Utilization Review Policy 248

POLICY: Oncology (Injectable) – Margenza Utilization Management Medical Policy
- Margenza® (margetuximab-cmkb intravenous infusion – MacroGenics)

EFFECTIVE DATE: 06/01/2021
LAST REVISION DATE: 02/19/2025

COVERAGE CRITERIA FOR: All UCare Plans

OVERVIEW

Margenza, a human epidermal growth factor receptor 2 (HER2)/neu receptor antagonist, in combination with chemotherapy, is indicated for the treatment of metastatic human epidermal growth factor receptor 2 (**HER2**)**-positive breast cancer** in adults who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease.[1]

Guidelines

The National Comprehensive Cancer Network (NCCN) breast cancer guidelines (version 1.2025 – January 31, 2025) recommend Margenza (category 2A) as a fourth-line and beyond treatment for recurrent unresectable (local or regional) or stage IV disease. Margenza should be used in combination with chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine). Other fourth-line and beyond therapies include trastuzumab + docetaxel or vinorelbine; trastuzumab + paclitaxel ± carboplatin; capecitabine + trastuzumab or lapatinib; trastuzumab + lapatinib (without cytotoxic therapy); trastuzumab + other chemotherapy agents; and Nerlynx® (neratinib tablets) + capecitabine (all category 2A). NCCN recommends the following therapies as first-line: Perjeta® (pertuzumab intravenous infusion) + trastuzumab + docetaxel (category 1; Preferred); and Perjeta + trastuzumab + paclitaxel (category 2A; Preferred). Enhertu® (fam-trastuzumab deruxtecan-nxki intravenous infusion) is the recommended therapy for second-line use (category 1; Preferred). Recommended third-line therapies are Tukysa® (tucatinib tablets) + trastuzumab + capecitabine (category 1; Preferred) or Kadcyla® (ado-trastuzumab emtansine intravenous infusion) [category 2A].

Safety

Margenza has a Boxed Warning regarding left ventricular dysfunction and embryo-fetal toxicity.[1] Margenza may lead to reductions in left ventricular ejection fraction; treatment should be discontinued for a confirmed clinically significant decrease in left ventricular function. Exposure to Margenza during pregnancy can cause embryo-fetal harm; patients should be advised of the risk and need for effective contraception.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Margenza. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case

basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Margenza as well as the monitoring required for adverse events and long-term efficacy, approval requires Margenza to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Margenza is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Breast Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, F, and G):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has recurrent or metastatic disease; AND
   - **C)** Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
   - **D)** Patient has tried at least three prior anti-HER2 regimens; AND
     Note: Some examples of anti-HER2 regimens are Perjeta (pertuzumab intravenous infusion) + trastuzumab + docetaxel, Perjeta + trastuzumab + paclitaxel, Kadcyla (ado-trastuzumab emtansine intravenous infusion), Enhertu (fam-trastuzumab deruxtecan-nxki intravenous infusion), Tukysa (tucatinib tablets) + trastuzumab + capecitabine, trastuzumab + lapatinib, trastuzumab + docetaxel, trastuzumab + vinorelbine, Nerlynx (neratinib tablets) + capecitabine.
   - **E)** At least one of the prior anti-HER2 regimens was used for metastatic disease; AND
   - **F)** The medication is used in combination with chemotherapy; AND
     Note: Examples of chemotherapy are capecitabine, eribulin, gemcitabine, vinorelbine.
   - **G)** The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 15 mg/kg administered as an intravenous infusion not more frequently than once every 3 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Margenza is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Margenza® intravenous infusion [prescribing information]. Rockville, MD: MacroGenics; May 2023.
2. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 1.2025 – January 31, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 16, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Breast Cancer.** The number of prior anti-HER2 regimens that the patient must try was changed from two to three regimens.	02/22/2023
Annual Revision	No criteria changes.	02/28/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
Annual Revision	No criteria changes.	02/19/2025