FDA Pulls Approval for Avastin in Breast Cancer

Commissioner points to lack of evidence that patients taking the drug will live longer or have an improved quality of life

Following months of deliberation, the U.S. Food and Drug Administration (FDA) on November 18 revoked approval of the breast cancer indication for bevacizumab (Avastin; Genentech), saying that the drug “has not been shown to be safe and effective for that use.” However, the drug will remain on the market as an approved treatment for certain colon, lung, kidney, and brain cancers. This means that doctors can recommend off-label use for patients with breast cancer, but insurers won’t necessarily pay for it. In the past, the U.S. Department of Health and Human Services has said that Medicare would continue to pay for it.

“After reviewing the available studies, it is clear that women who take Avastin for metastatic breast cancer risk potentially life-threatening side effects without proof that the use of Avastin will provide a benefit, in terms of delay in tumor growth, that would justify those risks,” said FDA Commissioner Margaret A. Hamburg, MD. “Nor is there evidence that use of Avastin will either help them live longer or improve their quality of life.”

The drug’s dangerous side effects include very high blood pressure; bleeding and hemorrhaging; heart attack and heart failure; and the development of perforations in the nose, stomach, and intestines.

Bevacizumab in combination with paclitaxel (Taxol; Bristol-Meyers Squibb) was approved for treatment of metastatic breast cancer in 2008, under the FDA’s accelerated approval program. This program provides an expedited, 6-month review of drugs for severe or life-threatening diseases for which there are few other therapies.

The drug’s manufacturer must then conduct additional studies to verify clinical benefit for the specific indication. If the drug doesn’t show a benefit, the FDA may revoke approval.

Initial approval of bevacizumab was based on a study that showed an increase in the amount of time it took a tumor to grow. Genentech subsequently completed 2 more clinical trials that showed a small effect on tumor growth but offered little evidence that patients lived longer or had a better quality of life than patients taking standard chemotherapy alone. Consequently, in December 2010, the FDA proposed to revoke approval for breast cancer.

Genentech requested a hearing to argue in favor of maintaining approval while more studies were conducted. But at that hearing, which took place in June, the FDA’s Oncologic Drugs Advisory Committee voted unanimously in favor of with-
drawing the breast cancer indication from the drug’s label. The final decision, however, rested with the Commissioner.

Through the end of 2010, oncology drugs for 5 indications that had been green-lighted under accelerated approval either failed to show a benefit in postmarketing clinical trials or were not further studied in a timely manner. The manufacturers voluntarily removed 4 of the 5 indications from the labels, according to the FDA. The fifth such agent, bevacizumab, represents the first time that the Commissioner has revoked approval.

“We are disappointed with the outcome,” Genentech’s Hal Barron, MD, chief medical officer and head of Global Product Development, said in a public statement. But he noted that the company “will start a new phase III study of Avastin in combination with paclitaxel in previously untreated metastatic breast cancer and will evaluate a biomarker that may help identify which patients will derive the most benefit from Avastin.”

Bevacizumab was the first angiogenesis inhibitor approved in the United States. – Suzanne Rose

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