Deep brain stimulation is proven for treating the following:

- Idiopathic Parkinson's disease when used according to U.S. Food and Drug Administration (FDA) indications
- Essential tremor when used according to U.S. Food and Drug Administration (FDA) indications
- Primary dystonia* (occurs apart from any other identifiable illness) including generalized and/or segmental dystonia, hemidystonia and cervical dystonia (torticollis) when used according to the U.S. Food and Drug Administration (FDA) indications
  *Primary dystonia may include genetic torsion dystonia, acquired torsion dystonia (not due to drugs), spasmodic torticollis, fragments of torsion dystonia, and unspecified torticollis.
Deep brain stimulation is unproven for treating secondary Parkinsonism (result of head trauma, metabolic conditions, toxicity, drugs, or other medical disorders).
Well-designed studies demonstrating the efficacy of deep brain stimulation for treating secondary Parkinsonism are not available. Clinical trials are needed to demonstrate the benefit of deep brain stimulation for this patient population.

Deep brain stimulation is unproven for treating secondary dystonia (occurs with illness, after trauma or following exposure to certain medications or toxins).
There is inadequate evidence of the safety and efficacy of deep brain stimulation for treating secondary dystonia. Questions remain with regard to patient selection criteria and long-term benefits and safety compared with standard treatments. Formal comparisons, with large randomized controlled or comparative trials of pallidotomy, thalamotomy, and deep brain stimulation, are required before conclusions can be drawn regarding the use of deep brain stimulation for patients with secondary dystonia.

Deep brain stimulation is unproven for treating conditions other than those listed as proven. This includes but is not limited to the following diagnoses:

- Depression
- Obsessive-compulsive disorder (OCD)
- Epilepsy
- Tourette syndrome
- Cluster headache
- Impulsive or violent behavior
- Chronic pain
- Trigeminal neuralgia
- Movement disorders caused by multiple sclerosis (MS)

Some studies have examined the use of deep brain stimulation for treating major depression, obsessive-compulsive disorder (OCD), epilepsy, Tourette syndrome, cluster headache, impulsive or violent behavior, stroke pain, chronic pain, phantom limb pain, trigeminal neuralgia and movement disorders of multiple sclerosis (MS). However, because of limited studies, small sample sizes, weak study designs and heterogenous patient characteristics, there is insufficient data to conclude that deep brain stimulation is safe and/or effective for treating these indications.

Information Pertaining to Medical Necessity Review (When Applicable)
Deep brain stimulation is medically necessary for idiopathic Parkinson's disease, essential tremor, or primary dystonia if signs or symptoms persist despite standard medical therapy.

BENEFIT CONSIDERATIONS

Consult benefit document for Humanitarian Use Device (HUD) coverage:

- 2001 Certificate of Coverage (COC): HUDs require Institutional Review Board (IRB) oversight, they are investigational and are not covered.
- 2007 Certificate of Coverage (COC): HUDs are not considered investigational and are covered when used for proven indication(s).

BACKGROUND

Deep brain stimulation (DBS) delivers electrical pulses to the brain via electrodes surgically implanted in the internal globus pallidus interna (GPI), subthalamic nucleus (STN) or ventral intermediate nucleus (VIM) of the thalamus. The mechanism of action is not completely understood, but the goal of DBS is to interrupt the pathways responsible for the abnormal movements associated with movement disorders such as Parkinson's disease and essential tremor. The exact location of electrodes depends on the type of movement disorder. Unlike standard surgical ablation, which causes permanent destruction of the targeted area, DBS is reversible and adjustable. The DBS device consists of an implantable pulse generator (IPG) or...
neurostimulator, an implantable lead with electrodes and a connecting wire. The neurostimulator is approximately the size of a stop watch and is similar to a cardiac pacemaker. Subcutaneous extension wires connect the lead(s) to the neurostimulator which is implanted near the clavicle or, in the case of younger primary dystonia patients, in the abdomen.

When used according to U.S. Food and Drug Administration (FDA) indications, deep brain stimulation is used to treat selected individuals with Parkinson's disease, essential tremor, and primary dystonia. Most forms of Parkinson's disease are idiopathic (having no specific known cause). In secondary Parkinsonism, the symptoms are a result of head trauma, metabolic conditions, toxicity, drugs, or other medical disorders. Primary dystonia occurs on its own, apart from any illness. Secondary dystonia can occur with illness, after trauma or following exposure to certain medications or toxins. Types of dystonia include:

- Generalized - affects multiple areas of the body
- Focal - affects one specific area of the body, such as the neck (cervical dystonia or torticollis), eyelid (blepharospasm) or hand (writer's cramp)
- Segmental - affects two or more adjacent parts of the body
- Multifocal - affects two nonadjacent parts of the body
- Hemidystonia - affects one side of the body
- Cervical dystonia or torticollis

Deep brain stimulation has been proposed for treating other disorders such as major depression, epilepsy, Tourette syndrome, cluster headache, impulsive or violent behavior, chronic pain and trigeminal neuralgia, phantom limb pain, and movement disorders of multiple sclerosis.

**CLINICAL EVIDENCE**

**Parkinson's Disease & Essential Tremor**

Evidence from available published studies indicates that deep brain stimulation (DBS) provides clinically and statistically significant improvements in patients with Parkinson's disease (PD) and essential tremor (ET).

Weaver et al. (2005) conducted a meta-analysis comparing DBS of the subthalamic nucleus (STN) and the globus pallidus interna (GPI) for treating Parkinson's disease. Motor function improved significantly following stimulation (54% in patients whose STN was targeted and 40% in those whose GPI was stimulated). After controlling for participant and study characteristics, patients who had undergone either STN or GPI DBS experienced comparable improved motor function following surgery. The performance of activities of daily living improved significantly in patients with either target (40%). Medication requirements were significantly reduced following stimulation of the STN but did not change when the GPI was stimulated.

The PD SURG trial is an ongoing randomized, open-label trial that includes 366 patients with Parkinson's disease who were randomly assigned to receive immediate surgery (lesioning or deep brain stimulation) and best medical therapy (n=183) or best medical therapy alone (n=183). All patients who had surgery had deep brain stimulation. The results of the study indicated that at 1 year, surgery and best medical therapy improved patient self-reported quality of life more than best medical therapy alone in patients with advanced Parkinson's disease. According to the investigators, these differences are clinically meaningful, but surgery is not without risk and targeting of patients most likely to benefit might be warranted (Williams, 2010).

Follett et al. (2010) randomly assigned 299 patients with idiopathic Parkinson's disease to undergo either pallidal stimulation (152 patients) or subthalamic stimulation (147 patients) and compared 24-month outcomes. Mean changes in the primary outcome did not differ significantly between the two study groups. There was also no significant difference in self-reported function. Patients undergoing subthalamic stimulation required a lower dose of dopaminergic agents than did those undergoing pallidal stimulation. One component of processing speed (visuomotor) declined more after subthalamic stimulation than after pallidal stimulation. The level of depression
worsened after subthalamic stimulation and improved after pallidal stimulation. Serious adverse events occurred in 51% of patients undergoing pallidal stimulation and in 56% of those undergoing subthalamic stimulation, with no significant between-group differences at 24 months. The investigators concluded that patients with Parkinson's disease had similar improvement in motor function after either pallidal or subthalamic stimulation. Non-motor factors may reasonably be included in the selection of surgical target for deep-brain stimulation.

In a randomized controlled trial, Odekerken et al. (2013) assessed whether globus pallidus pars interna (GPI) deep brain stimulation (DBS) gives greater functional improvement than does subthalamic nucleus (STN) DBS in patients with advanced Parkinson's disease. The authors enrolled 128 patients in the trial, randomly assigning 65 to GPI DBS and 63 to STN DBS. No statistically significant differences were found in either of the primary outcomes: mean change in weighted Academic Medical Center Linear Disability Scale (ALDS) and the number of patients with cognitive, mood, and behavioral side-effects. Secondary outcomes showed larger improvements in off-drug phase in the STN group compared with the GPI group. The authors concluded that although there was no difference in the primary outcomes, the findings suggest that STN could be the preferred target for DBS in patients with advanced Parkinson's disease.

Schuepbach et al. (2013) evaluated if neurostimulation is beneficial for early motor complications in patients with Parkinson's disease. In a 2-year trial, the authors randomly assigned 251 patients with Parkinson's disease and early motor complications to undergo neurostimulation plus medical therapy or medical therapy alone. For the primary outcome of quality of life, the mean score for the neurostimulation group improved by 7.8 points, and that for the medical-therapy group worsened by 0.2 points. Neurostimulation was superior to medical therapy with respect to motor disability, activities of daily living, levodopa-induced motor complications, and time with good mobility and no dyskinesia. Serious adverse events occurred in 54.8% of the patients in the neurostimulation group and in 44.1% of those in the medical-therapy group. Serious adverse events related to surgical implantation or the neurostimulation device occurred in 17.7% of patients. An expert panel confirmed that medical therapy was consistent with practice guidelines for 96.8% of the patients in the neurostimulation group and for 94.5% of those in the medical-therapy group. The authors concluded that subthalamic stimulation was superior to medical therapy in patients with Parkinson's disease and early motor complications. A limitation of this study is that patients in the trial did not represent the majority of patients with Parkinson's disease since all study participants had a good response to levodopa, were younger than 60 at the time of surgery, and had no dementia. Whether these results could be obtained in older patients with Parkinson's disease is unknown.

Weaver et al. (2012) compared the long-term outcomes of deep brain stimulation (DBS) of the globus pallidus interna (GPI) and subthalamic nucleus (STN) for patients with Parkinson's disease in a multicenter randomized controlled trial. Patients randomly assigned to GPI (n = 89) or STN DBS (n = 70) were followed for 36 months. Motor function improved between baseline and 36 months for GPI and STN. Improvements were similar between targets and stable over time. Health-related quality of life improved at 6 months on all subscales, but improvement diminished over time. The authors concluded that slight declines in quality of life following initial gains and gradual decline in neurocognitive function likely reflect underlying disease progression and highlight the importance of non-motor symptoms in determining quality of life.

Castrioto et al. (2011) assessed the 10-year motor outcome of deep brain stimulation of the subthalamic nucleus (STN-DBS) in 18 patients with Parkinson disease (PD). Patients were videotaped at baseline and 1, 5, and 10 years after surgery. An independent rater blinded to stimulation and medication condition scored the 10-year video assessments. In the 18 patients available for follow-up at 10 years, STN-DBS still significantly improved the Unified Parkinson's Disease Rating Scale (UPDRS), total motor score, resting and action tremor, and bradykinesia sub-scores. The UPDRS II scores in the medication and no medication conditions, UPDRS IV dyskinesia and motor fluctuations scores, and the levodopa equivalent daily dose were also significantly reduced compared with baseline. Axial signs showed the most progressive decline in
stimulation and levodopa response over the years. The authors concluded that this class III study provides evidence that stimulation-induced motor improvement was sustained overall at 10 years, although part of the initial benefit wore off over time.

To assess the current state of knowledge on essential tremor (ET) therapy and make recommendations based on the analysis of evidence, Zappia et al. (2013) reviewed the literature regarding pharmacologic and surgical therapies, providing a quality assessment of the studies and the strength of recommendations for each treatment. A systematic literature review was performed to identify all the studies conducted on patients with ET. Based on the results of the review, thalamic deep-brain stimulation was recommended for refractory ET.

