ado-trastuzumab emtansine (Kadcyla®)

Prior Authorization Drug Coverage Policy

Effective Date: 9/1/2020
Revision Date: n/a
Review Date: 10/4/2021
Lines of Business: Commercial
Policy type: Prior Authorization

This Drug Coverage Policy provides parameters for the coverage of ado-trastuzumab emtansine. Consideration of medically necessary indications are based upon U.S. Food and Drug Administration (FDA) indications, recommended uses within the Centers of Medicare & Medicaid Services (CMS) five recognized compendia, including the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium (Category 1 or 2A recommendations), and peer-reviewed scientific literature eligible for coverage according to the CMS, Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 titled, "Off-Label Use of Anti-Cancer Drugs and Biologics." This policy evaluates whether the drug therapy is proven to be effective based on published evidence-based medicine.

Drug Description[1]

Ado-trastuzumab emtansine is a HER2-targeted antibody-drug conjugate. The antibody is the humanized anti-HER2 IgG1, trastuzumab. The small molecule cytotoxin, DM1, is a microtubule inhibitor. Upon binding to sub-domain IV of the HER2 receptor, ado-trastuzumab emtansine undergoes receptor-mediated internalization and subsequent lysosomal degradation, resulting in intracellular release of DM1-containing cytotoxic catabolites. Binding of DM1 to tubulin disrupts microtubule networks in the cell, which results in cell cycle arrest and apoptotic cell death. In addition, in vitro studies have shown that similar to trastuzumab, ado-trastuzumab emtansine inhibits HER2 receptor signaling, mediates antibody-dependent cell-mediated cytotoxicity and inhibits shedding of the HER2 extracellular domain in human breast cancer cells that overexpress HER2.

FDA Indications[1]

ado-trastuzumab emtansine is FDA indicated for the following:

- ado-trastuzumab emtansine is a HER2-targeted antibody and microtubule inhibitor conjugate indicated, as a single agent for:
    - The treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination, Patients should have either:
        - received prior therapy for metastatic disease, ***OR***

        - developed disease recurrence during or within six months of completing adjuvant therapy.
    - The adjuvant treatment of patients with HER2-positive early breast cancer who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment.

NCCN Compendium Supported Indications[2]

- Head and Neck Cancer (Salivary Gland Tumors)
- Non-small Cell Lung Cancer

Coverage Determinations[1,2]

ado-trastuzumab emtansine will require prior authorization. This agent is considered medically necessary for the following oncology indications if all criteria below are met:

Breast Cancer

- The member will have a diagnosis of Metastatic HER2- Positive Breast Cancer (MBC), **AND**
    - ado-trastuzumab emtansine will be given as single agent therapy, **AND**
    - Member will have previously received trastuzumab and a taxane, separately or in combination, **AND**
    - Member received prior therapy for metastatic disease or developed disease recurrence during or within six months of completing adjuvant therapy, ***OR***
- The member will have a diagnosis of Early Breast Cancer (EBC) HER2-positive, **AND**
    - ado-trastuzumab emtansine will be given as single agent therapy, **AND**
    - Member experiences residual invasive disease after receiving neoadjuvant taxane and trastuzumab-based treatment, ***OR***
- The member will receive ado-trastuzumab emtansine as adjuvant systemic therapy for HER2-positive invasive breast cancer and ANY of the following clinical stages:
    - T1-3, N0-1, M0; OR
    - T0-3, N1, M0 disease; ***OR***
    - Any of the locally advanced clinical stages following completion of planned chemotherapy if residual disease are preoperative therapy:
        - T0-4, N1-3, M0; OR
        - T2-4, N0, M0; OR
- ado-trastuzumab emtansine will be given as single agent therapy for recurrent or stage IV HER2-positive invasive breast cancer for either hormone receptor negative or hormone receptor positive disease.

Recommended dose: 3.6 mg/kg given as in intravenous infusion every 21 days until disease progression or unacceptable toxicity, or a total of 14 cycles for patients with EBC.

Head and Neck Cancers – Salivary Gland Tumors

- The member must have diagnosis of recurrent, unresectable, or metastatic salivary gland tumors **AND**
- ado-trastuzumab emtansine will be given as single agent therapy, **AND**
- The tumor must express HER2-positive mutations.

Recommended dose: 3.6 mg/kg given as intravenous infusion every 21 days until disease progression or unacceptable toxicity.

Non-Small Cell Lung Cancer (NSCLC)

- The member must have diagnosis of non-small cell lung cancer, **AND**
- ado-trastuzumab emtansine will be given as single agent therapy, **AND**
- The tumor must express HER2-positive mutations.

Recommended dose: 3.6 mg/kg given as intravenous infusion every 21 days until disease progression or unacceptable toxicity.

All indications:

- ado-trastuzumab emtansine will be approved through clinical review for up to a 12-month duration

Coverage Limitations

Treatment with a is azo-trastuzumab emtansine will not considered medically necessary for members with the following concomitant conditions:

- The member will not receive a dose higher than 3.6 mg/kg.
- The member has experienced disease progression on ado-trastuzumab.
- Indications not supported by NCCN category 2A or higher recommendations may not be considered medically necessary

Contraindications/Warnings/Precautions[1]

- There are no contraindications listed in the US manufacturer's labeling.
- Warnings/precautions:
    - Pulmonary toxicity
    - Hepatotoxicity
    - Reductions in left ventricular ejection fraction
    - Infusion-Related Reactions
    - Embryo-Fetal Toxicity

For specific recommendations on contraindications, warnings and precautions, patient monitoring, and on dose adjustments and discontinuation, please refer to the current prescribing information.

Billing

- Description: ado-trastuzumab emtansine, 1 mg
  - J9354

Disclaimer

Drug Coverage Policies are developed as needed, regularly reviewed, updated at least annually, and are subject to change. Other policies and coverage determination guidelines may apply. Federal and state regulatory requirements and member specific benefit plan documents, if applicable, must be reviewed prior to this Drug Coverage Policy. This Drug Coverage Policy is for informational purposes only and does not constitute medical advice or dictate how providers should practice medicine. This policy should not be reproduced, stored in a retrieval system, or altered from its original form without written permission from Oncology Analytics, Inc.

References

1. Kadcyla [package insert]. Genentech, Inc., South San Francisco, CA. Available at: https://www.gene.com/download/pdf/kadcyla_prescribing.pdf
2. ado-trastuzumab emtansine. NCCN Drugs & Biologics Compendium. Available at https://www.nccn.org/professionals/drug_compendium/content/
3. von Minckwitz, G, Huang, C, Mano, MS, et al. Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer. N Engl J Med. 2019 Feb 14;380(7):617-628.
4. Dieras, V, ;18(6)Miles, Miles, D, Verma, S, et al. Trastuzumab Emtansine Verses Capecitabine Plus Lapatinib in Patients With Previously Treated HER2-positive Advanced Breast Cancer (EMILIA): A Descriptive Analysis of Final Overall Survival Results From a Randomised, Open-Label, Phase 3 Trial. Lancet Oncol. 2017 Jun;18(6):732-742.