

Deep Brain Stimulation

Effective: January 1, 2019

Next Review: March 2019

Last Review: December 2018

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Deep brain stimulation (DBS) involves the stereotactic placement of an electrode into the brain (i.e., hypothalamus, thalamus, globus pallidus or subthalamic nucleus [STN]).

MEDICAL POLICY CRITERIA

Notes:

- The use of spinal cord stimulation as a treatment of chronic pain is addressed in a separate policy (see Cross References section below).
 - This policy only applies to initial placement. This policy does not apply to revision(s) and replacement(s) after implantation.
- I. When a multidisciplinary evaluation has confirmed both the medical intractability of the patient's symptoms and the potential value of deep brain stimulation (DBS), unilateral or bilateral DBS may be considered **medically necessary** when **both** of the following criteria (A and B) are met:
- A. One of the following is met:
1. The request is for stimulation of the thalamus in patients with disabling, medically unresponsive tremor due to essential tremor or Parkinson's

disease. Disabling, medically unresponsive tremor defined as tremor causing significant limitation in daily activities AND inadequate symptom control despite optimal medical management for at least three months before implant.

2. The request is for stimulation of the subthalamic nucleus or globus pallidus in patients with previously levodopa-responsive Parkinson's disease and symptoms such as rigidity, bradykinesia, dystonia or levodopa-induced dyskinesias.
3. The request is for stimulation of the subthalamic nucleus or globus pallidus in patients seven years of age or above with disabling, medically unresponsive primary dystonias including generalized and/or segmental dystonia, hemidystonia and cervical dystonia (torticollis). Disabling, medically unresponsive dystonia defined as dystonia causing significant limitation in daily activities AND inadequate symptom control despite optimal medical management for at least three months before implant.

B. The patient does not have any of the following contraindications:

1. Patients who are not good surgical risks because of comorbid medical problems or because of the presence of a cardiac pacemaker; and
2. Patients who have medical conditions that require repeated MRI; and
3. Patients who have dementia that may interfere with the ability to cooperate.

II. Deep brain stimulation is considered **investigational** for all other conditions (see Policy Guidelines).

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and physical/chart notes
- Multidisciplinary evaluations
- Indication for DBS

Deep brain stimulation is considered investigational for indications that do not meet the policy criteria above including but not limited to the following:

- Cerebral Palsy
- Chronic pain (e.g., nociceptive pain; neuropathic pain)
- Cognitive decline/dementia due to Parkinson's Disease
- Epilepsy/intractable seizures
- Huntington's disease
- Multiple sclerosis
- Neuropsychiatric applications, including but not limited to the following:

- Tourette syndrome
- Depression
- Bipolar Disorder
- Obsessive-compulsive disorder
- Schizophrenia
- Anxiety
- Anorexia nervosa
- Other movement disorders
- Post-traumatic tremor
- Tardive dyskinesia and tardive dystonia
- Traumatic brain injury (TBI)

CROSS REFERENCES

1. [Dopamine Transporter Single-Photon Emission Computed Tomography \(DAT-SPECT\)](#), Radiology, Policy No. 57
2. [Spinal Cord and Dorsal Root Ganglion Stimulation](#), Surgery, Policy No. 45
3. [Implantable Peripheral Nerve Stimulation for Chronic Pain of Peripheral Nerve Origin](#), Surgery, Policy No. 205

BACKGROUND

Deep brain stimulation (DBS) involves the stereotactic placement of an electrode into the brain (i.e., hypothalamus, thalamus, globus pallidus or subthalamic nucleus [STN]). The electrode is initially attached to a temporary transcutaneous cable for short-term stimulation to validate treatment effectiveness. Several days later the patient returns to surgery for permanent subcutaneous implantation of the cable and a radiofrequency-coupled or battery-powered programmable stimulator. The electrode is typically implanted unilaterally on the side corresponding to the more severe symptoms. However, the use of bilateral stimulation using two electrode arrays is also used in patients with bilateral, severe symptoms.

After implantation, noninvasive programming of the neurostimulator can be adjusted to the patient's symptoms. This feature may be important for patients with Parkinson's disease, whose disease may progress over time, requiring different neurostimulation parameters. Setting the optimal neurostimulation parameters may involve the balance between optimal symptom control and appearance of side effects of neurostimulation, such as dysarthria, disequilibrium or involuntary movements.

DBS has been investigated for a variety of indications as discussed below:

- Alternative to permanent neuroablative procedures, such as thalamotomy and pallidotomy

The technique has been most thoroughly investigated as an alternative to thalamotomy for unilateral control of essential tremor, and tremor associated with Parkinson's disease (PD). More recently, there has been research interest in the use of deep brain stimulation of the globus pallidus or STN as a treatment of other Parkinsonian symptoms such as rigidity, bradykinesia or akinesia. Another common morbidity associated with PD is the occurrence of motor fluctuations, referred to as "on and off" phenomena, related to the maximum effectiveness of drugs (i.e., the "on" state) and the nadir response during drug troughs (i.e., the "off" state). In addition, levodopa, the most commonly used antiparkinson drug, may be associated with disabling drug-induced

dyskinesias. Therefore, the optimal pharmacologic treatment of Parkinson's disease may involve a balance between optimal effects on Parkinson's symptoms vs. the appearance of drug induced dyskinesias. The effect of DBS on both Parkinson's symptoms and drug-induced dyskinesias has also been studied.

- Treatment of primary and secondary dystonia

Dystonia is defined as a neurological movement disorder characterized by involuntary muscle contractions, which force certain parts of the body into abnormal, contorted, and painful movements or postures. In primary dystonia, dystonia is the only symptom and is unassociated with other pathology. Secondary dystonia is a dystonia brought on by an inciting event, such as a stroke, trauma, or drugs. Tardive dystonia is a form of drug-induced secondary dystonia. Dystonia can be classified according to age of onset, bodily distribution of symptoms, and cause. Age of onset can occur during childhood or during adulthood. Dystonia can affect certain portions of the body (focal dystonia and multifocal dystonia) or the entire body (generalized dystonia). Torticollis is an example of a focal dystonia. Treatment options for dystonia include oral or injectable medications (i.e., botulinum toxin) and destructive surgical or neurosurgical interventions (i.e., thalamotomies or pallidotomies) when conservative therapies fail.

