Policy #: 083 **Original policy date: 8/29/07** **Revised date: 11/1/09**

Title:

Spinal, Vagal, Deep Brain, Cerebellar Stimulation

Vagal Nerve Stimulation for Depression, is addressed in Behavioral Health policy #038

Description

Deep brain and spinal cord stimulation: Pain is very complicated, involving nerve endings in parts of the body, which connect up through the spinal cord to the brain. Scientists do not fully understand everything about the nerve cells that connect the body to the brain. However, there are some nerve cells (neurons) that control the "touch" sensation, and other neurons that send pain signals to the brain.

Most patients with pain are managed by treating the problem that causes the pain, or by exercises, medications, and other therapies. However, some patients do not respond to these treatments. Some have suggested that if the "touch" neurons can be gently stimulated, it might dull the pain signals from the "pain" neurons. To stimulate the "touch" neurons, some wires have to be placed directly on these cells, which are either deep in the brain, or inside the spinal cord. These cells are not on the body's surface. Once the wires are placed by surgery, electricity is used to stimulate the nerves. Note that these stimulators are not the same as TENS (transcutaneous nerve stimulators), which are devices placed over the skin near a painful body part. TENS devices do not pierce the skin to directly enter the spinal cord or brain.

Cerebellar stimulator or pacemaker is a device used to treat certain neurological disorders (problems of the body's nerve system). The cerebellum is part of the brain, near the back of the head toward the neck area. This brain part is responsible for coordination of movements, and posture. Problems with the cerebellum can lead to loss of coordination, abnormal movements, and spasticity. These diseases are mostly treated with medications to relieve spasticity, and occupational and physical therapy to help the patient function.

One theory to address these problems suggests that electrical impulses sent directly into the cerebellum might counteract the abnormal impulses already there. The intention is to imitate the normal electrical impulses made by the cerebellum, which are lacking in disease. Electrical stimulation (or electrical pacing) of the cerebellum requires drilling holes in the skull to place metal discs onto the brain surface. Wires connect these discs to a small electrical stimulator, surgically placed under the skin in the upper chest area.

Vagal nerve stimulators for seizures: Many patients with seizures are treated with medications. However, there are a small number of patients whose seizures cannot be treated with medicines, either because the medicines do not work well, or because the side effects of the medicines are too severe. In such cases, surgery is an option for some but not all patients. If surgery will not work, or has failed, another option is a device that is surgically implanted, called a vagal nerve stimulator. The vagus nerve is a nerve in the neck; if this nerve is stimulated with electricity, it has some effects on the brain that make it less likely to have a seizure.

Under general or local anesthesia, the left neck is opened, and wires are placed into the vagus nerve. The power pack for the electricity is surgically implanted on the front of the chest, just below the collar bone. The FDA has approved this type of device, for certain seizure patients, to be used along with seizure medications.

When services are covered for all products including Medicare HMO Blue, Medicare PPO Blue and Blue Medicare PFFS Plus Rx

We cover surgically-implanted electrical stimulators of the spinal cord or deep brain for severe and chronic intractable pain of the trunk or limbs, when all the following are met:[5,12,24,40]

- This treatment is a last resort when the pain is refractory to all other therapies (pharmacologic, surgical, psychological, and physical, when appropriate) or are considered unsuitable or contraindicated.
- A trial with a temporarily implanted electrode demonstrates good pain relief; the time period depends on the characteristic of the pain.
- Pain is neuropathic in nature; i.e., resulting from actual damage to the peripheral nerves. Common indications include, but are not limited to failed back syndrome, complex regional pain syndrome (i.e., reflex sympathetic dystrophy), arachoiditis, radiculopathies, phantom limb/stump pain, peripheral neuropathy. Spinal cord stimulation is generally not effective in treating nociceptive pain (resulting from irritation, not damage to the nerves) and central deafferentation pain (related to central nervous system damage from a stroke or spinal cord injury).
- No serious drug habituation exists;
- Demonstration of at least 50% pain relief with a temporarily implanted electrode precedes permanent implantation;
- All the facilities, equipment, and professional and support personnel required for the proper diagnosis, treatment, and follow-up of the patient are available.

We cover surgically-implanted electrical unilateral deep brain stimulators of the thalamus for tremor, when all the following are met:[15,22]

- The patient has either Parkinson's disease or essential tremor
- The patient's tremor is functionally disabling, and is refractory to medications
- The implanting physician is experienced in stereotactic and functional neurosurgery, and is using and FDA-approved implant.

We cover unilateral surgery to avoid potential complications, that may be associated with bilateral surgery.[20,22] We also cover **sequential** placement.[20]

We cover surgically-implanted electrical unilateral or bilateral deep brain stimulators of the globus pallidus or subthalamic nucleus in the following patients.[29, 38]

- Those with Parkinson's disease with all of the following:[29,38]
- A good response to levodopa[29]
- A minimal score of 30 points on the motor portion of the Unified Parkinson Disease Rating Scale when the patient has been without medication for approximately 12 hours[29]
- Motor complications not controlled by pharmacologic therapy.[29]
- Patients aged greater than 7 years with chronic, intractable (drug refractory) **Primary Dystonia**, including generalized and/or segmental dystonia, hemidystonia, and cervical dystonia (torticollis)[38].

We also cover unilateral or bilateral thalamic ventralis intermedius nucleus (VIN) deep brain stimulation (DBS) for the treatment of essential tremor (ET) and/or Parkinsonian tremor and unilateral or bilateral subthalamic nucleus (STN) or globus pallidus interna (GPi) DBS for the treatment of Parkinson's disease (PD) under the following conditions, for our **Medicare HMO Blue and Medicare PPO Blue members in accordance with the Centers for Medicare and Medicaid Services regulations**:[34] (Effective April 2003)

For thalamic VIN DBS to be considered reasonable and necessary, patients must meet **all** of the following criteria:

- Diagnosis of ET based on postural or kinetic tremors of hand(s) without other neurologic signs, or diagnosis of idiopathic PD (presence of at least 2 cardinal PD features (tremor, rigidity or bradykinesia)) which is of a tremor- dominant form.

- Marked disabling tremor of at least level 3 or 4 on the Fahn-Tolosa-Marin Clinical Tremor Rating Scale (or equivalent scale) in the extremity intended for treatment, causing significant limitation in daily activities despite optimal medical therapy.
- Willingness and ability to cooperate during conscious operative procedure, as well as during post-surgical evaluations, adjustments of medications and stimulator settings.

For STN or GPi DBS to be considered reasonable and necessary, patients must meet **all** of the following criteria:[34]

- Diagnosis of PD based on the presence of at least 2 cardinal PD features (tremor, rigidity or bradykinesia).
- Advanced idiopathic PD as determined by the use of Hoehn and Yahr stage or Unified Parkinson's Disease Rating Scale (UPDRS) part III motor subscale.
- L-dopa responsive with clearly defined "on" periods.
- Persistent disabling Parkinson's symptoms or drug side effects (e.g., dyskinesias, motor fluctuations, or disabling "off" periods) despite optimal medical therapy
- Willingness and ability to cooperate during conscious operative procedure, as well as during post-surgical evaluations, adjustments of medications and stimulator settings.

Note: Medicare will only consider DBS devices to be reasonable and necessary if they are FDA-approved for DBS or devices used in accordance with FDA- approved protocols governing Category B Investigational Device Exemption (IDE) DBS clinical trials.

We cover FDA-approved vagal nerve stimulators (VNS) for seizure, as an adjunct to anti-epileptic drugs, for patients with medically refractory partial onset seizures, when surgery is not recommended or when surgery has failed.[16,17,18, 25,26]

When services are not covered for all products, including Medicare HMOB, Medicare PPO Blue, and Blue Medicare PFFS Plus Rx

We do not cover **spinal cord stimulation** as a treatment for critical limb ischemia as a technique to forestall amputation is considered *investigational* and does not meet the BCBSMA Medical Technology Assessment Guidelines, #350.[40]

Electrical stimulators, H-wave electrical stimulators[1] or pacemakers of the cerebellum are not covered for any indication, because they have not been shown to improve the health outcome of patients with spastic cerebral palsy, epilepsy, or any other motor disorder.[6]

We do not cover surgically-implanted electrical deep brain stimulators of the thalamus for tremor, for the following:[15]

- Bilateral, rather than unilateral implantation
- Tremor not due to Parkinson's or essential tremor
- Tremor which is not functionally disabling.

We do not cover surgically implanted deep brain stimulators for other movement disorders, including but not limited to multiple sclerosis and post-traumatic dyskinesia. [38]

We do not cover surgically implanted deep brain stimulators for the treatment of chronic cluster headaches[38].

We do not cover deep brain stimulation for the treatment of psychiatric or neurologic disorders, including but not limited to:

- Tourette syndrome
- Depression

- Obsessive compulsive disorder
- epilepsy

We do not cover DBS for ET or PD for Medicare HMO Blue and Medicare PPO Blue members with any of the following, in accordance with the Centers for Medicare and Medicaid Services regulations: [34]

- Non-idiopathic Parkinson's disease or "Parkinson's Plus" syndromes.
- Cognitive impairment, dementia or depression, which would be worsened by or would interfere with the patient's ability to benefit from DBS.
- Current psychosis, alcohol abuse or other drug abuse.
- Structural lesions such as basal ganglionic stroke, tumor or vascular malformation as etiology of the movement disorder.
- Previous movement disorder surgery within the affected basal ganglion.
- Significant medical, surgical, neurologic or orthopedic co-morbidities contraindicating DBS surgery or stimulation.

We do not cover surgically-implanted vagal nerve stimulators (VNS) under the following circumstances, because there is not enough medical literature to make conclusions about health outcomes in these circumstances:[16,25,39]

- Patients with seizure types other than partial onset[16,25,39] **(see individual consideration guidelines below)**
- As a treatment of essential tremor[39]
- As a treatment of headaches.[39]

Individual consideration

All our medical policies are written for the majority of people with a given condition. Each policy is based on medical science. For many of our medical policies, each individual's unique clinical circumstances may be considered in light of current scientific literature. For consideration of an individual patient, physicians may send relevant clinical information to:

For services already billed	Prior to performance of service
Blue Cross Blue Shield of Massachusetts Provider Appeals PO Box 986065 Boston, MA 02298	Blue Cross Blue Shield of Massachusetts Case Creation/Medical Policy One Enterprise Drive Quincy, MA 02171 Tel: 1-800-327-6716 Fax: 1-888-641-5330

Managed care guidelines

- Medicare HMO Blue members: referrals are not required, however, the device must be medically necessary, prescribed by a plan physician and provided by a network provider.
- Any specialist visit requires a referral for Medicare HMO Blue
- For all other Managed Care plans, any specialist visit requires a referral
- Authorization for inpatient admission is required.
- Authorizations are required for outpatient services

Indemnity and PPO guidelines

All authorization requirements are determined by the individual's subscriber certificate, however:

- Authorizations are required for all inpatient services
- Authorizations are not required for most outpatient services as determined by the individual's subscriber certificate

- Referrals to a specialist are not required.

Coding information

Procedure codes are from current CPT, HCPCS Level II, Revenue Code, and/or ICD-9-CM manuals, as recommended by the American Medical Association, Centers for Medicare and Medicaid Services and American Hospital Associations. Blue Cross Blue Shield Association national codes may be developed when appropriate.

The following code is included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Spine, Deep Brain Stimulation, and Vagal Nerve Stimulator

- CPT code 63650, percutaneous implantation of neurostimulator, electrodes, epidural
- CPT code 63655, laminectomy for implantation of neurostimulator electrodes plate/paddle, epidural
- CPT code 63660, revision or removal of spinal neurostimulator electrode percutaneous array(s) or plate/paddle(s)
- CPT code 63685, insertion or replacement of spinal neurostimulator pulse generator or receiver, direct or inductive coupling
- CPT code 63688, revision or removal of implanted spinal neurostimulator pulse generator or receiver
- CPT code 61850, twist drill or burr hole(s) for implantation of neurostimulator electrodes; cortical
- CPT code 61860, craniectomy or craniotomy for implantation of neurostimulator electrodes, cerebral; cortical
- CPT code 61880, revision or removal of intracranial neurostimulator electrodes
- CPT code 61885, insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array.*
- CPT code 61886, insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to two or more electrode arrays. *
- CPT code 61888, revision or removal of cranial neurostimulator pulse generator or receiver*****
- CPT code 64585, revision or removal of peripheral neurostimulator electrodes
- CPT code 64595, revision or removal of peripheral or gastric neurostimulator pulse generator or receiver
- CPT code 95970, electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex brain, spinal cord, or peripheral (i.e., cranial nerve, peripheral nerve, autonomic nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming
- CPT code 95971, electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements);simple spinal cord, or peripheral (i.e., peripheral nerve, autonomic nerve, neuromuscular) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming
- CPT code 95972, electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements);complex spinal cord, or peripheral (except cranial nerve) neurostimulator pulse generator/transmitter, with intraoperative subsequent programming, first hour
- CPT code 95973: electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements);complex spinal cord, or

peripheral (except cranial nerve) neurostimulator pulse generator/transmitter, with intraoperative subsequent programming, each additional 30 minutes after first hour

***Payable for vagal nerve stimulator according to listed guidelines.** The services will deny, with no patient balance, if submitted with a diagnosis other than the listed covered indications for vagal nerve stimulator.

NOTE: For sacral nerve stimulator Medical Policy Guidelines and Coding Information please see Medical Policy #072.

For Inpatient Coding

- ICD-9-CM procedure code 02.93, implantation or replacement of Intracranial neurostimulator lead(s).
- ICD-9-CM procedure code 01.22, removal of intracranial neurostimulator lead(s).
- ICD-9-CM procedure code 02.93, removal of intracranial neurostimulator with synchronous replacement.
- ICD-9-CM procedure code 03.93, implantation or replacement of spinal neurostimulator lead(s).
- ICD-9-CM procedure code 03.94, removal of spinal neurostimulator lead(s).
- ICD-9-CM procedure code 04.92, implantation or replacement of peripheral neurostimulator lead(s).
- ICD-9-CM procedure code 04.93, removal of peripheral neurostimulator lead(s).

The following services will reject according to our Medical Technology Assessment Guidelines, **for all Plans,** leaving **no** patient balance.

- CPT code 61870, craniectomy for implantation of neurostimulator electrodes, cerebellar; cortical
- CPT code 61875, craniectomy for implantation of neurostimulator electrodes, cerebellar; subcortical

The following services will reject according to our Medical Technology Assessment Guidelines, **except for Medicare HMO Blue and Medicare PPO Blue,** leaving **no** patient balance.

The following services will reject according to our Medical Technology Assessment Guidelines, **for all Plans,** leaving ***no*** patient balance.

- HCPCS Level II code L8685, implantable neurostimulator pulse generator, single array, rechargeable, includes extension ***(New code effective 1/1/06)***
- HCPCS Level II code L8686, Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension ***(New code effective 1/1/06)***
- HCPCS Level II code L8687, Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension ***(New code effective 1/1/06)***
- HCPCS Level II code L8688, Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension ***(New code effective 1/1/06)***

Modifiers:

- modifier RR (rental)
- modifier NU (purchase)

Policy update history

Revised 9/95 to include specific indications for coverage. Deep brain stimulation policy was issued 2/91, and the cerebellar stimulation policy 3/91. Policies were combined 12/96; the deep brain stimulation policy was modified by removing specific types of pain diagnoses, and adding general characteristics about eligible candidates. Reviewed 4/97 after a literature review; no changes were made to coverage. Revised 6/96 to exclude coverage except for Medicare HMO Blue patients, in accordance with CMS regulations (DMERC). Reviewed 4/97 after a literature review; no changes were made to coverage. Reviewed 1/98; added coverage for deep brain stimulators for the thalamus in patients with Parkinson's and essential tremor. Updated 4/98 to include coverage for vagal nerve stimulators for certain seizure patients; effective 10/1/98. Updated 12/98 to include authorization information for managed care plans. Updated 1/99 to add individual consideration statement for children under age 12 with refractory partial onset seizures. Updated 7/99 to clarify billing information for vagal and sacral nerve stimulators. Updated 8/99 to include billing information for ICD-9-CM procedure codes 04.92-04.93. Updated 1/00 to include coverage for unilateral surgery for deep brain stimulators, and to include individual consideration for vagal nerve stimulations for patients with generalized seizures. Updated 1/01 to include individual consideration for patients with tremor-related multiple sclerosis who do not respond to other forms of treatment. Updated ½ to expand coverage for vagal nerve stimulation for children, and to exclude coverage for vagal nerve stimulation for the treatment of depression. Updated 2/02 to include individual consideration guidelines for vagal nerve stimulations for refractory depression; and to include coverage for unilateral or bilateral deep brain stimulation of the globus pallidus or subthalamic nucleus in patients with Parkinson's disease. Reviewed 1/03 MPG Neurology, no changes in coverage were made. Reviewed 7/03 MPG orthopedic, no changes in coverage were made. Reviewed ¼ MPG neurology, no changes were made. Reviewed 2/04 MPG Psychiatry, Ophthalmology and Endocrinology, no changes in coverage were made. Updated ¾ to include Medicare's policy guidelines on unilateral or bilateral deep brain stimulation for the treatment of essential tremor and/or Parkinsonian tremor for Medicare HMO Blue members; effective April 2003. Reviewed 7/04 MPG Orthopedic, no changes in coverage were made. Updated 11/04 to include coverage for NMES/FES for spinal cord injury (SCI) for Medicare HMO Blue members only, in accordance with CMS guidelines; effective immediately. 2/05 MPG Psychiatry, ophthalmology and endocrinology, no changes in coverage were made. Updated1/06 after review 9/05 based on National Policy 7.01.63-Deep Brain Stimulation to include coverage for Primary Dystonia and to exclude coverage for cluster headaches and for other movement disorders, including but not limited to multiple sclerosis and post-traumatic dyskinesia; effective 2/06; individual consideration for multiple sclerosis was deleted; references added. Reviewed 7/05 MPG-Orthopedic, no changes in coverage were made. Updated 1/06 after review 9/05 based on BCBSA national policy specific to vagal nerve stimulation to clarify non coverage of depression as well as coverage exclusion of VNS for treatment of headaches and essential tremors, effective 2/06. Reviewed 1/06 MPG-Neurology, no changes in coverage were made. 6/06 Footnote #38 (re: Deep Brain Stimulation) edited to include coverage/non-coverage rationale and updated literature from the BCBSA medical policy (issue 1:2006). Reviewed 7/06 MPG - Orthopedic/Rheumatology, no changes in coverage were made. 10/06 update information: 1. policy comparison review of National Policy # 7.01.29 conducted; no changes in coverage were noted. 2. June 2006, policy comparison review of National Policy # 7.01.63 *Deep Brain Stimulation*-references added, footnote #38. Updated 12/06 after review of BCBSA policy addressing vagal nerve stimulation without change in policy statements under footnote 39. Updated 12/06 to remove policy exclusion statement and IC policy guideline on vagal nerve stimulation for depression from this policy and separately address it under Behavioral Health policy #038. Reviewed 1/07 MPG Neurology, no changes in coverage were made. Reviewed 2/07 MPG Psychiatry, Ophthalmology and Endocrinology, no changes in coverage were made. 4/07 Comparison review of BCBSA policy 7.01.25 completed, BCBSMA covered and non-covered statements for spinal cord stimulation clarified; and footnote 40 developed to include BCBSA policy rationale, literature review, and references. Comparison review of BCBSA policy 7.02.09 completed, no change in policy statement; and footnote #32 in the BCBSMA medical policy expanded upon to reflect BCBSA national policy rationale, review of references, and updated reference list. Reviewed 7/07 MPG Neurology, no changes in coverage were made. 2/08, Comparison review of BCBSA policy 8.03.01 completed, no change in policy statement, references added. 2/08, Comparison review of BCBSA 1.01.27 completed, non-coverage for rheumatoid arthritis status added. Reviewed 1/08 MPG-Neurology, no changes in coverage were made. Updated during review of BCBSA #1.01.09 to add references 18-20 and 22-26. Policy remains unchanged. Updated based on BCBSA policy # 1.01.19 with literature review; reference 7 added; no change in policy statement. Updated 11/08 with removal of spinal, vagal, deep brain cerebellar stimulation information from medical policy #003 and creation of this stand alone policy. Reviewed 1/09 MPG – Neurology and Neurosurgery, no changes in coverage were made. Updated 2/09 to state authorization for inpatient admission and outpatient services are required. Updated 6/09, during review of BCBSA policy # 7.01.20, references and coding updated. Statement referencing BCBSMA Behavioral Health Policy #038,Vagal Stimulation for depression added. No change in policy statement. 3/09, Updated based on BCBSA policy #7.01.63 with non-coverage statement for listed psychiatric and selected neurologic disorders added. References 16-26 added. No change in policy statement. 11/09, Updated format, percutanuous implantation codes and definitions deleted. No change in policy statement.

Footnotes and References

[5] Based upon a TEC (Technology Evaluation Center) assessment from 1988, supplemented by a literature review from 1992 through 10/95 on deep brain and spinal cord stimulation for intractable pain. The 1988 TEC assessment reviewed 41 articles, including the following:
Young (1985) (n=48, 71 electrodes) deep brain stim for intractable pain. Average duration of pain management before surgery was 4.5 years. Complete or partial pain relief was achieved in 35 patients. 28 were able to discontinue narcotics, 12 returned to normal activity. No patient was worsened by stimulation, and the only complications were minor ones.

Shatin (1986) (n=90) dorsal spinal cord stim for intractable pain of the low back and legs. Significant relief was achieved in 70%, all of whom had failed previous standard pain management.

Hosobuchi (1986) (n=122) followed patients for 2-14 years. Pain of peripheral origin (n=65): 50 (76%) had significant relief with periaqueductal gray matter stimulation. Deafferentation pain syndrome (n=76): patients were stimulated in the somatosensory thalamus; 44 patients obtained complete relief from painful dysesthesias.

Vogel (1986) (n=50) treated low back/ leg pain with spinal cord stimulation. Of patients with proper electrode placement, 25/44 obtained at least temporary relief. Only 8 patients experienced pain relief sustained more than 3 years.

Broseta (1986) (n=41) treated chronic pain from peripheral arterial disease, with stimulation of the thoracic cord. Mean follow-up of 25 months showed that 29 (60%) experienced significant relief.
Conclusion: There is adequate clinical evidence to suggest that cases of severe, chronic pain refractory to other management may respond to electrical stimulation of CNS sites in the brain and cord.

[6] Based upon a TEC (Technology Evaluation Center) assessment from 1988, supplemented by a literature review from 1992 through 10/95 on cerebellar stimulation for various neurological disorders. The 1988 TEC assessment reviewed 19 articles, including the following:

Cerebral palsy: Schulman (1987) (n=20) and Davis (1987) (n=30) reported on electrical stimulation of the cerebellum with Neurolith 601[R] in patients with spastic cerebral palsy. Some of these patients may be reported on in both of these studies. In both, a double-blind protocol was used, with exams while stimulators were either on or off. Joint angle motion (AROM and PROM), motor performance (reaction time, hand dynamometry, grooved peg board placement, hand/foot tapping, and rotary pursuit) were assessed. In the Davis study, 14 patients finished (others dropped out due to technical failures, or stimulators in the “off” position throughout the study). 10/14 showed quantitative improvement less than 50%, 1 improved greater than 50%, and 3 showed no improvement. In the Schulman study, 23 patients dropped out due to infection, broken leads, unrelated medical problems, and refusal to participate. Evaluation was still underway for the remaining 7 patients. Davis (1985) (n=30) reported respiratory inductive plethysmography before and after stimulation, in patients with Hx paroxysmal and/or ataxic breathing patterns. Breathing patterns reverted to normal (n=5) within 5 months after the start of stimulation, and 3 others were thought to be markedly improved. Technical malfunction was a concern. These studies do not demonstrate that electrical stimulation of the cerebellum reduces spasticity in cerebral palsy as well as or better than standard therapy with PT and medications.

Epilepsy: 4 articles were reviewed, 2 of which were reviews (Spencer 1986, Ardern 1985). Another studied effects on beta-endorphin production, rather than spasticity (Madrazo 1985), and the other was a case study about a hematoma (Zuccarello 1986). No article presented substantial evidence that cerebellar stimulation was useful for epilepsy management.

2007-2008 Update: A search of the MEDLINE database for the period of October 2006 through January 2008 identified 1 controlled comparative effectiveness trial. (7) Sixty children with cerebral palsy were randomized to 1 hour daily of neuromuscular stimulation (n=18), overnight threshold electrical stimulation (n=20), or overnight sham stimulation (n=22). Blinded assessment following 16 weeks of treatment showed no difference among the groups as measured by peak torque or by a therapist-scored gross motor function. A parental questionnaire on the impact of disability on the child and family showed improvement for the 2 active groups, but not the sham control. Compliance in the threshold electrical stimulation group was 38%; compliance in the placebo group was not reported. Retrospective analysis indicated that the study would require 110 to 190 subjects to achieve 80% power for measures of strength and function. Evidence remains insufficient to determine if threshold electrical stimulation improves health outcomes in children with cerebral palsy. Therefore, the policy statement is unchanged.

References:

1. Steinbok P, Reiner A, Kestle JR. Therapeutic electrical stimulation (ThresholdES) following selective posterior rhizotomy in children with spastic diplegic cerebral palsy: a randomized clinical trial. Dev Med Child Neurol 1997; 39(8):515-20.
2. Dali C, Hansen FJ, Pedersen SA et al. Threshold electrical stimulation (TES) in ambulant children with CP: a randomized double-blind placebo-controlled clinical trial. Dev Med Child Neurol 2002; 44(6):364-9.
3. van der Linden ML, Hazlewood ME, Aitchison AM et al. Electrical stimulation of gluteus maximus in children with cerebral palsy: effects on gait characteristics and muscle strength. Dev Med Child Neurol 2003; 45(6):385-90.
4. Fehlings DL, Kirsch S, McComas A et al. Evaluation of therapeutic electrical stimulation to improve muscle strength and function in children with types II/III spinal muscular atrophy. Dev Med Child Neurol 2002; 44(11):741-4.
5. Ozer K, Chesher SP, Scheker LR. Neuromuscular electrical stimulation and dynamic bracing for the management of upper-extremity spasticity in children with cerebral palsy. Dev Med Child Neurol. 2006; 48(7):559-63.
6. Lannin N, Scheinberg A, Clark K. AACPDM systematic review of the effectiveness of therapy for children with cerebral palsy after botulinum toxin A injections. Dev Med Child Neurol 2006; 48(6):533-9.
7. Kerr C, McDowell B, Cosgrove A et al. Electrical stimulation in cerebral palsy: a randomized controlled trial. Dev Med Child Neurol 2006; 48(11):870-6.

[12] For a recent review, see *Deep brain stimulation for the relief of chronic pain*. Richardson DE. Neurosurg Clin N Am 1995 Jan;6(1):135-44. Good long-term results may be seen in 50-80% of patients, depending on etiology and site of stimulation. Best results are obtained in deafferentation pain, if internal capsule stimulation; and somatic pain with periventricular stimulation.

H-wave Electrical Stimulation:

2007-2008 Update based on BCBSA policy 1.01.13**,** a search of the MEDLINE database was performed for the period of February 2006 through December 2007. Two observational studies on the H-wave were identified; both were published by the same group of authors/consultants and consisted of patient's responses to 3 of 10 questions on a manufacturer's customer service questionnaire (i.e., warranty registration card). (5, 6) In the larger of the 2 reports, 80% of 8,498 patients with chronic soft-tissue injury and neuropathic pain who were given the H-wave device completed the questionnaire. (6) The answers were compared with an expected placebo response of 37% improvement. Following an average 87 days of use, 65% of respondents reported a decrease the amount of medication needed, 79% reported an increase in function and activity, and 78% of respondents reported an improvement in pain of 25% or greater. As indicated above, prospective controlled studies are needed; the policy statement remains unchanged.

Medicare Coverage Policy Position

The Centers for Medicare and Medicaid Services (CMS) currently has no national coverage policy on H-wave electrical stimulation.

References:
1. 1996 TEC Assessments, Tab 21.
2. Kumar D, Marshall HJ. Diabetic peripheral neuropathy: amelioration of pain with transcutaneous electrostimulation. Diabetes Care 1997; 20(11):1702-5.
3. Kumar D, Alvaro MS, Julka IS et al. Diabetic peripheral neuropathy. Effectiveness of electrotherapy and amitriptyline for symptomatic relief. Diabetes Care 1998; 21(8):1322-5.
4. Julka IS, Alvaro M, Kumar D. Beneficial effects of electrical stimulation on neuropathic symptoms in diabetes patients. J Foot Ankle Surg 1998; 37(3):191-4.
5. Blum K, DiNubile NA, Tekten T et al. H-wave, a nonpharmacologic alternative for the treatment of patients with chronic soft tissue inflammation and neuropathic pain: a preliminary statistical outcome study. Adv Ther 2006; 23(3):446-55.
6. Blum K, Chen TJ, Martinez-Pons M et al. The H-wave small muscle fiber stimulator, a nonpharmacologic alternative for the treatment of chronic soft-tissue injury and neuropathic pain: an extended population observational study. Adv Ther 2006; 23(5):739-49.

[15] Based on the 10/97 TEC (Technology Evaluation Center) assessment of medical literature on deep brain stimulation (DBS) of the thalamus, as an alternative to thalamotomy for patients with refractory tremors due to Parkinson's disease or essential tremor. The FDA, in 7/97, approved the Activa® Tremor Control system (Medtronic, Minnesota) for unilateral thalamic stimulation for suppression of Parkinsonian or essential tremor not adequately controlled by medications, when the tremor constitutes a significant functional disability. The FDA pre-market approval letter states that implanting physicians should be experienced in stereotactic and functional neurosurgery.

Available studies include a total of 179 patients at 4 centers in North America and Europe. Though only a case series, patient selection criteria and outcomes measures were adequate to permit conclusions about effectiveness. Because the device may be turned on and off once implanted, to a certain extent, additional information may be derived from each patient after implantation, with the device in on and off states. In addition to published literature, the Medtronic database includes 300 patients, some of whom are included in other published reports. Published literature includes 66 cases of bilateral deep-brain stimulation. Unfortunately, outcomes from these patients were not reported separately, so it is difficult to determine whether bilateral DBS is significantly better than unilateral implantation. The FDA has requested additional data on bilateral DBS before approving this bilateral implantation. There have been a few reports of patients with other types of tremors, such as multiple sclerosis and post-traumatic dyskinesia. These small numbers do not permit conclusions about improvements in health outcomes.

Outcomes: tremor suppression was total or clinically significant in 82-91% of operated sides of 179 patients. Results were durable for up to 8 years. Side effects were mild, and usually reversible. There was no intra-operative mortality in this patient group. Medtronic reported similar results to the FDA in their series of 300 patients (their series overlaps the published literature). Medtronic reported 9 deaths (2%) in their series, but only 2 of these were related to the DBS operation (1 post-op intracranial hemorrhage, 1 peri-op MI). Comparatively, thalamotomy tremor suppression ranges from 46-92%, with a higher percentage of successes in patients who underwent thalamotomy after 1970. Recurrence rate ranges from 5-10%. Unlike thalamotomy, tremor recurrence can sometimes be addressed with DBS by modulating the stimulation parameters. Intracranial hemorrhage rates range from 0.4-6% with thalamotomy, and DBS may carry a similar risk.

[16] Based on the 5/98 TEC (Technology Evaluation Center) assessment of medical literature on vagus nerve stimulation (VNS) as adjunctive treatment with antiepileptic drugs (AEDs). In July 1997, the FDA approved the NeuroCybernetic Prosthesis System (NCP®) for use in conjunction with drugs or surgery as an adjunctive treatment of adults and adolescents over 12 years of age with medically refractory partial onset seizures. The FDA has requested the manufacturer to evaluate its data to find out whether any factors predict which patients are most likely and/or least likely to benefit from the use of the device.

Data reviewed includes controlled studies of patients (n=454) at multiple medical centers in North America and Europe. For patients with medically refractory partial onset seizures, who have either failed surgery, or for whom surgery is not recommended, 2 blinded, randomized, active control, multicenter trials evaluated outcomes in 314 patients who had at least 6 partial onset seizures monthly despite optimal use of anti-epileptic drugs (AED). Seizure frequency was reduced by about 25% in the first 3 months following implantation. In those who do note an initial reduction in seizure frequency, the beneficial effect appears to be maintained or even improved with time. In one study, almost 30% of patients noted a 50% or more reduction in seizure frequency, at 3 months post-implantation. Long-term follow up in a smaller number of patients suggests that seizure frequency may be reduced by over 50% 18 months out.

For patients with seizure types other than partial onset, there is not sufficient published data to permit conclusions about reductions in seizure frequency.

[17] See JAMA August 26, 1998 vol 280, no. 8, Contempo, entitled "New Options for the Treatment of Epilepsy" by Herman and Pedley. The article points out that at the onset of an aura, patients can activate the device with a magnet, to abort or limit the spread of a seizure. Authors conclude that the role of VNS is not yet clear, and that in some studies of VNS as an adjunct, results are comparable to results obtainable from the newer anti-epileptic drugs. Since few patients are rendered seizure free with VNS, they conclude that this device will serve as an adjunct for those with refractory disease, who are not good candidates for surgery. They were unable to identify specific subgroups of patients for whom VNS is most appropriate. Authors state that adverse effects of Vagal Nerve Stimulators (VNS) include local irritation, hoarseness, cough, and swallowing difficulties while the device is turned on, and a 2-3% chance of infection at the implant site. They noted that neither cognitive nor autonomic nervous system effects (GI, cardiac) have been described in the literature.

[18] Based on a technology assessment by ECRI, a national non-profit technology assessment firm. Their analysis concluded that VNS has a modest effect on seizure frequency, with a mean reduction of about 30%. However, they point out that in individual patients, such improvements may be dramatic. they confirm that the efficacy of VNS as an adjunct is comparable to that achieved with some of the newer anti-epileptic drugs. They note that while seizure frequency is altered by VNS, neither duration nor intensity of seizures are affected. They concluded that adverse effects are also modest, and that the overall cost may be comparable to that of some anti-epileptic drugs. Hoarseness, cough, and paresthesia are typically well-tolerated, and may be reduced in some cases by altering the VNS parameters.

[20] Based on recommendations from Dr. Jeff Arle, Lahey Clinic, EBR 1/00, and Drs. Weinberg and Rizzoli, President and Vice President of the Massachusetts Neurologic Association, MPG 1/00.

[21] Based on recommendations from Dr. Andrew Blum, Harvard Medical School and Beth Israel Deaconess Medical Center, EBR 1/00.

[22] Evaluation of Surgery for Parkinson's Disease: A Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology, July 9, 1999. Neurology 1999;53:1910-1921

Deep brain stimulation (DBS) of the thalamus: The AAN report noted that DBS of the thalamus for tremor in patients with PD is safe and effective. While bilateral thalamic DBS appears safe and effective, it remains investigational because of only limited data. Brain stimulation of the thalamus was effective in reducing contralateral tremor, both short-term (3-12 mos.) and long-term (up to 8 years). Of 148 patients with PD, 90% had significant tremor reduction; 50% had complete tremor resolution. There may be minor loss of efficacy over the years, but generally tremor remained markedly reduced for periods up to 8 years. Response of tremor to contralateral stimulation: 80% of patients with PD had significant reduction in tremor contralateral to stimulation. 90% of patients rated their outcome as moderately to markedly improved after unilateral DBS of the thalamus.

