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5.21.032

Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	April 15, 2013
Subject:	Kadcyla	**Page:**	1 of 6

Last Review Date: June 13, 2024

Kadcyla

Description

Kadcyla (ado-trastuzumab emtansine)

Background
Kadcyla (ado-trastuzumab emtansine) is indicated for HER2-positive breast cancer. Kadcyla is a monoclonal antibody that targets and inhibits HER-2 receptor signaling. Kadcyla inhibits shedding of the HER2 extracellular domain in human breast cancer cells that overexpress HER2. Kadcyla binds to HER-2 receptors and undergoes internalization, which in turn releases cytotoxic catabolites that disrupt microtubule networks in the cell resulting in cell cycle arrest and apoptotic cell death (1).

Regulatory Status
FDA-approved indications:
Kadcyla 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 6 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 (1).

Kadcyla has a boxed warning citing the risk of hepatotoxicity, cardiac toxicity, and embryo-fetal toxicity. Serious hepatotoxicity has been reported, including liver failure and death in patients treated with Kadcyla. Serum transaminases and bilirubin levels should be obtained prior to initiation of treatment and prior to each dose. Kadcyla administration may lead to reductions in left ventricular ejection fraction (LVEF). Patients should be evaluated for left ventricular ejection fraction prior to and during treatment with Kadcyla (1).

Kadcyla can result in embryo-fetal harm when administered during pregnancy. Female patients of reproductive potential should be advised to use effective contraception during treatment and for 7 months following the last dose. Because of the potential for genotoxicity, male patients with female partners of reproductive potential should be advised to use effective contraception during treatment with Kadcyla and for 4 months following the last dose (1).

Kadcyla has warnings and precautions regarding pulmonary toxicity, infusion related reactions, hypersensitivity reactions, hemorrhage, thrombocytopenia, and neurotoxicity. Kadcyla should be discontinued in patients who develop interstitial lung disease (ILD) or pneumonitis. Kadcyla may cause thrombocytopenia and platelet counts should be monitored prior to initiation of therapy and prior to each dose (1).

Treatment with Kadcyla has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity. Treatment with Kadcyla is not recommended for these patients. Patients should be observed closely for IRR reactions, especially during the first infusion (1).

Safety and effectiveness in pediatric patients have not been established (1).

Related policies
Enhertu, Herceptin Hylecta, Margenza, Nerlynx, Perjeta, Phesgo, Trastuzumab, Tukysa, Tykerb

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Kadcyla may be considered **medically necessary** if the conditions indicated below are met.

Kadcyla may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have **ONE** of the following:

1. HER2-positive metastatic breast cancer
    a. Received prior therapy with trastuzumab or trastuzumab with a taxane **OR**
    b. Developed disease recurrence during or within six months of completing adjuvant therapy
2. HER2-positive early breast cancer
    a. Patient has residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment

AND ALL of the following:

a. Hepatic function and platelet counts monitored prior to initiation and prior to receiving each dose
b. Left ventricular ejection fraction (LVEF) monitored prior to initiation and every three months or more frequently as clinically indicated during treatment
c. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment and for 7 months after the last dose
d. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment and for 4 months after the last dose
e. Prescriber agrees to monitor for pulmonary toxicity

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. HER2-positive breast cancer

AND ALL of the following:

a. Patient has not been diagnosed with nodular regenerative hyperplasia (NRH)
b. Hepatic function and platelet count monitored prior to each dose
c. Left ventricular ejection fraction (LVEF) monitored every three months or more frequently as clinically indicated during treatment
d. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment and for 7 months after the last dose
e. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment and for 4 months after the last dose
f. Prescriber agrees to monitor for pulmonary toxicity

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Kadcyla (ado-trastuzumab emtansine) is indicated for HER2-positive breast cancer. Kadcyla is a monoclonal antibody that inhibits the HER2 receptor signaling and mediates antibody-dependent cell-mediated cytotoxicity. This inhibits the shedding of the HER2 extracellular domain in overexpressing HER2 breast cancer cells. Kadcyla carries a boxed warning citing the risk of hepatotoxicity, cardiac toxicity, and embryo-fetal toxicity. Kadcyla has warnings and precautions regarding pulmonary toxicity, infusion related reactions, hypersensitivity reactions, hemorrhage, thrombocytopenia, and neurotoxicity. The safety and efficacy of Kadcyla in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Kadcyla while maintaining optimal therapeutic outcomes.

References

1. Kadcyla [package insert]. San Francisco, CA: Genentech, Inc.; February 2022.
2. NCCN Drugs & Biologics Compendium® Ado-trastuzumab emtansine 2024. National Comprehensive Cancer Network, Inc. Accessed on May 3, 2024.

Policy History

Date	Action
March 2013	Addition to PA
June 2013	Clarified language in the Policy and Prior Approval Requirement Section
September 2014	Annual editorial review and reference update Removed weight-based dosing, do not substitute with trastuzumab and serum Transaminases and bilirubin limits
June 2015	Annual editorial review and reference update
June 2016	Annual editorial review and reference update Policy code changed from 5.04.32 to 5.21.32
June 2017	Annual editorial review and reference update Addition of age limit to renewal requirements
June 2018	Annual editorial review and reference update
May 2019	Addition of indication: HER2-positive early breast cancer. Addition of requirements for monitoring for pulmonary toxicity and embryo-fetal toxicity
June 2019	Annual review
December 2019	Annual review
March 2020	Annual review and reference update
June 2020	Annual review
September 2020	Annual review
December 2020	Annual review and reference update
June 2021	Annual editorial review and reference update
June 2022	Annual review and reference update
November 2022	Revised requirement for LVEF monitoring every 3 months or more frequently as clinically indicated, rather than before each dose. Reworded contraception requirement for consistency. Changed policy number to 5.21.032
December 2022	Annual review and reference update
June 2023	Annual review and reference update
June 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.