- Cluster headaches

Cluster headaches occur as episodic attacks of severe pain lasting from 30 minutes to several hours. The pain is usually unilateral and localized to the eye, temple, forehead, and side of the face. Autonomic symptoms that occur with cluster headaches include ipsilateral facial sweating, flushing, tearing, and rhinorrhea. Cluster headaches occur primarily in men and have been classified as vascular headaches that have been associated with high blood pressure, smoking, and alcohol use. However, the exact pathogenesis of cluster headaches is uncertain. PET scanning and MRI have shown the hypothalamic region may be important in the pathogenesis of cluster headaches. Alterations in hormonal/serotonergic function may also play a role. Treatment of cluster headaches includes pharmacologic interventions for acute episodes and prophylaxis, sphenopalatine ganglion (SPG) blockade and surgical procedures such as percutaneous SPG radiofrequency rhizotomy and gamma knife radiosurgery of the trigeminal nerve.

- Other Neurologic/Psychiatric Conditions

The role of DBS in treatment of other treatment-resistant neurologic and psychiatric disorders, particularly Tourette syndrome, epilepsy, obsessive-compulsive disorder (OCD), major depressive disorders, bipolar disorder, anorexia, and alcohol addiction, is also being investigated. Ablative procedures are irreversible and, though they have been refined, remain controversial treatments for intractable illness. Interest has shifted to neuromodulation through DBS of nodes or targets within neural circuits involved in these disorders. Currently, a variety of target areas are being studied.

REGULATORY STATUS

The U.S. Food and Drug Administration (FDA) has approved the Activa® Tremor Control System (Medtronic Corp.) for deep brain stimulation. The Activa® Tremor Control System and the Activa® Dystonia Therapy System consist of the following components:

1. The implantable pulse generator
2. The deep brain stimulator lead
3. An extension that connects the lead to the power source
4. A console programmer
5. A software cartridge to set electrical parameters for simulation
6. A patient control magnet, which allows the patient to turn the pulse generator on and off or change between high and low settings

In February 2009, the FDA approved deep brain stimulation with the Reclaim device (Medtronic, Inc.) via the Humanitarian Device Exemption (HDE) process for the treatment of severe obsessive-compulsive disorder (OCD).

In June 2015, the FDA approved deep brain stimulation with the Brio Neurostimulation System, (St. Jude Medical) under the Premarket Approval Application (PMA) process (#P140009) for the following conditions:^[1]

- Bilateral stimulation of the subthalamic nucleus (STN) as an adjunctive therapy to reduce some of the symptoms of advanced levodopa-responsive Parkinson's disease that are not adequately controlled by medications.
- Unilateral or bilateral stimulation of the ventral intermediate nucleus (VIM) of the thalamus for the suppression of disabling upper extremity tremor in adult essential tremor patients whose tremor is not adequately controlled by medications and where the tremor constitutes a significant functional disability.

In September 2016, the FDA approved the St. Jude Medical Infinity™ Deep Brain Stimulation (DBS) system under the PMA process (#P140009/S001) for the same indications above. The directional leads enable the clinician to “steer” current to different parts of the brain. This tailored treatment reduces side effects. The Infinity system can be linked to Apple's iPod Touch and iPad Mini.

In December 2017, a second system with directional leads, the Vercise Deep Brain Stimulation System (Boston Scientific), was approved by FDA. This system is to be used as an adjunctive therapy from reducing motor symptoms of moderate-to-advanced levodopa-responsive PD inadequately controlled with medication alone.

EVIDENCE SUMMARY

The principal outcome for deep brain stimulation (DBS) for any indication is symptom reduction and improved function. Assessment of the safety and efficacy of DBS requires well-designed and well-executed randomized controlled trials (RCTs) comparing DBS with sham or on-versus off- phases to determine the following:

- whether the benefits of DBS outweigh any risks
- whether DBS offers advantages over conventional treatments.

The evidence base is sufficient that deep brain stimulation (DBS) improves the net health outcomes of selected patients with symptoms related to Parkinson's disease, essential tremor,

or primary dystonias. DBS has become a standard of care for these patients and may be considered medically necessary when criteria are met. Therefore, the evidence for DBS for these indications will not be reviewed in this policy. Below is a brief synopsis of the evidence for Parkinson's disease, essential tremor, or primary dystonias.

SYMPTOMS ASSOCIATED WITH PARKINSON'S DISEASE

Systematic Reviews and Technology Assessments

The policy for PD and tremor was initially based on two BlueCross BlueShield Association Technology Evaluation Center (TEC) Assessments; a 1997 TEC Assessment focused on unilateral deep brain stimulation of the thalamus as a treatment for tremor^[2] and a 2001 TEC Assessment focused on the use of deep brain stimulation of the globus pallidus and subthalamic nucleus for a broader range of Parkinson symptoms.^[3]

A number of large systematic reviews have been published on the use of DBS for PD and tremor^[4-13] confirming the efficacy of DBS in the control of motor signs and improvement of patients' functionality and quality of life.

Randomized Controlled Trials

There have been additional published RCTs of deep brain stimulation for PD, which continue to report overall positive results^[14-22]. Some of these trials suggest that subthalamic stimulation was superior to medical therapy in patients with Parkinson's disease and early motor complications, while others did not find significant differences in overall health outcomes for patients. Surgery related adverse effects addressed in these RCTs indicate that the most common adverse effect is infection.

Nonrandomized Studies

Two new DBS systems with directional leads are currently available (approved by the Food and Drug Administration [FDA] in 2016 and 2017). Directional leads potentially enable clinicians to target more specific areas of the brain to be treated with the direct current. Published evidence consists of several small observational studies, with sample sizes ranging from 7 to 13.^[23-26] The studies showed that patients experienced improved tremor scores and improved quality of life (QOL). Compared with historical data from conventional DBS systems, directional DBS widened the therapeutic window and achieved beneficial effects using lower current level. Comparative, larger studies are needed to support the conclusions from these small studies. Data from a large study of 292 patients are expected in 2018.

PRIMARY DYSTONIA

DBS for the treatment of primary dystonia received FDA approval through the Humanitarian Device Exemption (HDE) process.^[27] The HDE approval process is available for those 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. As noted in the FDA's analysis of risk and probable benefit, the only other treatment options for chronic refractory primary dystonias are neurodestructive procedures. DBS 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 onset of dystonia occurs prior to the individual reaching their full adult size, the disease not only can affect normal psychological 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 DBS for dystonia appear to be similar to the risk associated with the performance of stereotactic surgery and the implantation of DBS systems for currently approved indications Parkinson's Disease and Essential Tremor), except when used in either child or adolescent patient groups.”

The FDA HDE approval was based on the results of DBS in 201 patients represented in 34 manuscripts. There were three studies that reported at least ten cases. Clinical improvement ranged from 50 to 88%. A total of twenty-one pediatric patients were studied; 81% were older than seven years. Among these patients there was approximately a 60% improvement in clinical scores.

Since the FDA approval, there have been additional published randomized controlled trials of deep brain stimulation for dystonia, which continue to report positive results.^[28-30] These trials included one with a long-term follow-up of five years. Two of the trials reported on the serious adverse effects of DBS, the majority of which were related to the implantation procedure. Dysarthria, involuntary movements and depression were common non-serious adverse events reported.

In 2017, Moro published a systematic review of literature published through November 2015 on primary dystonia (also known as isolated dystonia).^[31] Reviewers included studies with at least 10 cases. Fifty-eight articles corresponding to 54 unique studies were identified; most involved bilateral DBS of the GPi. There were only two controlled studies, one RCT (described below) and 1 study that included a double-blind evaluation with and without stimulation. Twenty-four studies reported data using the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) and were included in a meta-analysis. These studies enrolled a total of 523 patients (mean per study, 22 patients) and had a mean follow-up of 32.3 months (range, 6-72 months). In a pooled analysis of BFMDRS motor scores (scale range, 0-120) from 24 studies, the mean increase in scores at six months compared with baseline was 23.8 points (95% CI, 18.5 to 29.1 points). The mean increase in the motor score at last follow-up compared with baseline was 26.6 points (95% CI, 22.4 to 30.9 points). The mean percentage improvement was 59% at six months and 65% at last follow-up. Fourteen studies reported BFMDRS disability scores (scale range, 0-30). Compared with baseline, the mean absolute change in the score was 4.8 points (95% CI, 3.1 to 6.6 points) at six months and 6.4 points (95% CI, 5.0 to 7.8 points) at last follow-up. The mean percentage improvement was 44% at six months and 59% at last follow-up.

The remaining literature review below will focus on the use of DBS for the investigational indications in this policy.

TARDIVE DYSKINESIA AND TARDIVE DYSTONIA

Systematic Review

Tardive dyskinesia and dystonia (TDD) are severe side effects of dopamine-blocking agents, particularly antipsychotics. Little is known about the possible psychiatric complications of DBS in psychiatric patients. The mean improvement of TDD of the combined patients 3 to 76 months after implantation was 77.5% (95% CI, 71.4%-83.3%; $P < .000$) on the Burke-Fahn-

Marsden Dystonia Rating Scale.^[32] The data suggest DBS could be effective and relatively safe for patients with treatment-resistant TDD; however, these results should be interpreted with caution, as most of the data are from case reports and small trials.

Mentzel performed a systematic review to assess the effects and side-effects of deep brain stimulation (DBS) in patients that have developed a severe debilitating treatment-resistant form of TDD.^[33] This review included 19 case-reports and small-scale trials without randomization or blinding (N= 52 patients). Using the Burke Fahn Marsden Dystonia Rating Scale (BFMDRS), the Abnormal Involuntary Movement Scale (AIMS) and the Extrapyrimal Symptoms Rating Scale (ESRS), the investigators assessed the average improvement in the patients' condition, reporting that improvement as a result of DBS was statistically significant ($p < 0.00001$) on all scales. However, limited conclusions can be drawn from this review on the efficacy and safety of DBS in this population, since there were no randomized controlled trials identified.

Randomized Controlled Trials

Stimulation of the globus pallidus has been examined as a treatment of tardive dyskinesia in a phase II double-blinded (presence and absence of stimulation) multicenter study.^[34] The trial was stopped early due to successful treatment (greater than 40% improvement) in the first 10 patients.

No comparative trials were found for DBS for tardive dystonia.

Nonrandomized Studies

Pouclet-Courtemanche (2016) reported on a case series of 19 patients with severe pharmaco-resistant tardive dyskinesia treated with DBS.^[35] Patients were assessed after 3, 6, and 12 months after bilateral globus pallidus stimulation. At six months, all patients had experienced greater than 40% reduction in symptoms as measured on the Extrapyrimal Symptoms Rating Scale (ESRS). At 12 months, the mean decrease in ESRS score was 58% (range, 21%-81%). An additional small (n=9) case series reported improvement in motor and disability scores.^[36]

CEREBRAL PALSY

Koy (2013) reported data on the therapeutic outcomes of DBS in cerebral palsy.^[37] Twenty articles comprising 68 patients with cerebral palsy undergoing deep brain stimulation assessed by the Burke-Fahn-Marsden Dystonia Rating Scale were identified. Most articles were case reports reflecting great variability in the score and duration of follow-up. The mean Burke-Fahn-Marsden Dystonia Rating Scale movement score was 64.94 ± 25.40 preoperatively and dropped to 50.5 ± 26.77 postoperatively, with a mean improvement of 23.6% ($P < .001$) at a median follow-up of 12 months. The mean Burke-Fahn-Marsden Dystonia Rating Scale disability score was 18.54 ± 6.15 preoperatively and 16.83 ± 6.42 postoperatively, with a mean improvement of 9.2% ($P < .001$). There was a significant negative correlation between severity of dystonia and clinical outcome ($P < .05$). Authors suggest DBS can be an effective treatment option for dyskinetic cerebral palsy. In view of the heterogeneous data, a prospective study with a large cohort of patients in a standardized setting with a multidisciplinary approach would be helpful in further evaluating the role of deep brain stimulation in cerebral palsy.^[38]

EPILEPSY/INTRACTABLE SEIZURES

DBS has been investigated for the treatment of intractable seizures in patients who are not surgical candidates. To date studies show promise but these early reports of therapeutic success are not confirmed by controlled clinical trials. Questions regarding the best structures to stimulate, the most effective stimuli, and the contrasting effects of high-frequency and low-frequency stimulation remain unanswered.

