Genentech
IN BUSINESS FOR LIFE

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IMPORTANT DRUG WARNING
Regarding AVASTIN® (bevacizumab)

Dear Healthcare Provider:

Genentech, Inc. would like to inform you of important new safety information regarding AVASTIN® (bevacizumab). Cases of confirmed and possible reversible posterior leukoencephalopathy syndrome (RPLS) have been reported in patients receiving AVASTIN in clinical studies at a rate of <0.1%. RPLS is a rare brain-capillary leak syndrome associated with hypertension, fluid retention, and the cytotoxic effects of immunosuppressive drugs on the vascular endothelium. The syndrome can present as headache, seizures, visual disturbance, and altered mental function, and is characterized by its reversibility upon control of hypertension or other instigating factors. Cases of confirmed and possible RPLS have been reported in AVASTIN clinical studies and in post-marketing experience at a rate of <0.1%.

Based on these data, the following WARNING has been added to the prescribing information for AVASTIN:

Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

RPLS has been reported in clinical studies (with an incidence of <0.1%) and in post-marketing experience. RPLS is a neurological disorder which can present with headache, seizure, lethargy, confusion, blindness and other visual and neurologic disturbances. Mild to severe hypertension may be present, but is not necessary for diagnosis of RPLS. Magnetic Resonance Imaging (MRI) is necessary to confirm the diagnosis of RPLS. The onset of symptoms has been reported to occur from 16 hours to 1 year after initiation of AVASTIN.

In patients developing RPLS, discontinue AVASTIN and initiate treatment of hypertension, if present. Symptoms usually resolve or improve within days, although some patients have experienced ongoing neurologic sequelae. The safety of reinitiating AVASTIN therapy in patients previously experiencing RPLS is not known.

This information has also been included in the ADVERSE REACTIONS and DOSAGE and ADMINISTRATION sections of the prescribing information.

OTHER CHANGES TO PRESCRIBING INFORMATION

In addition, please note that the prescribing information has been revised to include nasal septum perforation based on seven cases of nasal septal perforation that have been reported in the post marketing setting. This event has been added to the Adverse Events, Other Serious Adverse Events section.

We have enclosed the revised 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 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 for 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.