SmartHealth Ascension

Ado-Trastuzumab Emtansine

(Kadcyla®) J9354 (1 mg)

Covered with prior authorization

Requests for Kadcyla® (ado-trastuzumab emtansine) may be approved if the following criteria are met:

- Individual has a diagnosis of HER2-positive (HER2+) breast cancer (NCCN1) confirmed by one of the following:
  - Immunohistochemistry (IHC) is 3+; **OR**
  - A positive fluorescence in situ hybridization (FISH) test (ratio greater than 2.2)
  - In situ hybridization (ISH) positive; **OR**
  - Single-probe in situ hybridization (ISH) test with average HER2 copy number greater than or equal to 6.0 signals/cell; **OR**
  - Dual-probe ISH test: HER2/CEP17 (chromosome enumeration probe 17) ratio greater than or equal to 2.0; **OR**
  - HER2/CEP17 ratio less than 2.0 and average HER2 copy number greater than or equal to 6.0 signals/cell;
    AND
  - Used in one of the following ways:
    - Individual has early breast cancer; **AND**
      - Individual is using as a single agent; **AND**
      - Individual is using as adjuvant treatment of early non-metastatic breast cancer for residual invasive disease in the breast or axilla after surgery after receiving at least 6 cycles (16 weeks) of neoadjuvant therapy containing a taxane (with or without anthracycline) and trastuzumab (or trastuzumab biosimilars);

      OR
    - Individual has metastatic breast cancer disease; **AND**
      - Individual is using as a single agent; **AND**
      - Individual has previously received trastuzumab and a taxane, separately or in combination; **AND**
      - Individual has either received prior therapy for metastatic disease or developed disease recurrence during or within 6 months of completing adjuvant therapy;

OR

- Individual has a diagnosis of limited or extensive brain metastases with HER2-positive breast cancer; **AND**
  - Using as initial or primary treatment; **OR**
  - As treatment for recurrent/relapsed disease with stable systemic disease or reasonable systemic treatment options;

OR

- Individual has a diagnosis of recurrent HER2+ salivary gland tumors (NCCN 2A); **AND**

  - Individual has had prior anti-HER2+ therapy (e.g., trastuzumab) (Clinical judgment); **AND**
  - Using as single-agent systemic therapy.

OR

- Individual has a diagnosis of non small cell lung cancer; **AND**
  - Patient has ERBB2 (HER2) mutation positive disease as determined by an FDA-approved or CLIA-complaint test; **AND**
  - Patient has metastatic disease; **AND**
  - Patient has adenocarcinoma histology.

Requests for Kadcyla® (ado-trastuzumab emtansine) may **not** be approved if the above criteria are not met and for all other indications not included above.

Initial and renewal authorizations are for up to 12 months.

Annual reauthorizations will require medical chart documentation that the patient has been seen within the past 12 months and that markers of disease are improved by therapy.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Exclusion criteria:

- Kadcyla® (ado-trastuzumab emtansine) may not be approved when the above criteria are not met and for all other indications.
- Doses, durations, or dosing intervals that exceed FDA maximum limits for any FDA-approved indication or are not supported by industry-accepted practice guidelines or peer-reviewed literature for the relevant off-label use.
- Individuals with significant known risk factors unless the record provides an assessment of clinical benefit that outweighs the risk.
- When Kadcyla® is used in combination with other targeted biologic agents or chemotherapy agents.