Systematic Review

Two systematic reviews published in 2018 on the use of DBS for drug-resistant epilepsy assessed many of the same studies. The larger review, by Li (2018), identified 10 RCTs and 48 uncontrolled studies.^[39] The literature search date was not reported. Meta-analyses were not performed. Summaries of the studies were discussed by area of the brain targeted by DBS. A review of the studies showed that DBS might be effective in reducing seizures when DBS targets the anterior nucleus of the thalamus or the hippocampus. Across studies, more than 70% of patients experienced a reduction in seizures by 50% or more. However, there were very few RCTs and the observational studies had small sample sizes. Individual responses varied, depending on seizure syndrome, presence or absence of structural abnormalities, and electrode position. Results were inconclusive when DBS targeted the centromedian nucleus of the thalamus, the cerebellum, and the subthalamic nuclei. Safety data on DBS was limited due to the small population sizes. The RCT in which DBS targeted the anterior nucleus of the thalamus (Fisher [2010] described below) reported paresthesias (23%), implant site pain (21%), and implant site infection (13%). Reviewers concluded that more robust clinical trials would be needed.

In a 2014 Cochrane review, updated in 2017, the safety, efficacy and tolerability of DBS and cortical stimulation were assessed in patients with refractory epilepsy.^[40,41] The reviews included RCTs comparing DPS to sham stimulation, resective surgery or further treatment with antiepileptic drugs. Of the 10 RCTs identified for inclusion in the 2014 review, three trials were specific to DBS (1 anterior thalamic DBS trial, n=109 treatment periods; two centromedian thalamic DBS trials, n=20, 40 treatment periods). The studies added in the 2017 update were a cross-over RCT of bilateral anterior thalamic stimulation (n=4) and a double blind RCT of hippocampal stimulation (n=6) that was not included in the meta-analysis due to missing detailed methodology. The primary outcome measures included the proportion of patients who were disease free and a 50% or greater reduction in seizure frequency after 1-3 months. The evidence was rated as moderate quality and no statistical or clinically significant differences were reported based upon the primary outcome measures. Authors concluded that there is insufficient evidence upon which to draw conclusions regarding the efficacy and safety of hippocampal DBS or centromedian DBS as a treatment for epilepsy.

Randomized Controlled Trials

Troster (2017) assessed neuropsychological adverse events from the SANTE trial during the three-month blinded phase, and at seven-year follow-up during the open-label noncomparative phase.^[42] At baseline, there were no differences in depression history between groups. During the three-month blinded phase of the trial, depression was reported in eight (15%) patients from the stimulation group and in one (2%) patient from the no stimulation group (p=0.02). Memory adverse events also occurred at significantly different rates between the treatment groups during the blinded phase (seven in the active group, one in the control group; p=0.03). At seven-year follow-up, after the treatment groups had been combined, there was no

statistically significant difference in Profile of Mood State depression score compared with baseline and most cognitive function tests did not improve over baseline measurements.

Cukiert (2017) conducted a double-blind, placebo-controlled randomized trial evaluating 16 patients with refractory temporal lobe epilepsy.^[43] Prior to treatment, all patients had focal impaired awareness seizures (FIAS, complex partial seizures), and 87% had focal aware seizures (FAS, simple partial seizures). All patients underwent DBS device implantation, and were followed for six months. Patients were seen weekly to receive the treatment or placebo. To maintain double-blind status, programming was performed by a nontreating assistant. Patients kept a seizure diary during the study period. Patients were considered seizure-free if no seizures occurred during the last 2 months of the trial. Responders were defined as patients experiencing a reduction of 50% or more in frequency reduction. There was a significant difference in FIAS frequency from the first month of full stimulation until the end of the blinded phase ($p < 0.001$) and FAS frequency for the same period except for the third month of the blinded phase.

Fisher (2010) reported results of a multicenter, RCT of bilateral stimulation of the anterior nuclei of the thalamus for epilepsy (SANTE).^[44] Fisher randomized patients who had failed at least three antiepileptic drugs to one of two groups, stimulation on or stimulation off. This was a 3-month double blind phase. After this phase, all patients received unblinded stimulation. During the first and second months of the blinded phase, the difference in seizure reduction between stimulation on and stimulation off was not significantly different (-42.1% vs. -28.7%, respectively). In the last month of the blinded phase, the stimulated group had a significantly greater reduction in seizures compared with the control group (-40.4% vs. -14.5%, respectively $p = 0.0017$). During the blinded phase, the stimulation group experienced significantly fewer seizure-related injuries than patients in the control group (7.4% vs. 25.5%, respectively $p = 0.01$). Cognition and mood showed no group differences, but participants in the stimulated group were more likely to report depression (8 vs. 1, respectively) or memory problems (7 vs. 1, respectively) as adverse events. Depression symptoms resolved in four of the eight stimulated patients over an average of 76 days (range 14-145). There was a progressive reduction in seizure frequency over long-term follow-up. On intention-to-treat analysis, the median change in seizure frequency was -44% at 13 months and -57% at 25 months. By two years, 54% of patients had a seizure reduction of at least 50%, and 14 patients (13%) were seizure-free for at least six months. The most common device-related adverse events were paresthesias in 18.2% of participants, implant site pain in 10.9%, and implant site infection in 9.1%. Eighteen participants (16.4%) withdrew from the study after the implantation because of adverse events. There were five deaths, none of which were considered to be device-related. Although some patients appeared to have benefited from treatment during the extended follow-up phase, the difference between groups in the blinded portion of the study, while significant, was modest.

