

# Registry Confirms Vagal Nerve Stimulation's Safety

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GAITHERSBURG, MD. — There have been no unexpected safety findings in the early phases of two postmarketing studies of the vagus nerve stimulation device in patients with depression, according to the manufacturer.

Updates on the studies of the implantable vagus nerve stimulation (VNS) system in patients with treatment-resistant depression were provided by the manufacturer, Cyberonics, and the Food and Drug Administration during a meeting of the FDA's Neurological Devices Panel in January.

In July 2005, the VNS device, previously approved for treating seizures, was approved for adjunctive long-term treatment of chronic or recurrent depression in patients aged 18 years and older who are experiencing a major depressive episode and



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DR. ZUCKERMAN

have not had an adequate response to four or more antidepressant treatments.

The approval came with several conditions, including that Cyberonics conduct a 1-year randomized dose-ranging study and a 5-year observational registry study.

Health advocacy groups have questioned the FDA's decision to approve the device for depression. A U.S. Senate Finance Committee investigation concluded last year that the device had been approved for the depression indication over the objections of FDA staff scientists and medical officers.

As of Dec. 31, 2006, 89 patients had been enrolled in the 1-year study, a multicenter, double-blind trial comparing the safety and effectiveness of adjunctive VNS administered at three electrical charges for 54 weeks in patients with treatment-resistant depression (TRD). The study is supposed to enroll 460 patients at 30 sites, but because of problems with reimbursement for the device and implantation surgery, the company is planning a voluntary program to donate the device and surgery so that the study can be completed in time, said Dr. Richard Rudolph, vice president of clinical and medical affairs, and chief medical officer at Cyberonics.

After the panel meeting, the Centers for Medicare and Medicaid Services said there was sufficient evidence to show vagus nerve stimulation was neither reasonable nor necessary for treating resistant depression. The agency said it planned to issue a national noncoverage determination for the use of VNS for this indication and requested public comments. VNS is covered by Medicare and Medicaid when used for epilepsy.

The 18-month report Cyberonics submitted to the FDA included serious adverse events reported through Jan. 9: There was one report of worsening depression after implantation, compared with five before

implantation. There were no reports of suicide ideation after implantation, compared with one before implantation. There has been one case each reported in patients after implantation of suicide attempt, wound infection, chest pain, death (a motor vehicle accident), and thyroid carcinoma, compared with no such cases reported preimplantation, Dr. Rudolph said. The FDA presented the same data.

To date, enrollment in the registry is on schedule, he said. As of Dec. 31, 264 pa-

tients (223 with implants) had been enrolled in the long-term prospective, observational, multicenter, patient outcome registry, which is following the clinical course and outcomes for patients with TRD, with and without adjunctive VNS therapy. The plan is to enroll 1,000 patients who receive VNS and follow them for 60 months, along with 1,000 patients with treatment-resistant depression who do not receive VNS, who will be followed for 24 months or 60 months.

During the public hearing session of the

meeting, Diana Zuckerman, Ph.D., president of the National Research Center for Women and Families, said postmarketing studies were critical because approval of the VNS device for depression was based on weak research. Dr. Peter Lurie of Public Citizen's Health Research Group said the need for a study comparing different electrical charges indicated the data submitted for approval were inadequate and that VNS efficacy will remain unresolved because the registry is uncontrolled and unblinded. ■

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Please see adjacent Brief Summary of Prescribing Information.