Genentech
A Member of the Roche Group

November 18th, 2011

IMPORTANT PRESCRIBING INFORMATION

FDA COMMISSIONER REVOKES APPROVAL OF AVASTIN FOR TREATMENT OF HER2-NEGATIVE METASTATIC BREAST CANCER (mBC) IN THE UNITED STATES

Dear Healthcare Professional:

This letter is to inform you about an important change to the Avastin® (bevacizumab) label for the treatment of metastatic breast cancer.

The FDA Commissioner announced this morning that she is revoking the approval of Avastin for the treatment of metastatic breast cancer in the United States, **This action is specific to Avastin's breast cancer indication and does NOT impact Avastin's approved uses for other cancer types in the United States.**

On February 22nd 2008, the US Food and Drug Administration (FDA) granted Avastin "Accelerated Approval" for use in combination with paclitaxel for the treatment of patients who have not yet received chemotherapy for metastatic HER2-negative breast cancer. Genentech completed two post-marketing randomized phase III trials in similar patient populations but with different chemotherapies combined with Avastin and with lesser magnitudes of benefit than the original one. FDA determined that the results of these additional studies did not justify continued approval.

The revised Avastin prescribing information is not yet available, but you will receive a follow-up letter with the updated full prescribing information as soon as it is available.

A "Dear Patient Letter" is also attached. Please share this letter with your patients who are currently receiving Avastin and discuss the impact the FDA's action may have on their treatment plans.

For additional information, you can consult our website at www.gene.com. If you have medical questions about Avastin, you can call Genentech's Medical Communications group at (800) 821-8590. For questions regarding reimbursement and active clinical trials, please call the **Genentech Resource Center** at 1-877-GENENTECH.

Roche and Genentech are disappointed with this outcome. We remain committed to developing therapies to improve outcomes for people with breast cancer. To that end, we will proceed with a new Phase III study of Avastin plus paclitaxel in previously untreated metastatic breast cancer and evaluate biomarker candidates that may identify people who derive more substantial benefit.

Sincerely,

Hal Barron, M.D., FACC
Chief Medical Officer
Head of Global Product Development
Genentech

Avastin® (bevacizumab) – Important Safety Information

BOXED WARNINGS and Additional Important Safety Information
People receiving Avastin may experience side effects. In clinical trials, some people treated with Avastin experienced serious and sometimes fatal side effects, including:

Gastrointestinal (GI) perforation: Treatment with Avastin can result in the development of a serious side effect called GI perforation, which is the development of a hole in the stomach, small intestine, or large intestine. In clinical trials, this event occurred in more people who received Avastin than in the comparison group (2.4 percent to 0.3 percent). In some cases, GI perforation resulted in fatality. Avastin therapy should be permanently stopped if GI perforation occurs.

Surgery and wound healing problems: Treatment with Avastin can lead to slow or incomplete wound healing (for example, when a surgical incision has trouble healing or staying closed). In some cases, this event resulted in fatality. Surgery and wound healing problems occurred more often in people who received Avastin than in the comparison group. In a controlled clinical trial, in patients with metastatic colorectal cancer who had surgery during the course of treatment, the incidence of wound healing complications, including serious and fatal complications, was 15 percent for patients who received Avastin and four percent for patients who did not receive Avastin.

Avastin therapy should not be started for at least 28 days after surgery and until the surgical wound is fully healed. The length of time between stopping Avastin and having voluntary surgery without the risk of wound healing problems following surgery has not been determined. Treatment with Avastin should be stopped at least 28 days before voluntary surgery and in people with wound healing problems following surgery that require medical treatment. Treatment with Avastin should be stopped in patients with slow or incomplete wound healing.

Severe bleeding: Treatment with Avastin can result in serious or fatal bleeding, including coughing up blood, bleeding in the stomach, vomiting of blood, bleeding in the brain, nosebleeds and vaginal bleeding. These events occurred up to five times more often in people who received Avastin compared to patients who received only chemotherapy. Across cancer types, 1.2 percent to 4.6 percent of people who received Avastin experienced severe to fatal bleeding. People who have recently coughed up blood (greater than or equal to a half teaspoon of red blood) or have serious bleeding should not receive Avastin. Treatment with Avastin should be permanently stopped if serious bleeding occurs.

In clinical trials for different cancer types, there were additional serious and sometimes fatal side effects that occurred in more people who received Avastin than in those in the comparison group. The formation of an abnormal passage from parts of the body to another part (non-GI fistula formation) was seen in 0.3 percent or less of people. Severe to life-threatening stroke or heart problems were seen in 2.4 percent of people. Too much protein in the urine that led to kidney problems was seen in less than one percent of people. Additional serious side effects that occurred in more people who received Avastin than those in the comparison group included severe to life-threatening high blood pressure, which was seen in five percent to 18 percent of people, and nervous system and vision disturbances (reversible posterior leukoencephalopathy syndrome), which was seen in less than 0.1 percent of people. Infusion reactions with the first dose of Avastin were uncommon and occurred in less than three percent of people, and severe reactions occurred in 0.2 percent of people. Avastin could cause a woman's ovaries to stop working and may impair her ability to have children.

Common side effects that occurred in more than 10 percent of people who received Avastin for different cancer types, and at least twice the rate of the comparison group, were nosebleeds, headache, high blood pressure, inflammation of the nose, too much protein in the urine, taste change, dry skin, rectal bleeding, tear production disorder, back pain, and inflammation of the skin (exfoliative dermatitis). Across all trials, treatment with Avastin was permanently stopped in 8.4 percent to 21 percent of people because of side effects.

Patients who are pregnant or thinking of becoming pregnant should talk with their doctor about the potential risk of loss of the pregnancy or the potential risk of Avastin to the fetus during and following Avastin therapy, and the need to continue an effective birth control method for at least six months

following the last dose of Avastin.

Women should be advised to discontinue nursing or discontinue treatment with Avastin, taking into account the importance of Avastin to the mother.

For full Prescribing Information and Boxed WARNINGS on Avastin please visit http://www.avastin.com.