Genentech
IN BUSINESS FOR LIFE
1 DNA Way, MS242
South San Francisco
CA 94080-4990

January 5, 2005

IMPORTANT DRUG WARNING

Dear Healthcare Provider:

This letter is a follow-up to the Important Drug Warning letter dated August 10, 2004, from Genentech, Inc., informing you of an increased risk of arterial thromboembolic events associated with the use of AVASTIN™ (Bevacizumab) in combination with chemotherapy. These events included cerebral infarction, transient ischemic attacks (TIAs), myocardial infarctions (MI), angina, and a variety of other arterial thromboembolic events. Some of these events were fatal.

Accompanying this letter you will find a new package insert for AVASTIN. Your attention is directed to the WARNINGS, PRECAUTIONS, ADVERSE EVENTS, and DOSAGE AND ADMINISTRATION sections, where important new information is provided regarding arterial thromboembolic events.

We ask that you review the information regarding arterial thromboembolic events contained in the revised label when making a medical judgment on the care and treatment of your patients. The risk of these events should be viewed in the context of AVASTIN's ability to improve overall survival in patients with metastatic colorectal cancer (median survival 20.3 vs. 15.6 months). AVASTIN should be discontinued in patients developing severe arterial thromboembolic events during treatment.

In randomized, active-controlled studies, the overall incidence of arterial thromboembolic events was increased with the use of AVASTIN in combination with chemotherapy (4.4% vs. 1.9%). The incidences of both cerebrovascular arterial events (1.9% vs. 0.5%) and cardiovascular arterial events (2.1% vs. 1.0%) were increased in patients receiving AVASTIN in combination with chemotherapy. In addition, there was a correlation between age (65 years and over) and the increase in risk of thromboembolic events.

The clinical benefit of AVASTIN, as measured by survival in the two principal arms, was seen in all subgroups tested. The subgroups examined were based on age, sex, race, ECOG performance status, location of primary tumor, prior adjuvant therapy, number of metastatic sites, and tumor burden.

Should you have any questions regarding the use of AVASTIN, please call our Medical Information/Communications Department at 1-800-821-8590.

Healthcare professionals should report any serious adverse events suspected to be associated with the use of AVASTIN to Genentech at 1-888-835-2555. Alternatively, this information may also be reported to the 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.

Sincerely,

Hal Barron, M.D.
Senior Vice President, Development
Chief Medical Officer
Genentech, Inc.