

# Genentech

*A Member of the Roche Group*

1 DNA Way  
South San Francisco, CA 94080  
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## Important Drug Information

**KADCYLA™ (ado-trastuzumab emtansine) 100 mg (NDC 50242-088-01)  
and  
KADCYLA™ (ado-trastuzumab emtansine) 160 mg (NDC 50242-087-01)**

Dear Pharmacist:

**Subject: KADCYLA (ado-trastuzumab emtansine) error on the carton**

This communication is to inform you that there is an error on the carton for both the 100 mg and 160 mg vial configurations of KADCYLA. The wording on the carton "Do not use if vacuum does not draw diluent into the vial" was included in error. This error is located only on the carton and is not found within the KADCYLA Package Insert. For complete and accurate instructions on how to reconstitute, dilute, and administer KADCYLA, please see Section 2.3 of the Package Insert.

KADCYLA vials are manufactured under a partial vacuum, which may or may not pull diluent into the vial during reconstitution. Diluent should be slowly injected into the vial. Absence of a vacuum strong enough to draw some or all of the Sterile Water For Injection (SWFI) into the vial is **not** an indication that the vial is defective or that the drug product is compromised. Genentech is working diligently with the FDA to revise this statement on the carton to reduce confusion and to ensure that KADCYLA is available to appropriate patients.

### Background

KADCYLA vials are manufactured with a slight vacuum to ensure that the stopper is properly sealed prior to capping. The vacuum level has **not** been designed to draw diluent into the vial during reconstitution. This does **not** indicate that the vial is defective.

### Instructions for Reconstitution

If the diluent is not spontaneously drawn into the vial, or if some but not all of the diluent is drawn in, reconstitution should be performed by depressing the plunger to introduce the required quantity of SWFI. Once the indicated amount of SWFI is in the vial, complete the preparation and administration process by following the remaining instructions in the KADCYLA Package Insert (Section 2.3).

**Please ensure all staff involved in the reconstitution and administration of KADCYLA receives a copy of this letter and reviews Section 2.3 of the Package Insert for appropriate instructions.**

Genentech encourages the reporting of adverse events expeditiously. To report adverse events, product quality complaints, or to request medical information related to KADCYLA, please contact Genentech Medical Communications at (800) 821-8590 (5:30 AM - 4:00 PM PST, M-F).

We will continue to work diligently to correct this error and ensure that KADCYLA is available to appropriate patients. For ongoing updates on KADCYLA, please visit **KADCYLA.com**. We appreciate your assistance in this matter and apologize for any inconvenience.

Sincerely,



Anthony Hurley  
Vice President, Head of Quality Biologics Drug Product  
Genentech, Inc.

**Please see following page for approved indication and Important Safety Information, including Boxed WARNINGS.**

## Indication

KADCYLA™ (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) 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

## Important Safety Information

### Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

### The following additional serious adverse reactions have been reported in clinical trials with KADCYLA:

- Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis
- Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR
- Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate
- Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to  $\leq$  Grade 2
- Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration

### Additional Important Safety Information:

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy
- Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother
- The most common adverse drug reactions (frequency  $>$  25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or calling 1-800-FDA-1088.