Thalamic stimulation for epilepsy is approved in several countries, but not presently in the U.S. Additional studies are needed to establish its role in treating patients with epilepsy and intractable seizures.

Nonrandomized Studies

Kim (2017) conducted a retrospective chart review of 29 patients with refractory epilepsy treated with DBS.^[45] Patients' mean age was 31 years, they had had epilepsy for a mean of 19 years, and had a mean preoperative frequency of tonic-clonic seizures of 27 per month. Mean

follow-up was 6.3 years. Median seizure reduction from baseline was 71% at year one, 74% at year two and ranged from 62% to 80% through 11 years of follow-up. Complications included one symptomatic intracranial hemorrhage, one infection requiring removal and reimplantation, and two lead disconnections.

Long-term outcomes of the SANTE trial, described above, were reported by Salanova in 2015.^[46] The uncontrolled open-label portion of the trial began after three months and, beginning at 13 months, stimulation parameters could be adjusted at the clinician's discretion. Of the 110 implanted patients, 105 (95%) completed the 13-month follow-up, 98 (89%) completed the three-year follow-up, and 83 (75%) completed five years. Among patients with at least 70 days of diary entries, the median change in seizure frequency from baseline was 41% at one year and 69% at five years ($p < 0.001$ for both). During the study, 39 (35%) of 110 patients had a device-related serious adverse event, most of which occurred in the first several months after implantation. The most frequently reported serious adverse events were implant site infection (10% of patients) and lead(s) not within target (8.2% of patients). Seven deaths occurred during the study and none were considered to be device-related. Depression was reported in 41 (37%) patients over the study; in three cases, this was considered device-related. Memory impairment (nonserious) was reported in 30 (27%) patients during the study, half of which had a history of the condition. Although some patients appear to have benefited from treatment during the extended follow-up phase, the difference between groups in the blinded portion of the study, while significant, was overall modest.

TRAUMATIC BRAIN INJURY

Central thalamic deep brain stimulation (CT-DBS) has been investigated as a therapeutic option to improve behavioral functioning in patients with severe traumatic brain injury (TBI)^[38]; however, there are no RCTs for this indication.

NEUROPSYCHIATRIC APPLICATIONS

In addition to the areas of research discussed above, DBS is being investigated for the treatment of Tourette syndrome, depression, addiction, alcohol addiction, anorexia, and obsessive compulsive disorder.^[47] Evidence remains insufficient to evaluate the efficacy of DBS for these disorders.^[48]

Tourette Syndrome

Systematic Reviews

Baldermann conducted a systematic review that included 57 studies on DBS for Tourette syndrome, four of which were randomized crossover studies. The studies included a total of 156 cases.^[49] Twenty-four studies included a single patient each and four had sample sizes of 10 or more (maximum, 18). Half of the patients ($n=78$) were stimulated in the thalamus and the next most common areas of stimulation were the global pallidus internus anteromedial part ($n=44$) and postventrolateral part ($n=20$). Two of the RCTs used thalamic stimulation, one used bilateral globus pallidus stimulation, and one used both. The primary outcome was the Yale Global Tic Severity Scale (YGTSS). In a pooled analysis of within subject pre-post data, there was a median improvement of 53% in the YGTSS, a decline from a median score of 83 to 35 at last follow-up. Moreover, 81% of patients showed at least a 25% reduction in the YGTSS and 54% and more than a 50% improvement. In addition, data were pooled from the four crossover RCTs; there were a total of 27 patients receiving DBS and 27 receiving a

control intervention. Targets included the thalamus and the globus pallidus. In the pooled analysis, there was a statistically significant between-group difference, favoring DBS (SMD=0.96; 95% CI, 0.36 to 1.56). The authors noted that the effect size of 0.96 is considered to be a large effect.

A 2012 systematic review by Pansaon identified 25 published studies, representing data from 69 patients that reported on the efficacy of DBS in the treatment of Tourette syndrome.^[50] However, only three studies with methodological quality ratings of fair to poor met the inclusion criteria for evidence-based analysis. The authors recommend that DBS continues to be considered an experimental treatment for severe, medically refractory tics.

Randomized Controlled Trials

Kefalopoulou (2015) reported on double-blind crossover trial that included 15 patients with severe medically refractory Tourette syndrome.^[51] They received surgery for bilateral globus pallidus internus DBS and were randomized to the off-position first or the on-position first for three months followed by the opposite position for the next three months. Fifteen patients underwent surgery 14 were randomized and 13 completed assessments after both on- and off-phases. For the 13 study completers, the mean YGTSS scores were 80.7 (SD=12.0) in the off-stimulation phase and 68.3 (SD=18.6) in the on-stimulation phase. Mean difference in YGTSS scores was 12.4 (95% CI, 0.1 to 24.7) which was statistically significant ($p=0.048$) after Bonferroni correction. There was no between-group difference in YGTSS scores in patients who were randomized to the on-phase first or second. Three serious adverse events were reported, two related to surgery and one related to stimulation. The authors noted that the most effective target for DBS in Tourette syndrome patients needs additional study.

Piedad (2012) analyzed patient and target selection for DBS of Tourette syndrome. The majority of clinical trials for DBS in Tourette syndrome have targeted the medial thalamus at the crosspoint of the centromedian nucleus, substantia periventricularis, and nucleus ventro-oralis internus.^[52] Other targets that have been investigated include the subthalamic nucleus, caudate nucleus, globus pallidus internus, and the anterior limb of the internal capsule and nucleus accumbens. The review found no clear consensus in the literature for the best target or for which patients should be treated. Additional study is needed to clarify these issues.

In 2011, Ackermans reported preliminary results of a double-blind crossover trial of thalamic stimulation in six patients with refractory Tourette syndrome.^[53] Tic severity during three months of stimulation was significantly lower than during the three months with the stimulator turned off, with a 37% improvement on the Yale Global Tic Severity Scale (mean 25.6 vs. 41.1) and a decrease in tic severity of 49% at one year after surgery compared to preoperative assessments (mean 21.5 vs. 42.2 – both respectively). Secondary outcomes (change in associated behavioral disorder and mood) were not altered by the stimulation. Serious adverse events included one small hemorrhage ventral to the tip of the electrode, one infection of the pulse generator, subjective gaze disturbances, and reduction of energy levels in all patients. The interim analysis led to the termination of the trial. The authors commented that further RCTs on other targets are urgently needed since the search for the optimal one is still ongoing.