**Professional Societies**

**American Academy of Neurology (AAN):**

In a practice parameter for the treatment of Parkinson's disease (PD), the AAN recommends the following:

- DBS of the subthalamic nucleus (STN) may be considered as a treatment option in PD patients to improve motor function and to reduce motor fluctuations, dyskinesia, and medication usage (Level C - possibly effective, ineffective, or harmful for the given condition in the specified population). Patients need to be counseled regarding the risks and benefits of this procedure. There is insufficient evidence to make any recommendations about the effectiveness of DBS of the GPi or ventralis intermedius (VIM) nucleus of the thalamus in reducing motor complications or medication usage, or in improving motor function in PD patients (Level U - data inadequate or conflicting given current knowledge, treatment is unproven).
- Preoperative response to levodopa should be considered as a factor predictive of outcome after DBS of the STN (Level B - probably effective, ineffective, or harmful for the given condition in the specified population). Age and duration of PD may be considered as factors predictive of outcome after DBS of the STN. Younger patients with shorter disease durations may possibly have improvement greater than that of older patients with longer disease durations (Level C). There is insufficient evidence to make any recommendations about factors predictive of improvement after DBS of the GPi or VIM nucleus of the thalamus in PD patients (Level U) (Pahwa, 2006).

In a practice parameter for essential tremor therapies, the AAN recommends the following:

- DBS of the VIM thalamic nucleus may be used to treat medically refractory limb tremor in essential tremor (Level C - possibly effective, ineffective, or harmful for the given condition in the specified population).
- There is insufficient evidence to make recommendations regarding the use of thalamic DBS for head or voice tremor (Level U - data inadequate or conflicting given current knowledge, treatment is unproven).
- DBS has fewer adverse events than thalamotomy (Level B - probably effective, ineffective, or harmful for the given condition in the specified population). However, the decision to use either procedure depends on each patient's circumstances and risk for intraoperative complications compared to feasibility of stimulator monitoring and adjustments (Zesiewicz, 2005).

The AAN issued an update of the 2005 American Academy of Neurology practice parameter on the treatment of essential tremor (ET) in 2011. Conclusions and recommendations for deep brain stimulation (Level C, possibly effective) were unchanged from the previous guideline. The guideline indicated that there were no additional trials (published between 2004 and April 2010) rated better than Class IV that examined the efficacy and safety of deep brain stimulation (DBS) of the thalamus for the treatment of ET (Zesiewicz, 2011).
Dystonia
Evidence from available published controlled trials and case series indicates that deep brain stimulation provides improvement in movement symptoms in patients with primary dystonia (Sarubbo et al. 2012; Vidailhet et al. 2005; Vidailhet et al. 2007; Kupsch et al. 2006; Houeto et al. 2007).

In a controlled multicentre trial, Volkmann et al. (2013) assessed the safety and efficacy of pallidal neurostimulation in patients with primary generalized or segmental dystonia who were prospectively followed up for 5 years. Forty patients were randomly assigned to either sham neurostimulation or neurostimulation of the internal globus pallidus for a period of 3 months and thereafter all patients completed 6 months of active neurostimulation. A total of 38 patients agreed to be followed up annually after the activation of neurostimulation, including assessments of dystonia severity, pain, disability, and quality of life. An intention-to-treat analysis including all patients from the parent trial showed significant improvements in dystonia severity at 3 years and 5 years compared with baseline. The improvement from 6 months to 3 years was significant and sustained at the 5-year follow-up. The authors concluded that 3 years and 5 years after surgery, pallidal neurostimulation continues to be an effective and relatively safe treatment option for patients with severe idiopathic dystonia. This long-term observation provides further evidence in favor of pallidal neurostimulation as a first-line treatment for patients with medically intractable, segmental, or generalized dystonia.

Andrews et al. (2010) analyzed combined published results of individual patient outcomes following DBS for all types of dystonia. Data was available in 157 studies for 466 patients with all forms of dystonia. The subclassification of these patients included 344 with primary forms of dystonia, 10 with myoclonus dystonia, 19 with heredodegenerative dystonias and 93 who had DBS for secondary dystonia. Patients with primary forms of dystonia, myoclonus dystonia, subtypes of heredodegenerative dystonia and tardive dystonia have a greater than 50% mean improvement in dystonia severity following DBS. Among patients with primary generalized dystonia, multiple regression analysis showed that a shorter duration of symptoms, a lower baseline severity score and DYT1 positive status were all independently associated with a significantly higher percentage improvement from surgery. Patients with other forms of heredodegenerative and secondary dystonia have variable responses, making prediction of response in future patients difficult.

Koy et al. (2013) performed a meta-analysis and analyzed the published literature regarding deep brain stimulation and secondary dystonia to evaluate the effect on cerebral palsy, a common cause of secondary dystonia. Twenty articles that included 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% at a median follow-up of 12 months. There was a significant negative correlation between severity of dystonia and clinical outcome. The authors concluded that deep brain stimulation can be an effective treatment option for dyskinetic cerebral palsy. The authors stated that 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.

In a systematic review, Mentzel et al. (2012) assessed the efficacy and safety, specifically the psychiatric side effects, of DBS in patients with medication-induced tardive dyskinesia and dystonia (TDD) (a form of secondary dystonia). Seventeen studies involving 50 patients with TDD who underwent DBS were included in the review. The mean improvement of TDD of the combined patients 3 to 76 months after implantation was 77.5% on the Burke-Fahn-Marsden Dystonia Rating Scale. Of the 50 patients, 1 experienced an exacerbation of depression, and 1 experienced an exacerbation of psychosis. The authors concluded that DBS seems to be
effective and relatively safe for patients with treatment-resistant TDD; however, the results should be interpreted with caution, as most of the data are from case reports and small trials.

Kim et al. (2011) applied a multimodal method to maximize the treatment effects of deep brain stimulation in patients with secondary dystonia. Four patients underwent bilateral globus pallidus internus (GPI) deep brain stimulation (DBS) and six patients underwent bilateral GPI DBS plus unilateral thalamotomy for treatment of cerebral palsy (CP). Among the patients with secondary dystonia without CP, five were also treated by DBS. Patients with generalized secondary dystonia with cerebral palsy were classified into group I and patients with focal dystonia without CP into group II. The movement and disability scores of group I-A had improved by 32.0% and 14.3%, respectively, at the last follow-up compared with baseline. The movement and disability scores of group I-B had improved by 31.5% and 0.18% at the last follow-up compared with baseline, respectively. In comparison with patients in group I-A, patients in group I-B showed a significant improvement in movement scores for the contralateral arm. Group II patients showed a marked improvement in movement and disability scores of 77.7% and 80.0%, respectively. The authors concluded that DBS plus unilateral ventralis oralis thalamotomy for CP patients with fixed states in the upper extremities is useful not only to treat secondary dystonic movement but also to improve quality of life. The authors concluded that excellent clinical outcomes were achieved using DBS in group II patients with post-traumatic dystonia and tardive dyskinesia. However, the conclusions that can be drawn from this study are limited by the extremely small number of study participants. These findings require confirmation in a larger study.

The National Institute for Health and Care Excellence (NICE) issued a guidance stating that the current evidence supports the safety and efficacy of DBS as a treatment modality for dystonia. Dystonia may be treated conservatively or surgically. Conservative treatment only treats the symptoms, and surgical intervention (i.e., thalamotomy and pallidotomy) may not render long-term benefits. Patient selection and management should be managed by a multidisciplinary team specializing in the long-term care of patients with movement disorders (NICE, 2006).

**Professional Societies**

**European Federation of Neurological Societies:** The European Federation of Neurological Societies Guidelines on Diagnosis and Treatment of Primary Dystonias state that pallidal deep brain stimulation is considered a good option, particularly for primary generalized or cervical dystonia, after medication or botulinum toxin have failed. Deep brain stimulation is less effective in secondary dystonia (Albanese et al., 2011).

**Other Conditions**

Deep brain stimulation (DBS) has been investigated for disorders including the following:

- Alzheimer’s disease (Laxton, 2010; Smith, 2012)
- Chronic pain (Bittar, 2005; Katayama, 2001a; Katayama, 2001; Nandi, 2002; Coffey, 2006; Rasche, 2006)
- Cluster headache (Seijo, 2011; Fontaine, 2010)
- Epilepsy (Oh, 2012; Fisher, 2010; Boex, 2011)
- Impulsive or violent behavior (Franzini, 2005)
- Treatment resistant and major depression (Holtzheimer, 2012; Bewernick, 2010; Malone, 2009; Mayberg, 2005; Lozano, 2008)
- Movement disorders of multiple sclerosis (Hosseini, 2012; Hyam, 2007; Thevathasan, 2011; Mandat, 2010)
- Obsessive compulsive disorder (Denye, 2010; Mallet, 2008; Appleby, 2007; Ooms et al. 2013)

While there is limited evidence to suggest that DBS may be an option for some of these conditions, there is not enough evidence to establish patient selection criteria and the safety and efficacy of DBS. Studies investigating DBS for treatment of other conditions are mainly case
series with small sample sizes and short-term follow-up. Further well-designed studies are needed to demonstrate the benefits of deep brain stimulation for these disorders.

**Tourette Syndrome**

Ackermans et al. (2011) evaluated 8 patients with intractable Tourette syndrome who were included in a double-blind randomized cross-over trial assessing the efficacy and safety of deep brain stimulation of the thalamus. After surgery, the patients were randomly assigned to 3 months stimulation followed by 3 months OFF stimulation (Group A) or vice versa (Group B). The cross-over period was followed by 6 months ON stimulation. Assessments were performed prior to surgery and at 3, 6 months and 1 year after surgery. Interim analysis was performed on a sample of six male patients with only one patient randomized to Group B. Tic severity during ON stimulation was significantly lower than during OFF stimulation, with substantial improvement (37%) on the Yale Global Tic Severity Scale. The effect of stimulation 1 year after surgery was sustained with significant improvement (49%) on the Yale Global Tic Severity Scale when compared with preoperative assessments. Secondary outcome measures did not show any effect at a group level, either between ON and OFF stimulation or between preoperative assessment and that at 1 year postoperatively. Cognitive re-assessment at 1 year after surgery showed that patients needed more time to complete the Stroop Color Word Card test. 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. According to the authors, the present preliminary findings suggest that deep brain stimulation may reduce tic severity in refractory Tourette syndrome, but there is the risk of adverse effects related to oculomotor function and energy levels. Further randomized controlled trials on other targets are needed since the search for the optimal DBS target is still ongoing.

Maciuñas et al. (2007) conducted a prospective double-blind crossover trial of bilateral thalamic deep brain stimulation (DBS) in five adults with TS. Bilateral thalamic electrodes were implanted. Subjective and objective results were assessed in a double-blind randomized manner for 4 weeks, with each week spent in one of four states of unilateral or bilateral stimulation. Results were similarly assessed 3 months after unblinded bilateral stimulator activation while repeated open programming sessions were permitted. In the randomized phase of the trial, a statistically significant reduction in the modified Rush Video-Based Rating Scale score was identified in the bilateral on state. Improvement was noted in motor and sonic tic counts as well as on the Yale Global Tic Severity Scale and TS Symptom List scores. Benefit was persistent after 3 months of open stimulator programming. Quality of life indices were also improved. Three of five patients had marked improvement according to all primary and secondary outcome measures. The authors concluded that bilateral thalamic DBS appears to reduce tic frequency and severity in some patients with TS who have exhausted other available means of treatment. These findings require confirmation in a larger study.

Piedad et al. (2012) evaluated which patients with Gilles de la Tourette syndrome (GTS) should be treated with DBS and what is the best target. To answer these questions, the authors conducted a systematic literature review of the published studies of DBS in GTS and critically evaluated the current evidence for both patient and target selection. The authors found that since 1999, up to 99 cases of DBS in GTS have been reported in the scientific literature, with varying selection criteria, stimulation targets, and assessment protocols. The vast majority of studies published to date are case reports or case series reporting successful outcomes in terms of both tic severity improvement and tolerability. The reviewed studies suggest that the best candidates are patients with significant functional impairment related to the tic symptoms, who did not respond to conventional pharmacological and behavioral interventions. The globus pallidus internus and thalamus appear to be the safest and most effective targets, especially for patients with “pure” GTS and patients with comorbid obsessive-compulsive symptoms, anxiety, and depression. The authors concluded that DBS is a promising treatment option for severe cases of GTS. According to the authors, there is a need to reach consensus on the definition of refractory treatment and to conduct larger double-blind randomized controlled studies on the most promising targets.

Deep Brain Stimulation: Medical Policy (Effective 02/01/2014)

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Saleh et al. (2012) analyzed 33 research articles reporting on DBS in patients with Gilles de la Tourette syndrome (GTS). The review included 88 patients with Tourette's syndrome who were treated since 1999 with DBS. The majority of patients received thalamic stimulation. Significantly fewer patients were treated with globus pallidus internus stimulation. Occasionally, the anterior limb of the internal capsule and the nucleus accumbens were implanted. The subthalamic nucleus was selected once. All targets were reported with positive results, but of variable extent. The majority of studies (n = 26) met only level 4 criteria (observational studies without control), while four studies met level 1 criteria (randomized control studies) and three studies met level 2 criteria (non-randomized controlled trials). This translates into level 1 evidence for 14 GTS patients, level 2 evidence for 38 patients, and level 4 evidence for 36 patients. The authors concluded that in light of the wide spectrum of associated behavioral co-morbidities in GTS, multiple networks modulation may result in the most efficacious treatment strategy. The optimal locations for DBS within the cortico-basal ganglia-thalamocortical circuits remain to be established. However, at the current stage, comparison between targets should be done with great caution. Significant differences between number of patients treated per target, methodological variability, and quality of reporting makes a meaningful comparison between targets difficult. According to the authors, randomized controlled trials with larger cohorts and standardization of procedures are needed.

In a prospective cohort study, Porta et al. (2009) assessed the long-term outcome (2 years) of 15 patients with severe and refractory Tourette syndrome (TS) who underwent bilateral thalamic deep brain stimulation (DBS). In addition to marked reduction in tic severity, 24-month follow-up ratings showed improvement in obsessive-compulsive symptoms, anxiety symptoms, depressive symptoms, and subjective perception of social functioning/quality of life in 15 patients. There were no substantial differences on measures of cognitive functions before and after DBS. The authors concluded that at 24-month follow-up, tic severity was improved in patients with intractable Tourette syndrome (TS) who underwent bilateral thalamic deep brain stimulation. According to the authors, controlled studies on larger cohorts with blinded protocols are needed to verify that this procedure is effective and safe for selected patients with TS.

As a follow-up to the previous study, Porta et al. (2012) assessed the long-term (5-6 years) outcome of bilateral thalamic deep brain stimulation in 18 patients with severe and refractory Tourette syndrome. The aim of the research was the assessment of long-term outcome on tics, obsessional behaviors, anxiety, mood, and on the overall general health of the patients and their general satisfaction. At 5-6 year follow-up, there was a significant reduction in tic severity, and significant improvements in obsessive compulsive behaviors, anxiety and depressive symptoms. Patients, in general, required less medication for tics, co-morbid conditions and/or co-existent psychopathologies. The long-term outcome and satisfaction were not unanimous between patients and the medical team. According to the authors, at long-term follow-up, DBS was very successful in terms of a significant improvement in tics and also a significant reduction in the potentially disabling symptoms of obsessionality, anxiety and depression. However, compared with the more positive overall results at 2 years, these later results demonstrate long-term difficulties as follows: non-compliance, long-term complications, and the differences in the opinions between the medical, the surgical teams and the post-DBS patients as to their outcome/satisfaction with the procedures. The authors indicated that this emphasizes the need for controlled studies, for long-term follow up, and the need to improve the selection of patients for DBS.

Steeves et al. (2012) conducted a systematic literature search for clinical trials on the treatment of tics. Three studies on deep brain stimulation (DBS) met the inclusion criteria. According to the authors, although evidence exists for the efficacy of DBS, the quality of this evidence is poor and the risks and burdens of the procedure are finely balanced with the perceived benefits. The author recommended that this intervention continues to be considered an experimental treatment for severe, medically refractory tics that have imposed severe limitations on quality of life.
According to the authors, the procedure should only be performed within the context of research studies and by physicians who are expert in DBS programming and in the management of tics.

In an open-label study, Cannon et al. (2012) evaluated the effectiveness of DBS of the anteromedial globus pallidus interna on tic severity and common comorbidities. Eleven patients (eight of them men, mean age=39 years) with severe and medically intractable Tourette's syndrome underwent implantation of Medtronic quadripolar electrodes in the globus pallidus interna bilaterally. Ten patients (91%) reported improvement in tic severity soon after DBS. Overall, there was a 48% reduction in motor tics and a 56.5% reduction in phonic tics at final follow-up. Six patients (54.5%) had a more than 50% reduction, sustained for at least 3 months, in Yale Global Tic Severity Scale score. Only two patients required ongoing pharmacotherapy for tics after surgery, and patients improved significantly on all secondary measures. One patient did not tolerate DBS and discontinued treatment after 3 months. Greater anxiety in two patients and hardware malfunction in three patients were noteworthy adverse outcomes. The authors concluded that the results suggest anteromedial globus pallidus interna DBS for Tourette's syndrome is an effective and well-tolerated treatment for a subgroup of patients with severe Tourette's syndrome. The small sample size of this study does not permit the examination of predictors of good response or a detailed examination of comorbidities. According to the authors, head-to-head studies comparing DBS with different targets would help establish the best anatomical sites for stimulation.

