(b) (4)

NDC 50242-088-01

Kadcyla™

(ado-trastuzumab emtansine)
For Injection

100 mg per vial

1 vial

Single-Dose Vial
KEEP REFRIGERATED

Genentech

Reconstitution, dosage, and administration: For single-use only. See enclosed full prescribing information for reconstitution. The vial is 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. Reconstitution with 5 mL Sterile Water for Injection, USP, yields a solution containing 20 mg/mL Kadcyla. Each reconstituted vial will deliver 100 mg of Kadcyla.

Reconstitute immediately before use.

Discard any unused solution.

DO NOT SHAKE.

Storage: Store at 2°C – 8°C (36°F – 46°F) prior to reconstitution.

Made in Switzerland

Manufactured by:
Genentech, Inc.
A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080-4990
US License No.: 1048

50242 08801 5

Contents: One single-use vial of Kadcyla containing 100 mg trastuzumab emtansine in 10 mM sodium succinate, 6% (w/v) sucrose, and 0.02% (w/v) polysorbate 20, pH 5.0. No preservative. Diluent is not provided. No U.S. standard of potency.

KEEP REFRIGERATED

10139360

LOT:
EXP:

NDC 50242-088-01

Kadcyla™

(ado-trastuzumab emtansine)
For Injection

100 mg per vial

For Intravenous Infusion Only
Reconstitute and Dilute prior to administration
Single-Dose Vial – Discard Unused Portion

KEEP REFRIGERATED

1 vial

℞ only

Genentech

10139360

(b) (4)

NDC 50242-087-01

Kadcyla™

(ado-trastuzumab emtansine)
For Injection

160 mg per vial

1 vial

Single-Dose Vial
KEEP REFRIGERATED

Genentech

Reconstitution, dosage, and administration:
For single-use only. For intravenous administration only. See enclosed full prescribing information for reconstitution. The vial is 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. Reconstitution with 8 mL Sterile Water for Injection, USP, yields a solution containing 20 mg/mL Kadcyla. Each reconstituted vial will deliver 160 mg of Kadcyla.

Reconstitute immediately before use.
Discard any unused solution.

DO NOT SHAKE.

Storage: Store at 2°C – 8°C (36°F – 46°F) prior to reconstitution.

Made in Switzerland
Manufactured by:
Genentech, Inc.
A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080-4990
US License No.: 1048

50242 08701 8

LOT:
EXP:

NDC 50242-087-01

Kadcyla™

(ado-trastuzumab emtansine)
For Injection

160 mg per vial

For Intravenous Infusion Only
Reconstitute and Dilute prior to administration
Single-Dose Vial – Discard Unused Portion

KEEP REFRIGERATED

1 vial

Rx only
Genentech

10139361

Contents: One single-use vial of Kadcyla containing 160 mg trastuzumab emtansine in 10 mM sodium succinate, 6% (w/v) sucrose, and 0.02% (w/v) polysorbate 20, pH 5.0. No preservative. Diluent is not provided. No U.S. standard of potency.

KEEP REFRIGERATED

10139361

Genentech
A Member of the Roche Group

1 DNA Way
South San Francisco, CA 94080
May 13, 2013

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.

Genentech
A Member of the Roche Group

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 ≤ 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 or calling 1-800-FDA-1088.

Genentech
A Member of the Roche Group

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

KATHLEEN A CLOUSE STREBEL
08/29/2013