BlueCross BlueShield Federal Employee Program

KADCYLA
(ado-trastuzumab emtansine)

RATIONALE FOR INCLUSION IN PA PROGRAM

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).

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 2025. National Comprehensive Cancer Network, Inc. Accessed on January 24, 2025.