VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Kadcyla® (ado-trastuzumab emtansine for intravenous [IV] injection – Genentech, Inc.)

TAC APPROVAL DATE: 06/27/2018

OVERVIEW

Kadcyla, as a single agent, is indicated for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-positive, metastatic breast cancer who previously received Herceptin® (trastuzumab for intravenous [IV] infusion) and a taxane, separately or in combination.[1] Patients should have either received prior therapy for metastatic disease, or developed disease recurrence during or within 6 months of completing adjuvant therapy. Kadcyla is a HER2-targeted antibody-drug conjugate (ADC) which contains trastuzumab covalently linked to the microtubule inhibitory drug DM1 (a maytansine derivative) via the stable thioether linker MCC. Emtansine refers to the MCC-DM1 complex. The antibody trastuzumab is a well characterized recombinant monoclonal antibody product produced by mammalian (Chinese hamster ovary) cells, and the small molecule components (DM1 and MCC) are produced by chemical synthesis.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Kadcyla to recommend pharmacogenomic testing in patients with breast cancer to ensure patients have HER2-positive disease. All approvals are provided for 3 years in duration unless otherwise noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Breast Cancer that is Human Epidermal Growth Factor Receptor 2 (HER2)-Positive.** Approve for 3 years.

   The National Comprehensive Cancer Network (NCCN) breast cancer guidelines (version 1.2018) indicate that Kadcyla, as a single agent, is recommended for the treatment of patients with HER2-positive recurrent or Stage IV (M1) disease with symptomatic visceral disease or visceral crisis or that is hormone receptor-negative or hormone receptor-positive and endocrine therapy refractory.[2]

   In the pivotal Phase III study (EMILIA), eligible patients had documented progression of unresectable, locally advanced or metastatic HER2-positive breast cancer previously treated with a taxane and Herceptin.[1,3] Patients were randomized to receive Tykerb plus capecitabine or Kadcyla. Median progression-free survival (PFS) was 9.6 months with Kadcyla and 6.4 months with Tykerb plus capecitabine (hazard ratio [HR] 0.65; 95% confidence interval [CI]: 0.55, 0.77; $P < 0.0001$). Median overall survival was 30.9 months with Kadcyla and 25.1 months with Tykerb plus capecitabine (HR 0.682; 95% CI: 0.548, 0.849; $P = 0.0006$).

In one Phase III trial (MARIANNE), 1,095 patients with HER2-positive advanced breast cancer and no prior therapy for advanced disease were randomized to receive Herceptin plus a taxane, Kadcyla plus placebo, or Kadcyla plus Perjeta.[4] The primary end point was PFS. Kadcyla alone and Kadcyla plus Perjeta were non-inferior compared with Herceptin plus a taxane; median PFS was 13.7 months with Herceptin plus a taxane, 14.1 months with Kadcyla alone, and 15.2 months with Kadcyla plus Perjeta. Efficacy of Kadcyla was non-inferior but not superior to Herceptin plus a taxane.

Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for Kadcyla therapy because these were the only patients studied and for whom benefit has been shown.[1] Details on testing are reviewed in guidelines.[2,5] Treatment guidelines indicate that HER2-tumor status should be determined for all newly diagnosed invasive breast cancers and for first recurrences of breast cancer whenever possible if previously unknown or negative.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Kadcyla has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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. Kadcyla® for intravenous injection [prescribing information]. South San Francisco, CA: Genentech, Inc.; July 2016.
2. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (Version 1.2018 – March 20, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed June 22, 2018.
3. Verma S, Miles D, Gianni L, et al; for the EMILIA Study Group. Trastuzumab emtansine for HER2-positive advanced breast cancer. *N Engl J Med*. 2012;367:1783-1791.
4. Perez EA, Barrios C, Eiermann W, et al. Trastuzumab emtansine with or without pertuzumab versus trastuzumab plus taxane for human epidermal growth factor receptor 2-positive, advanced breast cancer: Primary results from the phase III MARIANNE study. *J Clin Oncol*. 2017;35(2):141-148.
5. Wolff AC, Hammond MEH, 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 May 30. [Epub ahead of print]

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	No changes to criteria.	04/06/2016
Annual revision	No changes to criteria.	05/24/2017
Annual revision	No changes to criteria.	06/27/2018

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx.