Neurology® Clinical Practice

Vagus nerve stimulation in the treatment of epilepsy

Payment policy perspectives

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Summary

This article is presented as a companion to the recent American Academy of Neurology (AAN) guideline update on use of vagus nerve stimulation (VNS) for treating epilepsy. The guideline update reaffirms the efficacy of VNS for intractable epilepsy. Whereas it upholds the value of VNS for its originally approved indications, the guideline reminds us of existing evidence gaps and unmet research needs. This companion identifies ambiguities in the definition of intractable epilepsies and discusses the use of VNS in children under age 12 years and in persons with intellectual disabilities (mental retardation). Many payers require prior authorization and fulfillment of criteria for coverage of VNS. This article provides guidance and background information to reduce obstacles for coverage, especially where uncertainties exist and levels of evidence are lower.

Three important events mark the progress of vagus nerve stimulation (VNS) therapy. The first is the US Food and Drug Administration (FDA) approval of VNS in 1997 "… as an adjunctive therapy in reducing the frequency of seizures in adults and adolescents over 12 years of age with partial onset seizures that are refractory to antiepileptic medications."

The second occurred in 1999, when the Centers for Medicare & Medicaid Services (CMS) determined that "VNS is reasonable and necessary for patients with medically refractory partial onset seizures for whom surgery is not recommended or for whom surgery has failed."

The third was a 1999 American Academy of Neurology (AAN) technology assessment of VNS that concluded "VNS is indicated for adults and adolescents aged >12 years with

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medically intractable partial seizures who are not candidates for potentially curative surgical resections such as lesionectomies or mesial temporal lobectomies."

The 2013 AAN guideline update[1] reviews the evidence accumulated since the 1999 assessment, and is helpful in several ways: foremost, it reaffirms the validity of the original indications for which this therapy was approved, and it draws attention to more recent evidence for use in children and in Lennox-Gastaut syndrome (LGS). The guideline updates adverse effect profiles and stimulation parameter characteristics, and describes areas where evidence is weak or unavailable. This companion expands on the policy implications of some of the latter aspects of the guideline.

The guideline update reasserts the value of VNS under very specific circumstances. The basic tenets of VNS and the original indications for which it was approved in 1997 remain valid. No convincing contrary evidence has emerged since the publication of the AAN's 1999 assessment of the efficacy of VNS. More than a decade has passed since FDA approval and inception of Medicare coverage. There is little or no reason to deny payment for its use for these initially established indications, although a few payers may still require prior authorization.

The guideline update is also useful in pointing out where evidence gaps exist. The accrual of more experience in the use of VNS since 1999 has spawned questions that have no clear evidence-based answers. Whereas this could spur future research, payers still expect data and rationale to satisfy their current coverage requirements. In the rest of this article, we suggest potential solutions to ambiguous coverage situations that result from incomplete evidence.

Identification and labeling of refractory seizures

Clinicians and patients face difficult decisions when seizures become refractory. Short on options and long on hope, they may resort to tested and untested treatment venues, including the possible off-label use of VNS.

What constitutes "refractory" seizures remains a matter of consensus. The terms "refractory" and "intractable" epilepsy are generally accepted as synonymous, although a "precise definition has remained elusive."[2] Many payer coverage policies use 1 of the 2 terms, and only occasionally do they recognize explicitly their interchangeable status. A taskforce by the International League Against Epilepsy (ILAE) put forth a nonprescriptive, adaptable consensus definition of drug resistant epilepsy: "…a failure of adequate trials of 2 tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom."[2] Many payers would cover VNS for "medically refractory" seizures; however, some spell out explicit qualifying coverage criteria such as the number of drugs tried, duration and frequency of seizures, and the length of intractability. Such rigid qualifying criteria may not always align with decisions made by neurologists and epileptologists.

The prerogative of labeling a patient's condition as refractory rests mainly with the treating neurologist or epileptologist. The methods the physician uses to label a patient's condition as such should be transparent and consistent. Simple declarative statements of intractability without explicative data are insufficient to convince reviewers. The ILAE report includes illustrative case examples of intractability that are applicable in clinical practice. The

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chronicity of the disease requires an adaptable definition. If the clinical circumstances of a patient are akin to those described in any of the ILAE examples, then that similarity should be cited to fulfill the adaptable criteria for identification of intractable epilepsy. In addition, it is worthwhile to describe expectations and outcomes of interest to individual patients.[2,3] Patients may already be aware that complete elimination of seizures, while desirable and ideal, may not be possible. In these instances, their goal may be "reducing symptoms or improving function, rather than offering cure for a given condition."[3] In view of the inherent variables in consensus definitions and payer requirements, it is best to document treatments chosen, doses administered, therapeutic levels achieved, and the reasons for discontinuation of a drug. Inclusion of seizure diaries and caregiver narratives is also advisable.