[23] Recommendations from Dr. David Weinberg, MD, President of the Massachusetts Neurologic Association and Paul Rizzoli, MD, Vice President of the Massachusetts Neurologic Association.

[24] See also Blue Cross Blue Shield Association July 2000 *Tecnologica* newsletter. *The Use of Spinal Cord Stimulation for Chronic Reflex Sympathetic Dystrophy.* In this study by Kemler and Furnee at Maadstricht University Hospital, patients were randomized to receive either spinal cord stimulation (SCS) + physical therapy (n=36) or physical therapy alone. The purpose was to find out the effectiveness and cost effectiveness of SCS and physical therapy vs. physical therapy alone. Researchers found that during the first year of therapy, SCS is more expensive that physical therapy alone. However, lifetime analysis showed it to be both more effective and less costly than just physical therapy alone. They concluded that there is compelling evidence for its adoption and appropriate utilization.

[25] Based on the Blue Cross Blue Shield Association national policy 7.01.20, issued 11/20/01. Medical literature that was reviewed included: Amar (2001), Murphy (1999), Morris (1999), Hornig (1997).

Vagal nerve stimulation in children with refractory seizures: FDA-approval in 1997 limited the use of vagal nerve stimulation to patients over 12 years old. Since then, some trials reported results supporting the safety of the device in children with refractory seizures. One study reported on 60 pediatric patients who were treated as part of the double-blind clinical trials done to support the FDA application. Median reduction in seizure frequency was 50% at 18 months, which was similar to outcomes reported in adults. Also, adverse events were similar to those reported in adults. Another study reported on 38 patients (11 mos.-16 years old). 29% had 90% decrease in seizure frequency, while 39% had 50%- 90% reductions.

[26] See the 1999 Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology: Reassessment: Vagus nerve stimulation for epilepsy. See also Neurology 1999;53:66-669.

This report concluded that the degree of improvement in seizure control from vagal nerve stimulation remains comparable to new anti-epileptic drugs, but is lower than that of temporal lobectomy in suitable candidates for surgical resection. Although the report noted that the effectiveness of vagal nerve stimulation in less severely affected populations remains to be evaluated, it was concluded that there is sufficient evidence to grade vagal nerve stimulation for epilepsy as effective and safe, based on Class I evidence. Class I: Evidence provided by 1 or more well-designed randomized, controlled clinical trials.

[29] Based on the 2001 TEC (Technology Evaluation Center) assessment on bilateral deep brain stimulation of subthalamic nucleus or the globus pallidus interna for treatment of advanced Parkinson's disease, including review of the medical literature from 1985 through January 2002. Also, based on the 2002 Blue Cross Blue Shield Association national policy 7.01.63, issued 2/15/02.

Unilateral or bilateral stimulation of the globus pallidus or subthalamic nucleus: The TEC assessment and the national policy concluded that studies consistently established that deep brain stimulation of the globus pallidus or subthalamic nucleus resulted in significant improvements as measured by standardized rating scales of neurologic function. Improvements consisted of increased waking hours spent in a state of mobility without dyskinesia, improved motor function during "off" periods when levodopa is not effective, reduction in frequency and severity of levodopa-induced dyskinesia during periods when levodopa is working ("on" periods), improvement in cardinal symptoms of Parkinson's disease during periods when medication is not working, and in the case of bilateral deep brain stimulation of the subthalamic nucleus, reduction in the required daily dosage of levodopa and/or its equivalents. They concluded that the degree of these changes is both statistically significant and clinically important.

It was also noted that the beneficial treatment effect lasted 6–12 months in most trials. While there is not a great deal of long-term follow-up, the available data are generally positive. Adverse effects and morbidity are similar to those known to occur with thalamic stimulation. Deep brain stimulation possesses advantages to other treatment options. In comparison to pallidotomy, deep brain stimulation can be performed bilaterally. The procedure is non-ablative and reversible.

[38] Based on Blue Cross Blue Shield Association National Policy, 7.01.63, *Deep Brain Stimulation*.

June 2006 Review
Based on Blue Cross Blue Shield Association National Policy, 7.01.63, Deep Brain Stimulation. Literature review update for the period of 2005 through January 2006, references #4 and 5.

Rationale
The policy is based on 2 TEC Assessments; a 1997 TEC Assessment that focused on unilateral deep brain stimulation of the thalamus as a treatment for tremor (1) and a 2001 TEC Assessment that focused on the use of deep brain stimulation of the globus pallidus and subthalamic nucleus for a broader range of Parkinson symptoms. (2) The observations and conclusions of the TEC assessment are summarized here. Articles published since these two assessments continue to report positive outcomes for deep brain stimulation for tremor and Parkinson disease.

Unilateral Deep Brain Stimulation of the Thalamus for Tremor (1)

Tremor suppression was total or clinically significant in 82%–91% of operated sides in 179 patients who underwent implantation of thalamic stimulation devices. Results were durable for up to 8 years, and side effects of stimulation were reported as mild and largely reversible.

These results are at least as good as those associated with thalamotomy. An additional benefit of deep brain stimulation is that recurrence of tremor may be managed by changes in stimulation parameters.

Unilateral or Bilateral Stimulation of the Globus Pallidus or Subthalamic Nucleus for Parkinson Symptoms (2)
A wide variety of studies consistently demonstrate that deep brain stimulation of the globus pallidus or subthalamic nucleus results in significant improvements as measured by standardized rating scales of neurologic function. The most frequently observed improvements consist of increased waking hours spent in a state of mobility without dyskinesia, improved motor function during "off" periods when levodopa is not effective, reduction in frequency and severity of levodopa-induced dyskinesia during periods when levodopa is working (on periods), improvement in cardinal symptoms of Parkinson's disease during periods when medication is not working, and in the case of bilateral deep brain stimulation of the subthalamic nucleus, reduction in the required daily dosage of levodopa and/or its equivalents. The magnitude of these changes is both statistically significant and clinically meaningful.

The beneficial treatment effect lasts at least for the 6–12 months observed in most trials. While there is not a great deal of long-term follow-up, the available data are generally positive.

Adverse effects and morbidity are similar to those known to occur with thalamic stimulation.

Deep brain stimulation possesses advantages to other treatment options. In comparison to pallidotomy, deep brain stimulation can be performed bilaterally. The procedure is non-ablative and reversible.