Depression

Systematic Reviews

In a recent systematic review, the literature was identified and reviewed for research findings related to treatment-resistant BD.^[54] Therapeutic trials for treatment-resistant bipolar mania are uncommon, and provide few promising leads other than the use of clozapine. Far more pressing challenges are the depressive-dysthymic-dysphoric-mixed phases of BD and long-term prophylaxis. Therapeutic trials for treatment-resistant bipolar depression have assessed various pharmacotherapies, behavioral therapies, and more invasive therapies including electroconvulsive therapy (ECT), transcranial magnetic stimulation, and deep brain stimulation—all of which are promising but limited in effectiveness. Most studies identified in the review were small, involved supplementation of typically complex ongoing treatments, varied in controls, randomization, and blinding, usually involved brief follow-up, and lacked replication. Clearer criteria for defining and predicting treatment resistance in BD are needed, as well as improved trial design with better controls, assessment of specific clinical subgroups, and longer follow-up. Due to significant limitations within literature the effectiveness of DBS for bipolar treatment is not known at this time.

Randomized Controlled Trials

In 2016, a crossover RCT evaluating active and sham phases of DBS stimulation in patients with treatment-resistant depression was published by Bergfeld.^[55] Twenty-five patients were enrolled. Prior to the randomized phase, all patients received 52 weeks of open-label DBS treatment with optimization of the settings. Optimization ended when patients achieved a stable response of at least four weeks or after the 52-week period ended. At the end of the open-label phase, 10 (40%) patients were classified as responders ($\geq 50\%$ decrease in the Hamilton Depression Rating Scale [HAM-D] score) and 15 (60%) patients were classified as nonresponders. After the 52 weeks of open-label treatment, patients underwent six weeks of double-blind active and sham stimulation. Sixteen (64%) of 25 enrolled patients participated in the randomized phase (nine responders, seven nonresponders). Nine patients were prematurely crossed over to the other intervention. Among all 16 randomized patients, HAM-D scores were significantly higher at the end of the active stimulation phase (mean HAM-D score, 16.5) than the sham stimulation phase (mean HAM-D score, 23.1; $p < 0.001$). Mean HAM-D scores were similar after active and sham phases in initial nonresponders (19.0 vs 23.0, respectively). Among initial responders, mean HAM-D score was 9.4 after active stimulation and 23 after sham stimulation. Trial limitations include a small number of patients in the randomized phase and potential bias from having an initial year of open-label treatment; patients who had already responded to DBS over a year of treatment were those who were likely to respond to active than sham stimulation in the double-blind randomized phase; findings may not be generalizable to treatment-resistant depressed patients who are DBS-naive.

Dougherty published an industry-sponsored, double-blind RCT evaluating DBS of the ventral capsule/ventral striatum in patients with chronic treatment resistant depression, including 30 patients with a major depressive episode lasting at least two years and inadequate response to at least four trials of antidepressant therapy.^[56] Participants were randomized to 16 weeks of active ($n=16$) versus sham ($n=14$) DBS, followed by an open-label continuation phase. One patient, who was assigned to active treatment, dropped out of the study during the blinded treatment phase. The primary outcome was clinical response at 16 weeks, defined as 50% or greater improvement from baseline on the Montgomery-Asberg Depression Rating Scale (MADRS). A response was identified in 3 (20%) of 15 patients in the active treatment group and 2 (14%) of 14 patients in the sham control group. The between-group difference in response was not statistically significant ($p=0.53$). During the blinded treatment phase,

psychiatric adverse events occurring more frequently in the active treatment group included worsening depression, insomnia, irritability, suicide ideation, hypomania, and mania. Psychiatric adverse events occurring more frequently in the sham control group were early morning awakening and purging. Findings of this study do not support the conclusion that DBS is effective for treating treatment-resistant depression.

Obsessive-compulsive Disorder

Systematic Reviews

Kisely conducted a systematic review and meta-analyses pooling study findings evaluating DBS for OCD, including only double-blind RCTs of active versus sham DBS.^[57] Five trials (total N=50 patients) met eligibility criteria and data on 44 patients were available for meta-analysis. Three were parallel group RCTs with or without a crossover phase and two were only crossover trials. The site of stimulation was the anterior limb of the internal capsule (3 studies), the nucleus accumbens (1 study) and the subthalamic nucleus (1 study). Duration of treatment ranged from 2 to 12 weeks. All studies reported scores on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). This is a 10-item scale in which higher scores reflect more intense symptoms, and a score of 24 or more (of a possible 40) is considered severe illness. Most studies designate a therapeutic response as a Y-BOCS reduction of 35% or more from the pretreatment baseline, with a reduction of 25-35% or more considered a partial response. Only one of the five studies reported proportion of responders Y-BOCS as an outcome measure and that study did not find a statistically significant difference between active and sham stimulation groups. All studies reported the outcome measure, mean reduction in Y-BOCS. When data from the five studies were pooled, there was a statistically significantly greater reduction in the mean Y-BOCS in the active versus sham group (mean difference, -8.49; 95% CI, 12.18 to -4.80). The outcome measure, however, does not allow conclusions on whether the difference between groups is clinically meaningful. Trial authors reported 16 serious adverse events including one cerebral hemorrhage and two infections requiring electrode removal. Additionally, nonserious transient adverse events were reported including 13 reports of hypomania, five of increase in depressive or anxious symptoms and six of headaches.

