

## **IMPORTANT DRUG WARNING**

Dear Healthcare Provider:

It is important that Genentech, Inc. informs you of updated serious adverse event information related to the use of AVASTIN™ (Bevacizumab). Specifically, there is evidence of an increased risk of serious arterial thromboembolic events including cerebrovascular accidents (stroke), myocardial infarctions, transient ischemic attacks, and angina, related to the use of AVASTIN. The risk of fatal arterial thrombotic events is also increased. Patients who experience an arterial thromboembolic event during treatment should permanently discontinue AVASTIN. In randomized, active-controlled studies conducted in patients with metastatic colorectal cancer, the risks of a serious arterial thrombotic event was approximately two-fold higher in patients receiving infusional 5-FU based chemotherapy plus AVASTIN, with an estimated overall rate of up to 5%. Risk factors for the development of arterial thromboembolic events included a history of arterial thromboembolism prior to AVASTIN exposure, age 65 years and above, and AVASTIN therapy. These events occur at a higher rate in these high-risk groups.

A revised AVASTIN package insert containing more detailed information on arterial thromboembolic events is in development. In the interim we have enclosed the current AVASTIN package insert for your review. 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, FACC  
Senior Vice President, Development  
Chief Medical Officer  
Genentech, Inc.