Genentech
A Member of the Roche Group

February 22, 2013

Submission Request
c/o Joan McClure
National Comprehensive Cancer Network (NCCN)
275 Commerce Dr, Suite 300
Fort Washington, PA 19034

Dear Ms. McClure:

Enclosed are copies of the Kadcyla™ (ado-trastuzumab emtansine) prescribing information and the corresponding pivotal trial publication in *New England Journal of Medicine* for your product information updating needs. Genentech, Inc. received approval for Kadcyla on February 22, 2013.

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 (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

Kadcyla was approved based on results of a randomized, international, multicenter, 2-arm, open-label, Phase III study (EMILIA), which evaluated the safety and efficacy of Kadcyla compared with lapatinib plus capecitabine in locally advanced breast cancer (LABC) and MBC HER2-positive patients.[1,2] Kadcyla demonstrated a statistically significant improvement in both primary endpoints of progression free survival (PFS) and overall survival (OS). Data on patient-reported outcomes from the EMILA study were also presented at a recent congress meeting.[3] The most common adverse drug reactions (frequency >25%) with Kadcyla were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased tranasminases, and constipation.[4]

Please be aware of a potential name confusion between ado-trastuzumab emtansine (Kadcyla) and trastuzumab (Herceptin®). Kadcyla should not be substituted for or with trastuzumab.

Additional Phase II data is available for previously treated[5,6] and previously untreated patients[7] with HER2-positive MBC.

Refer to the enclosed full prescribing information for complete product indication and safety information.

I hope this information is helpful to you in updating your drug information publications. If you have any questions or need additional assistance, please contact me directly at (650) 225-8084 or by email at costerison.emily@gene.com.

Sincerely,

Emily C. Costerison

Emily Costerison, PharmD, Scientist
Medical Communications, Medical Affairs
Genentech, Inc.

1 DNA Way, South San Francisco, CA 94080
Phone (800) 821-8590 | Email mc-mc-d@gene.com

cc: Iris Tam, PharmD, Director, Genentech Medical Communications

Enclosures

Verma S, Miles D, Gianni L, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer [supplementary appendix available online]. N Engl J Med 2012;367:1783-1791. http://www.ncbi.nlm.nih.gov/pubmed/23020162.

Kadcyla Prescribing Information

References:

1. Verma S, Miles D, Gianni L, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer [supplementary appendix available online]. N Engl J Med 2012;367:1783-1791. http://www.ncbi.nlm.nih.gov/pubmed/23020162.
2. Verma S, Miles D, Gianni L, et al. Updated overall survival results from EMILIA, a Phase 3 study of trastuzumab emtansine (T-DM1) vs capecitabine and lapatinib in HER2-positive locally advanced or metastatic breast cancer. Presented at the European Society for Medical Oncology in Vienna, Austria; September 28 - October 2, 2012. ESMO Oral Presentation #LBA12
3. Welslau M, Diéras V, Sohn J-H, et al. Patient-reported outcomes from EMILIA, a phase 3 study of trastuzumab emtansine (T-DM1) vs capecitabine and lapatinib in HER2-positive locally advanced or metastatic breast cancer. Presented at: European Society for Medical Oncology (ESMO) Congress; September 28–October 2, 2012; Vienna, Austria. Poster 329P. http://www.esmo.org
4. Kadcyla Prescribing Information
5. Krop IE, Lorusso P, Miller KD, et al. A Phase II Study of Trastuzumab Emtansine in Patients With Human Epidermal Growth Factor Receptor 2-Positive Metastatic Breast Cancer Who Were Previously Treated With Trastuzumab, Lapatinib, an Anthracycline, a Taxane, and Capecitabine. J Clin Oncol. 2012;30(26):3234-3241. http://www.ncbi.nlm.nih.gov/pubmed/22649126
6. Burris HA, 3rd, Rugo HS, Vukelja SJ, et al. Phase II study of the antibody drug conjugate trastuzumab-DM1 for the treatment of human epidermal growth factor receptor 2 (HER2)-positive breast cancer after prior HER2-directed therapy. J Clin Oncol. 2011;29(4):398-405. http://www.ncbi.nlm.nih.gov/pubmed/21172893
7. Hurvitz SA, Dirix L, Kocsis J, et al. Phase II randomized study of trastuzumab emtansine versus trastuzumab plus docetaxel in patients with human epidermal growth factor receptor 2-postive metastatic breast cancer. J Clin Oncol. E-pub Date: [published online ahead of print] 2013. DOI # 10.1200/JCO.2012.44.9694.