A 2015 systematic review and meta-analysis by Alonso included studies of any type (including case reports) evaluating DBS for OCD and reporting changes on the Y-BOCS.^[58] The authors identified 31 studies (total N=116 patients). They did not report study type (ie, controlled vs uncontrolled); however, the meta-analysis was only of patients who received active treatment. Twenty-four (77%) studies included 10 or fewer patients. Most studies (24, including 83 patients) involved DBS of striatal areas including the anterior limb of the interior capsule, the ventral capsule and ventral striatum, the nucleus accumbens or the ventral caudate nucleus. Of the remaining studies, five (27 patients) addressed subthalamic nucleus stimulation and two (6 patients) addressed stimulation of the inferior thalamic peduncle. Data were available from 14 studies (105 patients) on percentage of responders (ie, >35% reduction in posttreatment Y-BOCS scores). Twelve studies provided patient-level data. A pooled analysis yielded a global percentage of responders of 60% (95% CI, 49% to 69%). The most frequent adverse events reported were worsening anxiety (25 patients), disinhibition (23 patients), throbbing or flushing (12 patients) and feeling the extension leads (10 patients). The study reported benefits and risks of DBS stimulation but conclusions cannot be drawn about stimulation to any particular region or about the safety or efficacy of DBS for OCD compared with sham stimulation or an alternative therapy.

In 2014, the American Society for Stereotactic and Functional Neurosurgery and the Congress of Neurological Surgeons conducted a systematic review which served as the basis of their evidence-based guideline regarding DBS as a treatment of OCD.^[59] The group made the following conclusions:

1. There is Level I evidence, based on a single Level I study, for the use of bilateral subthalamic nucleus DBS for the treatment of medically refractory OCD.
2. There is Level II evidence, based on a single Level II study, for the use of bilateral nucleus accumbens DBS for the treatment of medically refractory OCD.
3. There is insufficient evidence to make a recommendation for the use of unilateral DBS for the treatment of medically refractory OCD.

However, the Level I and II evidence used to support the groups conclusions were based upon studies with small sample sizes (n=18, 16) which limit the ability to rule out the possibility of chance as an explanation of findings.

In 2011, de Koning published a systematic review of clinical trials for DBS for treatment resistant obsessive-compulsive disorder (OCD).^[60] Nine case studies and seven controlled studies with a blinded on-off phase were included. Inclusion criteria were use of the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) as an outcome measure, and “some estimate of efficacy” included in the study report. The authors concluded that DBS may be a beneficial and safe therapy for refractory OCD, but further research is needed to establish appropriate patient selection criteria, determine the more effective target location, and optimize postoperative patient management. Of note, the systematic review discussed the reported outcomes of the selected studies, but failed to critically appraise their quality.

Of the studies included in the systematic review:

- Nine case studies consisted of observational case reports of one to two patients, or small (<10 patients) non-comparative case series. Conclusions cannot be reached from these studies as randomized trials with an appropriate comparison group are needed to control for any placebo effect and for potential patient selection and treatment bias. In addition, the lack of blinding of patients and investigators fails to control for the placebo effect and potentially leads to additional bias.
- All seven RCTs included in the systematic review were double-blind crossover studies in which both the patient and the investigators were blinded to whether the DBS was turned on or off.^[61-67] However, these RCTs are considered unreliable for the following reasons:
 - Small study populations (n= 4 to 16) limit the ability to rule out the role of chance as an explanation of findings
 - Heterogeneity of study participants (e.g., comorbidities) and procedures (e.g., five different brain target areas) limits meaningful comparison of outcomes
 - Inability to isolate the contribution of DBS from the impact of other treatments (e.g., medications) during the study period
 - Short-term follow-up does not permit conclusions related to the durability of any initial beneficial effects

Anorexia Nervosa

Anorexia nervosa is an eating disorder characterized by a chronic course that is refractory to treatment in many patients and has one of the highest mortality rates of any psychiatric

disorder. In a recent systematic review by McClelland et al., two case series and two case reports that applied DBS to anorexic patients were identified and reviewed with mixed results.^[68] There are no RCTs investigating DBS for this indication.

Alcohol Addiction

Alcohol dependency can be considered as a chronic mental disorder characterized by frequent relapses even when treated with appropriate medical or psychotherapeutic interventions.

A 2012 systematic review by Herremans and Baeken investigated several neuromodulation techniques including deep brain stimulation in the treatment of alcohol addiction.^[69] Previous studies investigating these neuromodulation techniques in alcohol addiction remain to date rather limited. Overall, the clinical effects on alcohol addiction were modest. Neuromodulation techniques have only recently been subject to investigation in alcohol addiction and methodological differences between the few studies restrict clear conclusions. Nevertheless, the scarce results encourage further investigation in alcohol addiction.

OTHER APPLICATIONS

There is interest in applications of DBS beyond that for essential tremors, primary dystonia and Parkinson's disease. Clinical trials are being pursued; however, at this time, FDA approval is limited to the above indications and severe obsessive-compulsive disorder. The following discussion focuses on randomized controlled trials (RCTs) for the investigational indications noted in Policy Criteria II. above.

Chronic Pain, Pain Syndromes, and Cluster Headaches

DBS for the treatment of chronic pain was investigated and largely abandoned in the 1980's due to poor results in two trials. With improved technology and surgical techniques there has been a resurgence of interest in DBS for intractable pain. DBS of the posterior hypothalamus for the treatment of chronic cluster headaches has also been investigated as functional studies have suggested cluster headaches have a central hypothalamic pathogenesis. However, due to the lack of RCTs, conclusions cannot be reached on the effectiveness of DBS as a treatment of any type of pain, including but not limited to cluster headaches, chronic spinal pain, failed back surgery syndrome, phantom limb pain, facial deafferentation pain, and central or peripheral neuropathic pain.

Morbid Obesity

The study of DBS of the hypothalamus and nucleus accumbens for cluster headache and obsessive-compulsive disorder (OCD) has prompted interest in DBS for obesity and addiction, which are thought to be associated with those brain regions. However, patients with unilateral subthalamic nucleus or globus pallidus internus DBS for PD were found to have gained a mean 4.86 pounds following initiation of DBS.^[70] There are currently no studies of DBS in any brain region for the treatment of obesity.

