |
| J (10) | TN, GA, AL | Palmetto GBA, LLC |
| M (11) | NC, SC, WV, VA (excluding below) | Palmetto GBA, LLC |
| L (12) | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc. |
| K (13 & 14) | NY, CT, MA, RI, VT, ME, NH | National Government Services, Inc. (NGS) |
| 15 | KY, OH | CGS Administrators, LLC |