Genentech
A Member of the Roche Group

IMPORTANT DRUG WARNING

Subject: Direct Healthcare Professional Communication on Cases of Severe Hemorrhage Reported with Kadcyla® (ado-trastuzumab emtansine)

November 2013

Dear Healthcare Provider,

Genentech, a member of the Roche Group, would like to inform you of the following important safety information:

Summary

- Severe hemorrhage with fatal outcomes including central nervous system bleeding has been reported in patients receiving Kadcyla.
- Kadcyla should be used with caution in patients with thrombocytopenia. Please refer to the prescribing information for management of decreased platelet count.
- Anti-coagulation therapy and anti-platelet agents may increase the risk of bleeding. Avoidance of these agents, or additional monitoring with concomitant use, may be indicated.

You are advised to discuss the risks that may be associated with Kadcyla therapy with patients and their caregivers.

Genentech is working closely with health authorities to update the product label.

Further information on the safety concern

Kadcyla, as a single agent, is indicated 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 six months of completing adjuvant therapy.

Current prescribing information for Kadcyla (based on data from the 884 patients included in clinical trials) contains information in the "WARNINGS AND PRECAUTIONS" section stating that Kadcyla may cause thrombocytopenia and the incidence of severe hemorrhagic events in patients treated with

Kadcyla was low. However, new data (from more than 4,200 patients exposed to Kadcyla in the clinical trial setting only) showed that some of the severe bleeding events, including central nervous system hemorrhage, resulted in fatal outcome. In some of the observed cases, the patients were also receiving anti-coagulation therapy or anti-platelet agents. Based on these findings, the Kadcyla prescribing information will be updated.

Call for Reporting

Healthcare professionals should report any serious adverse events suspected to be associated with the use of Kadcyla to: Genentech at 1-888-835-2555. Alternatively, this information may be reported to FDA's MedWatch reporting system by phone (1-800-FDA-1088), by facsimile (1-800-FDA-0178), online (https://www.accessdata.fda.gov/scripts/medwatch/) or mailed, using the MedWatch form FDA 3500, to the FDA Medical Products Reporting Program, 5600 Fishers Lane, Rockville, MD 20852-9787.

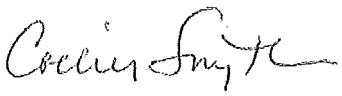
Company Contact Point

Should you have any questions regarding the use of Kadcyla, please feel free to contact us at: Genentech Medical Information/Communications Department at 1-800-821-8590.

The important safety information in this letter is not comprehensive. Please refer to the full Prescribing Information.

Yours sincerely,

Genentech, a Member of the Roche Group



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