VNS in patients with intellectual disabilities

It has long been recognized that there is a higher prevalence of epilepsy in persons with intellectual disabilities (mental retardation [MR]).[4] In this section, we use the terms "mental retardation" and "intellectual disability" in an inclusive and interchangeable manner without specific emphasis on individual syndromes. Intellectual disability is the preferred phrase used in recent publications.[5] The benefit of VNS in individuals with intellectual disabilities is not easy to assess because behavioral manifestations of MR could mimic seizure phenomena. Reduction in seizure frequency, improvement in quality of life, and satisfaction from employment or useful vocation are reasonable prerogatives for people who have intellectual impairments as well as people who do not have such impairments.[6] Thus, intellectual disability should not be an absolute contraindication for VNS. A few payers already recognize this as such; however, many, including Medicare, are silent on this issue. If an affirmative statement of coverage is absent, the possibility for post hoc denial exists. Therefore, providers should seek clarification about coverage in selected instances for their patients with intellectual disabilities. If an implant is planned in this situation, the anticipated health benefits need to be documented thoroughly in preparation for prior authorization or postsurgery payer review. Documentation should include caregivers' input. It will be helpful to provide copies of relevant publications that discuss VNS implantation in patients with MR even with the realization that such publications, as are available, consist only of multicenter case series or single-center open-label prospective studies.[7–10] Evidence included in the guideline update and earlier multicenter data showing reduction in seizure frequency in LGS might be helpful.[1,9] Even with this degree of preparation, appeals for exceptions either pre or postimplantation may not be successful.

VNS viewed as a form of step therapy

Step therapy requires a trial of less expensive drugs, usually generic, before administration of more expensive or brand-name agents. It is a construct generally applied to pharmacologic treatments. VNS is approved for patients who have not improved after a trial of 2 or more drugs or surgery. The original FDA approval label does not address failed surgery. Medicare and most other payers, however, include failed surgery among the indications for VNS. Approval also includes use in patients for whom surgery is not recommended (i.e., when the patient is not

an ideal resective surgery candidate, or the patient refuses resective surgery). Thus, VNS becomes a step within a hierarchy of escalating therapies that include surgical excision, callosotomy, hemispherectomy, and ketogenic diet. After failed drug therapy, providers should have the freedom to position VNS among these modalities, wherever clinically appropriate for individual patients. Workup for different types of surgeries, or diet modification, should not be an absolute prerequisite to VNS coverage.

Use in children under age 12 years

After a thorough analysis of evidence, the guideline update concludes that VNS is "possibly effective," and therefore, "may be considered" in children with refractory seizures and in LGS seizures. This less than robust recommendation plus the current FDA-labeled lower age limit of 12 years require provider attention. Outside the United States, VNS is recognized as an acceptable indication for use in children.[11] Payers are unlikely to relax or expand their stated policy limitations for implantation in children under age 12 years. It is best to ascertain respective payers' positions before undertaking the procedure below this age limit. Providers must be willing to hold candid discussions with payers about both merits and shortcomings of their plans. During interactive discussions, the following issues are likely to come up: cumulative longitudinal benefits, potential for reduced management costs and hospitalizations,[12,13] funding source of publications, increased rates of infection, approved usage in non–United States settings, and the advantages of VNS as measured against additional pharmacotherapy. Relevant sections of the guideline update will be helpful as a thorough neutral source of evidence.

Other considerations

Medicare and a majority of payers do not cover VNS for treatment-resistant depression even though this indication received FDA approval in 2005. It is prudent not to present improvement of depression or mood as the primary reason when one is considering VNS therapy. This benefit, however, could weigh in as an additive factor.

The 2013 guideline update recommends research on stimulus parameters, and rightly so, for future developments. Payers depend on already established codes for payments, and these codes have been processing claims well for several years. Stimulus parameter alterations, although important as therapeutic endeavors, will not affect current payments, unless they earn independent status as new codes.

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