Clinical Policy Title:	ado-trastuzumab emtansine
Policy Number:	RxA.179
Drug(s) Applied:	Kadcyla®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Kadcyla® is a human epidermal growth factor receptor 2 protein (HER2)-targeted antibody and microtubule inhibitor conjugate. It is indicated as a single agent for the:

- Adjuvant treatment of patients with HER2-positive early breast cancer who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment.
- 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
ado-trastuzumab emtansine (Kadcyla®)	Breast cancer	Adjuvant therapy for early breast cancer with residual disease 3.6 mg/kg IV Q3WK (21-day cycle) for a total of 14 cycles unless there is disease recurrence or unmanageable toxicity. Metastatic breast cancer 3.6 mg/kg IV Q3WK (21-day cycle) until disease progression or unmanageable toxicity.	3.6 mg/kg

Dosage Forms

- Single-use vial: 100 mg, 160 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Breast Cancer (must meet all)**:**

1. Diagnosis of HER2-positive breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as a single-agent therapy;
5. Documentation of prior use of trastuzumab-based therapy and a taxane;
6. Request meets one of the following (a, b, or c):
   a. As adjuvant: Dose does not exceed 3.6 mg/kg every 21 days for a maximum of 14 doses;
   b. For metastatic: Dose does not exceed 3.6 mg/kg every 21 days;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Non-Small Cell Lung Cancer (off-label) (must meet all)**:**

1. Diagnosis of HER2-positive non-small cell lung cancer (NSCLC);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 3.6 mg/kg every 21 days;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

C. Head and Neck Cancers - Salivary Gland Tumors (off-label) (must meet all)**:**

1. Diagnosis of HER2-positive Salivary Gland Tumor;
2. Useful in certain circumstances as single-agent systemic therapy for human epidermal growth factor receptor 2 (HER2)-positive recurrent disease with (a or b):
   a. Distant metastases in patients with a performance status (PS) of 0-3;
3. Unresectable locoregional recurrence or second primary with prior radiation therapy.
4. Prescribed by or in consultation with an oncologist;
5. Age ≥ 18 years;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 3.6 mg/kg every 21 days;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration

Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. As adjuvant for breast cancer: New dose does not exceed 3.6 mg/kg every 21 days for a maximum of 14 doses;
   b. For metastatic breast cancer or NSCLC or Salivary Gland Tumor (SG: New dose does not exceed 3.6 mg/kg every 21 days;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval Duration
Commercial: 6 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HER2: Human Epidermal Growth Factor Receptor 2 Protein
NSCLC: Non-Small Cell Lung Cancer
LVEF: Left Ventricular Ejection Fraction

APPENDIX B: Therapeutic Alternatives
Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - Hepatotoxicity, liver failure and death have occurred in Kadcyla®-treated patients. Monitor hepatic function prior to initiation and prior to each dose. Institute dose modifications or permanently discontinue as appropriate.
  - Kadcyla® may lead to reductions in left ventricular ejection fraction (LVEF). Assess LVEF prior to initiation. Monitor and withhold dosing or discontinue as appropriate.
  - Embryo-Fetal Toxicity: Exposure to Kadcyla® during pregnancy can result in embryo-fetal harm. Advise patients of these risks and the need for effective contraception.

APPENDIX D: General Information

- Pulmonary Toxicity: Permanently discontinue Kadcyla® in patients diagnosed with interstitial lung disease or pneumonitis. For patients with radiation pneumonitis in the adjuvant setting, permanently discontinue Kadcyla® for Grade ≥ 3 or for Grade 2 not responding to standard treatment.
- Infusion-Related Reactions, Hypersensitivity Reactions: Monitor for signs and symptoms during and after

infusion. If significant infusion related reactions or hypersensitivity reactions occur, slow or interrupt the infusion and administer appropriate medical therapies.

- Hemorrhage: Fatal cases of hemorrhage occurred in clinical trials among patients with no known identified risk factors, as well as among patients with thrombocytopenia and those receiving anti-coagulation and antiplatelet therapy.

References

1. Kadcyla® Prescribing Information. South San Francisco, CA: Genentech, Inc.; September 2020. Available at: https://www.gene.com/download/pdf/kadcyla_prescribing.pdf . Accessed March 01, 2021.
2. Minckwitz GV, Huang CS, Mano MS, et al. Trastuzumab emtansine for residual invasive HER2-positive breast cancer. N Engl J Med 2019; 380:617-28. Available at: Accessed March 01, 2021.
3. Correa TS, Matos GD, Segura M, Dos Anjos CH. Second-line treatment of HER2-positive salivary gland tumor: ado-trastuzumab emtansine (T-DM1) after progression on trastuzumab. Case reports in oncology. 2018;11(2):252-7.
4. Li BT, Shen R, Offin M, Buonocore DJ, Myers ML, Venkatesh A, Razavi P, Ginsberg MS, Ulaner GA, Solit DB, Hyman DM. Ado-trastuzumab emtansine in patients with HER2 amplified salivary gland cancers (SGCs): Results from a phase II basket trial. Available at: https://ascopubs.org/doi/abs/10.1200/JCO.2019.37.15_suppl.6001. Accessed March 01, 2021.
5. National Comprehensive Cancer Network. Head and Neck Cancers Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed March 01, 2021.
6. National Comprehensive Cancer Network. Breast Cancer Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed March 01, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 2. Initial Therapy Criteria Approval duration updated to 6 months for Commercial, Added MEDICAID-6 months 3. Continued Therapy Approval Duration updated to 6 months for Commercial and Added MEDICAID-12 months 4. Reference reviewed and updated	06/19/2020	09/14/2020
Policy was reviewed: 1. Initial approval criteria updated for new off label indication “Head and Neck	03/01/2021	06/10/2021

Cancers - Salivary Gland Tumors". 2. Continued Therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 3. Continued Therapy approval criteria II.A.3.b updated for indication "Salivary Gland Tumors". 4. Appendix C: box warning was updated to "Hepatotoxicity, liver failure and death have occurred and Embryo-Fetal Toxicity…" 5. Appendix D added to policy. 6. References were reviewed and updated		