Okun et al. (2013) performed a small National Institutes of Health-sponsored clinical trials planning study of the safety and preliminary efficacy of implanted DBS in the bilateral centromedian thalamic region for Tourette syndrome in 5 patients. The study used a cranially contained constant-current device and a scheduled, rather than the classic continuous, DBS paradigm. Baseline vs 6-month outcomes were collected and analyzed. In addition, the study compared acute scheduled vs acute continuous vs off DBS. Baseline vs 6-month data revealed that reductions in the Yale Global Tic Severity Scale (YGTSS) total score did not achieve the pre-study criterion of a 50% improvement in the YGTSS total score on scheduled stimulation settings. However, statistically significant improvements were observed in the YGTSS total score, impairment score, and motor score, the Modified Rush Tic Rating Scale Score total score; and the phonic tic severity score. Continuous, off, and scheduled stimulation conditions were assessed blindly in an acute experiment at 6 months after implantation. The scores in all 3 conditions showed a trend for improvement. Trends for improvement also occurred with continuous and scheduled conditions performing better than the off condition. Tic suppression was commonly seen at ventral (deep) contacts, and programming settings resulting in tic suppression were commonly associated with a subjective feeling of calmness. The authors concluded that this study provides safety and proof of concept that a scheduled DBS approach could improve motor and vocal tics in Tourette syndrome. Refinements in neurostimulator battery life, outcome measure selection, and flexibility in programming settings can be used to enhance outcomes in a future larger study. According to the authors, scheduled stimulation holds promise as a potential first step for shifting movement and neuropsychiatric disorders toward more responsive neuromodulation approaches.

A European guideline on DBS was developed by a working group of the European Society for the Study of Tourette Syndrome (ESSTS). A systematic literature search was conducted and expert opinions of the guidelines group contributed also to the recommendations. Of 63 patients reported so far in the literature, 59 had a beneficial outcome following DBS with moderate to marked tic improvement. However, randomized controlled studies including a larger number of patients are still lacking. Although persistent serious adverse effects (AEs) have hardly been reported, surgery-related (e.g., bleeding, infection) as well as stimulation-related AEs (e.g., sedation, anxiety, altered mood, changes in sexual function) may occur. According to the ESSTS working group, at the present time, DBS in TS is still in its infancy. Due to both different legality and practical facilities in different European countries these guidelines, therefore, need to be understood as recommendations of experts. However, among the ESSTS working group on DBS in TS there is general agreement that, at present time, DBS should only be used in adult,
treatment resistant, and severely affected patients. It is highly recommended to perform DBS in the context of controlled trials (Müller-Vahl et al. 2011).

**Chronic Pain**

Bittar et al. (2005) performed a meta-analysis of DBS for pain relief that included 6 studies (n = 424 patients) published from 1977-1997. DBS was more effective for nociceptive than deafferentation pain (63% vs 47% long-term success). Long-term success was attained in over 80% of patients with intractable low back pain (failed back surgery) following successful trial stimulation. Trial stimulation was successful in approximately 50% of those with post-stroke pain, and 58% of patients permanently implanted achieved ongoing pain relief. Higher rates of success were seen with phantom limb pain and neuropathies. The authors concluded that DBS is frequently effective when used in well-selected patients. Neuroimaging and neuromodulation technology advances complicate the application of these results to modern practice.

Katayama et al. (2001a) conducted a non-randomized comparative study of 43 patients with post-stroke pain and reported a pain reduction greater than 60% in 25% (3/12) of patients treated with DBS and 48% (15/31) of patients treated with motor cortex stimulation (MCS). Follow-up information was not reported in the study.

In another non-randomized comparative study, Katayama et al. (2001) evaluated 19 patients with phantom limb pain. The patients reported a pain reduction greater than 80% in 60% (6/10) of patients treated with DBS and 20% (1/5) of patients treated with motor cortex stimulation (MCS). Follow-up ranged from 2 to 18 years. These findings require confirmation in a larger study.

In a National Institute for Health and Care Excellence (NICE) Guidance for refractory chronic pain syndromes (excluding headache), NICE stated that current evidence on the safety of deep brain stimulation for refractory chronic pain syndromes (excluding headache) shows that there are serious but well-known risks. There is evidence that the procedure is efficacious in some patients who are refractory to other forms of pain control. Therefore, NICE recommends that this procedure may be used provided that normal arrangements are in place for clinical governance, consent and audit (NICE 2011).

**Trigeminal Autonomic Cephalalgias**

In a National Institute for Health and Care Excellence (NICE) Guidance for deep brain stimulation for intractable trigeminal autonomic cephalalgias, NICE stated that current evidence on the efficacy of deep brain stimulation for intractable trigeminal autonomic cephalalgias (TACs) is limited and inconsistent, and the evidence on safety shows that there are serious but well-known side effects. Therefore, NICE recommends that this procedure should only be used with special arrangements for clinical governance, consent and audit or research (NICE 2011).

**Cluster Headache**

Fontaine et al. (2010) performed a prospective crossover, double-blind, multicenter study assessing the efficacy and safety of unilateral hypothalamic DBS in 11 patients with severe refractory chronic cluster headache (CCH). The randomized phase compared active and sham stimulation during 1-month periods, and was followed by a 1-year open phase. During the randomized phase, no significant change in primary and secondary outcome measures was observed between active and sham stimulation. At the end of the open phase, 6/11 patients responded to the chronic stimulation (weekly frequency of attacks decreased by at least 50%), including three pain-free patients. There were three serious adverse events, including subcutaneous infection, transient loss of consciousness and micturition syncopes. According to the investigators, randomized phase findings of this study did not support the efficacy of DBS in refractory CCH, but open phase findings suggested long-term efficacy in more than 50% patients, confirming previous data. Discrepancy between these findings justifies additional controlled studies.

**Depression**

Deep Brain Stimulation: Medical Policy (Effective 02/01/2014)
Blomstedt et al. (2011) conducted a review of the literature on DBS in the treatment of major depressive disorder (MDD). According to the authors, the results of DBS in MDD have been presented in 2 case reports and 3 studies of 47 patients operated upon in 5 different target areas. Positive effects were presented in all studies and side effects have been minor. DBS in the nucleus accumbens resulted in a mean reduction of Hamilton depression rating scale (HDRS) of 36% after 1 year and 30% of the 10 patients achieved remission. DBS in the internal capsule/ventral striatum resulted in a reduction of 44% after 1 year, and at the last evaluation after in mean 2 years, 40% of the 15 patients were in remission. The 20 patients with subcallosal cingulated gyrus DBS had a reduction of HDRS of 52% after 1 year, and 35% were within 1 point from remission or in remission. The authors concluded that DBS is a promising treatment for therapy-refractory MDD. However, the authors also stated that the published experience is limited, and the method is at present an experimental therapy.