Deep Brain Stimulation for the Treatment of Dystonia
Deep brain stimulation for the treatment of primary dystonia received FDA approval through the Humanitarian Device Exemption (HDE) process. The HDE approval process is available for conditions that affect less than 4,000 Americans per year. According to this approval process, the manufacturer is not required to provide definitive evidence of efficacy, but only probable benefit. The approval was based on the results of DBS in 201 patients represented in 34 manuscripts. (3) There were 3 studies that reported at least 10 cases of primary dystonia. In these studies, clinical improvement ranged from 50% to 88%. A total of 21 pediatric patients were studied; 81% were older than 7 years. Among these patients there was about a 60% improvement in clinical

scores. As noted in the analysis of risk and probably benefit, the only other treatment options for chronic refractory primary dystonia are neuro-destructive procedures. Deep brain stimulation provides a reversible alternative. The FDA Summary of Safety and Probable Benefit states, "Although there are a number of serious adverse events experienced by patients treated with deep brain stimulation, in the absence of therapy, chronic intractable dystonia can be very disabling and, in some cases, progress to a life-threatening stage or constitute a major fixed handicap. When the age of dystonia occurs prior to the individual reaching their full adult size, the disease not only can affect normal psychosocial development but also cause irreparable damage to the skeletal system. As the body of the individual is contorted by the disease, the skeleton may be placed under constant severe stresses that may cause permanent disfigurement. Risks associated with deep brain stimulation for dystonia appear to be similar to the risk associated with the performance of stereotactic surgery and the implantation of deep brain stimulation systems for currently approved indications, except when used in either child or adolescent patient groups."

Since the FDA approval, there have been additional published trials of deep brain stimulation for dystonia, which continue to report positive results. (4,5) Vidailhet and colleagues reported the results of a prospective multi-institutional case series of 22 patients with primary generalized dystonia. Symptoms were evaluated prior to surgery and at several points up to 1 year of follow-up, in a double-blind fashion with the stimulator turned on and off. Dystonia scores were significantly better with the neurostimulator turned on.

Deep Brain Stimulation for the Treatment of Headaches

Deep brain stimulation of the posterior hypothalamus for the treatment of chronic cluster headaches has been investigated since recent functional studies have suggested cluster headaches have a central hypothalamic pathogenesis. Franzini and colleagues and Leone et al, reported deep brain stimulation with long-term, high-frequency, electrical stimulation of the ipsilateral posterior hypothalamus resulted in long-term pain relief (1–26 months of follow-up) without significant adverse effects in 5–8 patients with chronic cluster headaches. (6-8) The results from these reports seem promising; however, the authors note further studies are needed to determine the long-term safety and effectiveness of this treatment.

Update 2005

Literature review for the period of 2003 through February 2005. Information and policy statement added on deep brain stimulation for cluster headaches as investigational.

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[39] Based upon BCBSA National Policy 7.01.20 addressing Vagus Nerve Stimulation issued 6/05. Added headaches to investigational policy statement; otherwise policy statement unchanged.

Vagus Nerve Stimulation as a Treatment of Seizures
This policy is based in part on a 1998 TEC Assessment (1) that offered the following conclusions.
1. Published evidence from 2 large, well-designed multicenter trials involving over 300 patients demonstrates that the use of vagus nerve stimulation as an adjunct to optimal use of antiepileptic drugs in the treatment of medically refractory patients with at least 6 partial-onset seizures/month reduces seizure frequency by approximately 25% after 3 months of treatment. In patients who achieve an initial reduction in seizure frequency, the beneficial treatment effect appears to be maintained and may increase with time.
2. Adverse effects are mild and consist primarily of hoarseness or voice change during "on" periods of stimulation.
3. There is limited information about the use of vagus nerve stimulation in patients with other types of seizure disorders.

Vagus Nerve Stimulation in Children for Treatment of Seizures
The original FDA approval limited the use of vagus nerve stimulation (VNS) to those over the age of 12 years. Since that time, there has been interest in expanding the use of VNS to younger patients. Several studies have now reported results that support the safety of the device in children with refractory seizures. (2) For example,

60 pediatric patients were treated as part of the double-blind clinical trials conducted to support the FDA application. (3) At 18 months, the median reduction in seizure frequency was 50%, similar to the results achieved in adults. Adverse events were also similar to those recently reported in adults (4), and none resulted in termination of stimulation. Hornig and colleagues reported on a case series of 19 pediatric patients, with observation periods ranging up to 30 months. (5) Overall, 50% of patients had a 50% reduction in seizure frequency. Patwardhan and colleagues reported that among 38 patients aged 11 months to 16 years, 29% had a greater than 90% reduction in seizure frequency, while 39% had 50% to 90% reduction. (6) The major limitations of VNS are the facts that stimulation generally does not completely eliminate seizures, and it is not possible to predict which patients will optimally respond. Therefore, some authors suggest that VNS may be most appropriately used in patients with refractory seizures who are not candidates for surgery (i.e., bilateral or unresectable foci or no identified structural abnormality).

Additional published studies were identified that support the safety and effectiveness of the device for adults and children with partial-onset seizures refractory to medical therapy. (7,8)

Vagus Nerve Stimulation as a Treatment of Refractory Depression
Interest in the application of VNS for treatment of refractory depression is related to reports of improvement in depressed mood among epileptic patients undergoing VNS. (9) However, studies examining VNS for the treatment of depression are limited, and all published and unpublished data concerning clinical outcomes of VNS therapy for the indication of treatment-resistant depression come from company-sponsored clinical studies. A June 2005 TEC Assessment on Vagus Nerve Stimulation for Treatment-Resistant Depression concluded that evidence was insufficient to permit conclusions of the effect of VNS therapy on health outcomes. (10) The available evidence for the TEC Assessment included study groups assembled by the manufacturer of the device, Cyberonics, and reported on in various publications. Analyses from these study groups were presented for FDA review and consisted of a case series of 60 patients receiving VNS (Study D-01), a short-term (i.e., 3-month) randomized sham-controlled clinical trial of 221 patients (Study D-02), and an observational study comparing 205 patients on VNS therapy compared to 124 patients receiving ongoing treatment for depression (Study D-04). (11) Patients who responded to sham treatment in the short-term randomized, controlled trial (approximately 10%) were excluded from the long-term observational study.

The primary outcome evaluated in the TEC Assessment was the relief of depression symptoms that can usually be assessed by any one of many different depression symptom rating scales. A 50% reduction from baseline score is considered to be a reasonable measure of treatment response. An improvement in depression symptoms may allow reduction of pharmacologic therapy for depression, with a reduction in side effects related to that form of treatment. In the studies evaluating VNS therapy, the 4 most common instruments used were the Hamilton Rating Scale for Depression, Clinical Global Impression, Montgomery and Asberg Depression Rating Scale, and the Inventory of Depressive Symptomatology (IDS).

The case series data show rates of improvement, as measured by a 50% improvement in depression score of 31% at 10 weeks to greater than 40% at 1 to 2 years, but there are some losses to follow-up. (11-14) Natural history, placebo effects, and patient and provider expectations make it difficult to infer efficacy from case series data.

The randomized study (D-02), which compared VNS therapy to a sham control (implanted but inactivated VNS), showed a non-statistically significant result for the principal outcome. (11) Fifteen percent of VNS subjects responded, versus 10% of control subjects ($p=0.31$). The IDS-SR was considered a secondary outcome, and showed a difference in outcome that was statistically significant in favor of VNS (17.4% versus 7.5%, $p=0.04$).

The observational study comparing patients participating in the randomized clinical trial and a separately recruited control group (D-04 vs. D-02) evaluated VNS therapy out to 1 year and showed a statistically significant difference in the rate of change of depression score. (11) However, issues such as unmeasured differences between patients, nonconcurrent controls, differences in sites of care between VNS therapy patients and controls, and differences on concomitant therapy changes raise concern about this observational study. Analyses performed on subsets of patients cared for in the same sites, and censoring observations after treatment changes, generally showed diminished differences in apparent treatment effectiveness of VNS and almost no statistically significant differences. Given these concerns about the quality of the observational data, these results did not provide strong evidence for the effectiveness of VNS therapy.