Multiple Sclerosis

No randomized controlled trials were found for DBS in the treatment of multiple sclerosis (MS) tremors. Three small nonrandomized comparative trials were found, one^[71] comparing stimulation off versus on (n=9), and two^[19,72] comparing thalamic stimulation versus

thalamotomy (n=12 total MS patients). The small study populations do not permit conclusions on efficacy of DBS for MS tremors.

PRACTICE GUIDELINE SUMMARY

AMERICAN ACADEMY OF NEUROLOGY

In the 2013 American Academy of Neurology (AAN) guidelines on the treatment for tardive syndromes (TDS), indicated there is insufficient evidence to support or refute DBS for TDS.^[73] This recommendation is based on Level U evidence (evidence is insufficient to support or refute the use of any other treatment over another). The 2011 AAN guideline regarding essential tremor was reaffirmed in 2014 indicating that, “no high quality, long-term studies exist regarding the efficacy and safety of (DBS) for ET.”^[74]

The American Academy of Neurology (AAN) updated its guidelines on the treatment of essential tremor (ET) in 2011.^[74] This update did not change the conclusions and recommendations of AAN 2005 practice parameters on DBS for ET.^[75] The guidelines stated that bilateral DBS of the thalamic nucleus may be used to treat medically refractory limb tremor in both upper limbs (level C, possibly effective), but that there were insufficient data on the risk/benefit ratio of bilateral vs unilateral DBS in the treatment of limb tremor. There was insufficient evidence to make recommendations on the use of thalamic DBS for head or voice tremor (level U, treatment is unproven).

The 2010 guidelines from AAN on the treatment of nonmotor symptoms of PD found insufficient evidence for the treatment of urinary incontinence with DBS of the STN.^[76] AAN found that DBS of the STN possibly improves sleep quality in patients with advanced PD. However, none of the studies performed DBS to treat insomnia as a primary symptom, and DBS of the STN is not currently used to treat sleep disorders.

AMERICAN PSYCHIATRIC ASSOCIATION

In a 2007 the American Psychiatric Association (APA) published an evidence-based guideline, which was reaffirmed in 2012, on the treatment of patients with obsessive-compulsive disorder.^[77] The APA gave their lowest level recommendation for DBS, among a list of other therapies with limited published evidence, for OCD that remains refractory “after first- and second-line treatment and well-supported augmentation strategies have been exhausted.” In the 2010 APA guideline for the treatment of major depression, DBS is listed as a search term in the literature review; however, no recommendations for DBS are mentioned.^[78]

VETERANS HEALTH ADMINISTRATION, DEPARTMENT OF DEFENSE (VA/DoD)

A 2017 evidence-based update of the VA/DoD practice guideline for the management of post-traumatic stress is silent on the use of deep brain stimulation for treatment of post-traumatic stress disorder.^[79]

SUMMARY

There is enough research to show that deep brain stimulation (DBS) improves health outcomes in select patients with symptoms related to Parkinson's disease, essential tremor, or primary dystonias. DBS has become a standard of care for these patients and therefore

may be considered medically necessary when policy criteria are met.

There is not enough research to determine the safety and effectiveness of deep brain stimulation (DBS) for other conditions. Current practice guidelines do not recommend the use of deep brain stimulation for the treatment of various neurologic and psychiatric disorders. Therefore, DBS is considered investigational for all other indications when policy criteria are not met.

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CODES

Codes	Number	Description
CPT	61850	Twist or burr hole(s) for implantation of neurostimulator electrode(s), cortical
	61860	Craniectomy or craniotomy for implantation of neurostimulator electrodes, cerebral, cortical
	61863	Twist drill, burr hole, craniotomy, or craniectomy for stereotactic implantation of neurostimulator array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), without use of intraoperative microelectrode recording; first array
	61864	Twist drill, burr hole, craniotomy, or craniectomy for stereotactic implantation of neurostimulator array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), without use of intraoperative microelectrode recording; each additional array (List separately in addition to primary procedure).
	61867	Twist drill, burr hole, craniotomy, or craniectomy for stereotactic implantation of neurostimulator array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), with use of intraoperative microelectrode recording; first array
	61868	Twist drill, burr hole, craniotomy, or craniectomy for stereotactic implantation of neurostimulator array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), with use of intraoperative microelectrode recording; each additional array (List separately in addition to primary procedure)
	61885	Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array
	61886	;with connection to two or more electrode arrays
	61888	Revision or removal of cranial neurostimulator pulse generator or receiver
	95970	Electronic analysis of implanted neurostimulator pulse generator/transmitter (eg, contact group[s], interleaving, amplitude, pulsewidth, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional;

Codes	Number	Description
		with brain, cranial nerve, spinal cord, peripheral nerve, or sacral nerve, neurostimulator pulse generator/transmitter, without programming
	95978	Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, battery status, electrode select ability and polarity, impedance and patient compliance measurements), complex deep brain neurostimulator pulse generator/transmitter, with initial or subsequent programming, first hour (Deleted 1/1/2019)
	95979	;complex deep brain neurostimulator pulse generator/transmitter, with initial or subsequent programming, each additional 30 minutes after first hour (Deleted 1/1/2019)
	95983	Electronic analysis of implanted neurostimulator pulse generator/transmitter (eg, contact group[s], interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with brain neurostimulator pulse generator/transmitter programming, first 15 minutes face-to-face time with physician or other qualified health care professional
	95984	;with brain neurostimulator pulse generator/transmitter programming, each additional 15 minutes face-to-face time with physician or other qualified health care professional (List separately in addition to code for primary procedure)
HCPCS	C1820	Generator, neurostimulator (implantable), with rechargeable battery and charging system
	L8679	Implantable neurostimulator, pulse generator, any type
	L8680	Implantable neurostimulator electrode, each
	L8681	Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
	L8682	Implantable neurostimulator radiofrequency receiver
	L8683	Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver
	L8685	Implantable neurostimulator pulse generator, single array, rechargeable, includes extension
	L8686	Implantable neurostimulator pulse generator, single array, nonrechargeable, includes extension
	L8687	Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
	L8688	Implantable neurostimulator pulse generator, dual array, nonrechargeable, includes extension
	L8689	External recharging system for battery (internal) for use with implantable neurostimulator

Date of Origin: April 1998