Lakhan et al. (2010) systematically reviewed reports on clinical trials of DBS for obsessive-compulsive disorder (OCD) and treatment-resistant depression (TRD). The authors concluded that DBS is considered a promising technique for OCD and TRD. The authors stated that outstanding questions about patient selection and electrode placement may be resolved by larger studies.

Bewernick et al. (2012) reported the results of long-term follow-up of Deep brain stimulation (DBS) to the nucleus accumbens (NAcc-DBS). Results of long-term follow-up of up to 4 years of NAcc-DBS are described in a group of 11 patients: 12 months (n=11), 24 months (n=10), and last follow-up (maximum 4 years, n=5). Analyses were performed in an intent-to-treat method with last observation carried forward, thus 11 patients contributed to each point in time. In all, 5 of 11 patients (45%) were classified as responders after 12 months and remained sustained responders without worsening of symptoms until last follow-up after 4 years. Both ratings of depression and anxiety were significantly reduced in the sample as a whole from first month of NAcc-DBS on. All patients improved in quality of life (QoL) measures. One non-responder committed suicide. No severe adverse events related to parameter change were reported. The authors concluded that first-time, preliminary long-term data on NAcc-DBS have demonstrated a stable antidepressant and anxiolytic effect and an amelioration of QoL in this small sample of patients suffering from TRD. None of the responders of first year relapsed during the observational period (up to 4 years). This study is limited by a small patient population and lack of a controlled comparator group.

Kennedy et al. (2011) reported on the extended follow-up of 20 patients with treatment-resistant depression who received DBS to the subcallosal cingulate gyrus. After an initial 12-month study of DBS, patients were seen annually and at a last follow-up visit to assess depression severity, functional outcomes, and adverse events. The average response rates 1, 2, and 3 years after DBS implantation were 62.5%, 46.2%, and 75%, respectively. At the last follow-up visit (range=3-6 years), the average response rate was 64.3%. Functional impairment in the areas of physical health and social functioning progressively improved up to the last follow-up visit. No significant adverse events were reported during this follow-up, although two patients died by suicide during depressive relapses. The authors concluded that these data suggest that in the long term, DBS remains a safe and effective treatment for treatment-resistant depression. The authors state that additional trials with larger samples are needed to confirm these findings (Kennedy, 2011).

A Comparative Effectiveness Review was prepared for the Agency for Healthcare Research and Quality (AHRQ) on Nonpharmacologic Interventions for Treatment-Resistant Depression in Adults. The report indicated that clinical trial data on some of the developing nonpharmacologic interventions, such as deep brain stimulation were insufficient (from the published literature) to include them in the report. The authors stated that as the evidence bases grow to support the efficacy of such nonpharmacologic interventions, the newer strategies should be included in comparative effectiveness study designs (Gaynes et al. 2011).

Professional Societies
The Canadian Psychiatric Association and the Canadian Network for Mood and Anxiety Treatments (CANMAT): In 2008-2009, the Canadian Psychiatric Association and the CANMAT partnered to produce evidence-based clinical guidelines for the treatment of depressive disorders. Among the four forms of neurostimulation for depression reviewed in the guidelines, electroconvulsive therapy (ECT) had the most extensive evidence, spanning seven decades. The investigators indicated that deep brain stimulation remains an investigational treatment (Kennedy, 2009).

The American Psychiatric Association (APA): In a clinical practice guideline for the treatment of patients with major depressive disorder, the APA states that electroconvulsive therapy remains the treatment of best established efficacy against which other stimulation treatments (e.g., VNS, deep brain stimulation, transcranial magnetic stimulation, other electromagnetic stimulation therapies) should be compared. The APA did not assign a rating for the use deep brain stimulation in treating depression (Gelenberg et al. 2010).

Epilepsy
Deep brain stimulation has also been investigated for treatment of epilepsy. Fisher et al. (2010) reported on a multicenter, double-blind, randomized trial of bilateral stimulation of the anterior nuclei of the thalamus using the Medtronic DBS System for Epilepsy. One hundred ten participants with epilepsy were included in the study referred to as the SANTE trial. Half received stimulation and half no stimulation (control group) during a 3-month blinded phase; then all received unblinded stimulation. In the last month of the blinded phase the stimulated group had a 29% greater reduction in seizures compared with the control group. Unadjusted median declines at the end of the blinded phase were 14.5% in the control group and 40.4% in the stimulated group. By 2 years, there was a 56% median percent reduction in seizure frequency; 54% of patients had a seizure reduction of at least 50%, and 14 patients were seizure-free for at least 6 months. Thirty-six percent (40 of 110) of patients experienced serious adverse events, including 6 deaths, 10 cases of suicidality (2 events occurred in patients who discontinued the trial during the baseline phase), 4 intracranial hemorrhages, 6 device-related infections requiring device removal, and 5 cases of status epilepticus. The FDA panel reviewing the SANTE results expressed particular concern about an increased risk of depression and suicidal thoughts in some trial patients. One patient who was not receiving active stimulation due to battery depletion committed suicide while awaiting further surgery to replace the neurostimulator. Two more patients either attempted suicide or intentionally injured themselves. Five other patients reported having suicidal thoughts. Thus, the company added the following warning to proposed device labeling: “Depression monitoring - During treatment, patients should be monitored closely for new or changing symptoms of depression.”

In a National Institute for Health and Care Excellence (NICE) Guidance for deep brain stimulation for refractory epilepsy, NICE stated that the evidence on the efficacy of deep brain stimulation for refractory epilepsy is limited in both quantity and quality. NICE recommends that this procedure should only be used with special arrangements for clinical governance, consent and audit or research (NICE 2012).