Adverse effects of VNS therapy included voice alteration, headache, neck pain, and cough, which are known from prior experience with VNS therapy for seizures. Regarding specific concerns for depressed patients such as mania, hypomania, suicide, and worsening depression, there does not appear to be a greater risk of these events during VNS therapy.

Vagus Nerve Stimulation as a Treatment of Essential Tremor
Handforth and colleagues studied VNS in 9 patients with essential tremor. (15) Four weeks after implantation of the VNS device, tremor assessment using a masked videotape of patients was performed. Raters found no improvement in upper extremity tremors. Therefore, the authors of the study concluded that VNS is not likely to have any clinically meaningful effect in essential tremor treatment.

Vagus Nerve Stimulation as a Treatment of Headaches
Drawing on the analgesic effects noted with VNS in the treatment of depression, Mauskop evaluated VNS in 5 patients with severe, refractory chronic cluster and migraine headaches. (16) Mauskop reported excellent results in 1 patient who was able to return to work and significant improvement in 2 patients. Other than nausea developed by 1 patient, VNS was well tolerated. However, this study is too small to draw conclusions on the effects of VNS for the treatment of headache, and further study is needed.

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2006 Update
Based on Blue Cross Blue Shield National policy 7.01.20 issued 10/06. The policy was updated with June 2006 TEC Assessment (treatment-resistant depression) and literature review for other indications; policy statement is unchanged.

Review of the literature for the period of June 2005 through July 2006 did not locate any studies which would alter the conclusions or policy statements for use of VNS for other indications.

Medicare coverage policy notes that “Clinical evidence has shown that vagus nerve stimulation is safe and effective treatment for patients with medically refractory partial onset seizures, for whom surgery is not recommended or for whom surgery has failed. Vagus nerve stimulation is not covered for patients with other types of seizure disorders which are medically refractory and for whom surgery is not recommended or for whom surgery has failed.”

NOTE: Refer to Medical Policy #38 for references/rationale of BCBSA national policy 7.01.20 specific to VNS for treatment resistant depression.

[40] Based on Blue Cross Blue Shield National policy 7.01.25, Spinal Cord Stimulation.

Rationale
The bulk of published literature regarding spinal cord stimulation (SCS) consists of case series. In a systematic literature synthesis of these studies, Turner and colleagues reported that in patients with chronic low back pain, an average of 59% of patients had 50% or greater pain relief. (1)

Preliminary results of a randomized controlled trial reported that a significantly greater proportion of patients initially randomized to repeat lumbosacral surgery opted to cross over to the spinal cord stimulation arm of the trial, compared to those initially in the spinal cord stimulation of the trial crossing over to lumbosacral surgery. (2) A prospective multicenter study of spinal cord stimulation in 219 patients with chronic back and extremity pain reported successful management of pain in 55% of patients. (3) Most recently, Kemler and colleagues reported on favorable outcomes of SCS among patients with chronic reflex sympathetic dystrophy who were randomized to the SCS arm, as compared to those treated with physical therapy alone. (4) The favorable outcomes were still present at 2 years' follow-up. (5)

2005 Update
A literature search was performed on the MEDLINE database for the period of 1998 through June 2005, with a specific focus on spinal cord stimulation (SCS) as a treatment of limb ischemia.

Critical limb ischemia is described as pain at rest or the presence of ischemic limb lesions. If the patient is not a suitable candidate for limb revascularization (typically due to insufficient distal runoff), it is estimated that amputation will be required in 60%–80% of these patients within a year. Spinal cord stimulation has been investigated in this small subset of patients as a technique to relieve pain and decrease the incidence of amputation. Klomp and colleagues conducted a study that randomized 120 patients with critical limb ischemia not suitable for vascular reconstruction to undergo either best medical care or medical care in addition to spinal cord stimulation. The primary endpoint was limb survival at 2 years. (6) Amputation-free survival was not improved nor was the risk of major amputation significantly reduced. Both groups also reported similar levels of pain reduction. In both groups, the rates of amputation were highest within the first 3 months of the study, reflecting the limitations with both treatment options.

References:

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2. Burchiel KJ, Anderson VC, Brown FD et al. Prospective, multicenter study of spinal cord stimulation for relief of chronic back and extremity pain. Spine 1996; 21(23):2786-94.
3. North RB, Kidd DH, Lee MS et al. A prospective, randomized study of spinal cord stimulation versus reoperation for failed back surgery syndrome: initial results. Stereotact Funct Neurosurg 1994; 62(1-4):267-72.
4. Kemler MA, Barendse GA, van Kleef M et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. N Engl J Med 2000; 343(9):618-24.
5. Kemler MA, De Vet HC, Barendse GA et al. The effect of spinal cord stimulation in patients with chronic reflex sympathetic dystrophy: two years' follow-up of the randomized controlled trial. Ann Neurol 2004; 55(1):13-8.
6. Klomp HM, Spincemaille GH, Steyerberg EW et al. Spinal cord stimulation in critical limb ischemia: a randomized trial. Lancet 1999; 353(9158):1040-4.
7. Ubbink DT, Vermeulen H. Spinal cord stimulation for non-reconstructable chronic critical leg ischaemia. Cochrane Database Syst Rev 2005; 3:CD004001.
8. Klomp HM, Steyerberg EW, van Urk H et al. ESES Study Group. Spinal cord stimulation is not cost-effective for non-surgical management of critical limb ischaemia. Eur J Vasc Endovasc Surg. 2006; 31(5):500-8.
9. The British Pain Society. Spinal cord stimulation for the management of chronic pain: Recommendations for best clinical practice. http://www.britishpainsociety.org/SCS 2005.pdf .

2006 Update

A search of the MEDLINE database was performed for the period of January 2005 through September 2006 with a focus on SCS as a treatment of limb ischemia. There are no new clinical studies on this topic.

A systematic review from the Cochrane group on use in peripheral vascular diseases was updated in 2005. Included were 6 European studies of generally good quality with a total of 444 patients. (7) None of the studies were blinded due to the nature of the treatment. At 12 months' follow-up, limb salvage improved by 11% compared with any form of conservative treatment with a number needed to treat (NNT) of 9. The SCS patients required significantly less analgesics, and more patients reached Fontaine stage II than in the conservative group. There was no difference in ulcer healing. The overall risk of complications or additional SCS treatment was 17%, with a number needed to harm (NNH) of 6. The report concludes that there is evidence to favor SCS over standard conservative treatment to improve salvage and clinical situation in patients with critical leg ischemia and that, "The benefits of SCS against the possible harm of relatively mild complications and costs must be considered." Analysis of data and cost calculations from a previously published study (6) showed that the difference in amputation rate at 12 months was no longer present at 24 months. (8) There was no difference in survival rate at 24 months.

Evidence supports a decrease in pain with a short-term decrease in limb amputations following treatment with SCS. Complications include the need for operative repositioning procedures. There is no scientific evidence for improvement in pain and limb salvage at an endpoint of 24 months.

The use of SCS for other conditions such as visceral pain has been reported. The British Pain Society recommends that its use in this and other emerging indications be carefully audited (9).