

### Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab-related infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment should be interrupted for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 14.5% and 3.3%, respectively.
- KADCYLA treatment should be interrupted in patients with severe IRR and/or a life-threatening IRR. Patients should be closely monitored for IRR reactions.

### Thrombocytopenia

- In EMILIA, the incidence of  $\geq$  Grade 3 thrombocytopenia was 14.5% in the KADCYLA group and 3.3% in the comparator group (overall incidence 31.2% and 3.3%, respectively).
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA infusion. Modify KADCYLA dose or delay KADCYLA administration as appropriate.

### Neurotoxicity

- In EMILIA, the incidence of  $\geq$  Grade 3 peripheral neuropathy was 2.2% in the KADCYLA group and 13.5% in the comparator group (overall incidence 21.2% and 13.5%, respectively).
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to  $\leq$  Grade 2.

### HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency.

### Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been reported. The infusion site should be closely monitored for possible subcutaneous infiltration. Specific treatment for KADCYLA extravasation is unknown.

### Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the benefits and risks to the mother and child.

### Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency  $>$  25%) were musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and fatigue. The most common NCI-CTCAE (version 3)  $\geq$  Grade 3 ADRs (frequency  $>$  2%) were thrombocytopenia, transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue.

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech at 1-800-438-2555. You may contact the FDA by visiting [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or calling 1-800-FDA-1088.

Click here for full [Prescribing Information](#) for additional important safety information and **WARNINGS**.

Reference: 1. KADCYLA Prescribing Information. Genentech, Inc. May 2013.

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From Reuters Health Information

## US Gives States Flexibility on

By Alina Selyukh and Anna Yukhananov

WASHINGTON (Reuters) Jul 11 - The Obama adm

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The proposal calls for the exchanges to operate spe

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INFORMATION FROM INDUSTRY



**KADCYLA<sup>®</sup> (ado-trastuzumab emtansine) v**  
**maintain the HER2 suppression and antica**  
**trastuzumab and to provide the cytotoxic**

Learn the full MOA story on KADCYLA

#### Indication

KADCYLA<sup>®</sup> (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, sep  
have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuva

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## INFORMATION FROM INDUSTRY

KADCYLA<sup>®</sup> (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separate from each other, and who have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy.

## Proposed mechanism of action, based on preclinical data

### 1 HER2 binding

KADCYLA selectively binds to HER2 receptor at subdomain IV

### 2 Trastuzumab activities

- Inhibits HER2 receptor signaling
- Triggers the ADCC immune response
- Inhibits HER2 shedding

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**3 Internalization**  
Once bound, the KADCYLA/HER2 receptor complex is internalized via endocytosis

**4 DM1\* release**  
is degraded inside the tumor to release DM1

**5 DM1\* cytotoxicity**  
DM1 binds to microtubules and inhibits their polymerization, causing cell-cycle arre  
and cell death

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ADCC=antibody-dependent cell-mediated cytotoxicity.

\*Cytotoxic DM1-containing catabolites (primarily lysine-bound emtansine).

## 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. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases.
- **Cardiac Toxicity:** KADCYLA administration may lead to reductions in left ventricular function in all patients prior to and during treatment with KADCYLA. Monitor for decrease in left ventricular function.
- **Embryo-Fetal Toxicity:** Exposure to KADCYLA can result in embryo-fetal death or malformations and the need for effective contraception.

## Additional Important Safety Information

## Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD was observed in 10.3% in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVD is observed.

## Pregnancy Registry

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