U.S. Food and Drug Administration:
This section is to be used for informational purposes. FDA approval alone is not a basis for coverage. Kadcyla®, an antibody-drug conjugate (ADC) that utilizes the HER2- targeting properties of trastuzumab to selectively deliver chemotherapy to HER2- overexpressing tumor cells. This targeted approach minimizes toxicity by limiting exposure of DM1 to normal cells. Breast cancer is a type of tumor composed of malignant (cancerous) cells that start to grow in the breast and may spread (metastasize) to surrounding tissues and other areas of the body (American Cancer Society, 2016). Breast cancer is commonly treated by various modalities which include combinations of surgery, radiation therapy, chemotherapy and hormone therapy (National Cancer Institute, 2019). The prognosis and selection of therapies can be affected by

clinical and pathologic features of the tumor. One of these includes the human epidermal growth factor receptor 2 gene ERBB2 which is commonly referred to as HER2. Other names for this gene include NEU, Her-2, HER-2/neu and c-erb B2. Initially the HER2 gene was detected in frozen breast tumor samples. Amplification of the HER2 gene was later correlated to overexpression of protein levels in samples of breast cancer. The FDA approved indication for Kadcyla® includes use as a single agent to treat those with HER2-positive, metastatic breast cancer who previously received trastuzumab and/or taxane therapy, or had disease recurrence within 6 months of completing adjuvant therapy. The National Comprehensive Cancer Network (NCCN) provides additional recommendations with a category 2A level of evidence for the use of Kadcyla® as a preferred option for treatment of individuals with HER2-positive metastatic breast cancer that progresses on first-line trastuzumab-containing regimen. The guidelines do not recommend the use of Kadcyla® in the neoadjuvant setting. The updated NCCN guideline provides a category 1 recommendation for use of Kadcyla® as a preferred regimen as preferred adjuvant systemic therapy in individuals with HER2-positive tumors and locally advanced disease following completion of planned chemotherapy and following mastectomy or lumpectomy. NCCN also provides a level category 2A rating for Kadcyla's® use as single-agent therapy for recurrent or metastatic HER2-positive disease that is HR-negative or HR-positive. NCCN also provides a 2A recommendation for the use in limited or extensive brain metastases in those with HER2-positive breast cancer.

Other Uses

In the NCCN clinical practice guideline for Head and Neck cancers the NCCN Panel recommends the use of Kadcyla® at a category level 2A rating (previously level 2B rating) in certain circumstances as a single-agent, systemic therapy for HER2-positive-recurrent disease with distant metastases or unresectable locoregional recurrence or second primary with prior radiation therapy. At this time the guideline's discussion section updates are under progress and there are no published trials discussing the recommendation. There is one clinical study in progress under clinicaltrials.gov. In the NCCN clinical practice guideline for non-small cell lung cancer the NCCN Panel now recommends use of Kadcyla® (category 2A) in treatment of individuals with HER2 mutations in lung cancer based on recent unpublished data from a small phase 2 basket trial (Li, 2018). The NCCN guidelines for gastric cancer (2019) do not recommend the use of Kadcyla® to treat these cancer types. There is a lack of published data from large randomized controlled trials to demonstrate long-term efficacy and safety for these off-label uses. NCCN also provides a 2A recommendation for use in salivary gland tumors. The evidence comes from two basket trials for a total of 13 individuals. At this time, there is a lack of published data from large, randomized trials for both efficacy and safety for off-label use.

Key References Accessed 8/2022:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.

5. Li BT, Shen R, Buonocore D, et al. Ado-trastuzumab emtansine in patients with HER2 mutant lung cancers. Results from a phase II basket trial. J.Clin Oncol 2018:36:2532-2537.
6. NCCN Clinical Practice Guidelines in Oncology™. © 2021 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp.
    a. Breast Cancer. V2.2022. Revised December 20, 2021.
    b. Central Nervous System Cancer. V2.2021. Revised September 8, 2021. C
    c. Head and Neck Cancers. V1.2022. Revised December 8, 2021.
    d. Non-Small Cell Lung Cancer. V1.2022. Revised December 7, 2021.

Date	Summary of Changes
August 2022	Criteria for use summary developed by the Ascension Medical Specialty Prior Authorization Team.
September 2022	Criteria for use summary approved by the Ascension Ambulatory Care Expert Review Panel.
October 2022	Criteria for use summary approved by the Ascension Therapeutic Affinity Group.

If you have questions, call 833-980-2352 to speak to a member of the Ascension Rx prior authorization team or, email your questions to smarthealthspecialty@ascension.org.