Obsessive Compulsive Disorder
Bilateral deep brain stimulation of the anterior limb of the internal capsule (AIC) has been investigated as an adjunct to medications and as an alternative to anterior capsulotomy for treatment of chronic, severe, treatment-resistant obsessive compulsive disorder (OCD) (Abelson, 2005; Greenberg, 2006; Nuttin, 2003; Rauch, 2006). While there is limited evidence to suggest that DBS may be an option for OCD, there is not enough evidence to establish patient selection criteria and the safety and efficacy of DBS. Further well-designed studies with larger patient populations are needed to demonstrate the benefits of deep brain stimulation for OCD. Blomstedt et al. (2012) review the literature on DBS for OCD and found 25 reports with 130 patients. Five of these reports included at least 5 individual patients not presented elsewhere. Sixty-eight of these patients underwent implantation in the region of the internal capsule/ventral striatum, including the nucleus accumbens. The target in this region has varied between groups
and over time, but the latest results from bilateral procedures in this area have shown a 50% reduction of OCD scores, depression, and anxiety. The subthalamic nucleus has been suggested as an alternative target. Although beneficial effects have been demonstrated, the efficacy of this procedure cannot be decided, because only results after 3 months of active stimulation have been presented so far. The authors concluded that DBS is a promising treatment for therapy-refractory OCD, but the published experience is limited and the method is at present an experimental therapy.

Appleby et al. (2007) conducted a meta-analysis is to characterize the risks and benefits of DBS and to assess its possible use within the psychiatric setting. A total of 808 articles met inclusion criteria for the meta-analysis; 98.2% of studies that specifically assessed motor function reported some level of improvement. Most reported side effects were device or procedure related (e.g., infection and lead fracture). The prevalence of depression was 2-4%, mania 0.9-1.7%, emotional changes 0.1-0.2%, and the prevalence of suicidal ideation/suicide attempt was 0.3-0.7%. The authors concluded that DBS is an effective treatment for Parkinson's disease, dystonia, and essential tremor, and case reports suggest that major depression and OCD may also respond to DBS. According to the authors, there is a need for further clinical studies to assess its efficacy and safety before it can be offered as routine care for psychiatric illnesses such as depression, OCD, and anxiety disorders.

Denye et al. (2010) evaluated whether bilateral deep brain stimulation of the nucleus accumbens is an effective and safe treatment for treatment-refractory OCD in 16 patients. The study consisted of an open 8-month treatment phase, followed by a double-blind crossover phase with randomly assigned 2-week periods of active or sham stimulation, ending with an open 12-month maintenance phase. In the open phase, the mean Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score decreased by 46%, from 33.7 at baseline to 18.0 after 8 months. Nine of 16 patients were responders, with a mean Y-BOCS score decrease of 23.7 or 72%. In the double-blind, sham-controlled phase (n = 14), the mean Y-BOCS score difference between active and sham stimulation was 8.3 or 25%. This study is limited by a small study population.

In a 10-month, crossover, double-blind, multicenter study, 8 patients with highly refractory obsessive-compulsive disorder (OCD) were randomly assigned to undergo active stimulation of the subthalamic nucleus followed by sham stimulation and eight to undergo sham stimulation followed by active stimulation. After active stimulation of the subthalamic nucleus, the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score (on a scale from 0 to 40, with lower scores indicating less severe symptoms) was significantly lower than the score after sham stimulation, and the Global Assessment of Functioning (GAF) score (on a scale from 1 to 90, with higher scores indicating higher levels of functioning) was significantly higher. The ratings of neuropsychological measures, depression, and anxiety were not modified by stimulation. There were 15 serious adverse events overall, including 1 intracerebral hemorrhage and 2 infections; there were also 23 non-serious adverse events. The investigators concluded that these preliminary findings suggest that stimulation of the subthalamic nucleus may reduce the symptoms of severe forms of OCD but is associated with a substantial risk of serious adverse events (Mallet et al., 2008).

Professional Societies

American Psychiatric Association (APA): In a practice guideline for the treatment of patients with obsessive-compulsive disorder, the APA states that data regarding treatment of obsessive-compulsive disorder (OCD) with deep brain stimulation is limited and further research is needed. Two small, double-blind trials and several case reports have investigated the efficacy of DBS in OCD. Given the preliminary promising results in treatment-resistant OCD, the procedures reversibility and adjustability in comparison with ablative neurosurgery, and the absence to date of serious adverse events, DBS deserves investigation in severe, treatment-resistant OCD. Nonetheless, DBS is an invasive procedure, and the risks must be kept in mind. DBS should be considered only after first- and second-line treatments and well-supported augmentation strategies have been exhausted. For the time being, DBS and ablative neurosurgical treatment.
for OCD should be performed only at sites with expertise in both OCD and these treatment approaches (Koran, 2007).

**Additional Search Terms**
paroxysmal, myoclonic, myoclonus, paralysis agitans

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**U.S. FOOD AND DRUG ADMINISTRATION (FDA)**

Deep brain stimulation is a procedure and, therefore, not subject to FDA regulation. However, any medical devices, drugs, and/or tests used as part of this procedure may require FDA regulation.

**Parkinson’s disease and Essential Tremor**
The FDA approved the Activa® Tremor Control System (Medtronic) on July 31, 1997. The device is indicated for unilateral thalamic stimulation for the suppression of tremor in the upper extremity in patients who are diagnosed with essential tremor or Parkinsonian tremor not adequately controlled by medications and where the tremor constitutes a significant functional disability. Available at: [http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm083894.htm](http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm083894.htm), Accessed October 2013.

A January 14, 2002 Premarket Approval (PMA) supplement (S007) expanded use to include bilateral stimulation of the internal globus pallidus (GPI) or the subthalamic nucleus (STN) as an adjunctive therapy in reducing some of the symptoms of advanced, levodopa-responsive Parkinson’s disease that are not adequately controlled with medication. Available at: [http://www.accessdata.fda.gov/cdrh_docs/pdf/P960009S007b.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf/P960009S007b.pdf) Accessed October 2013.

**Dystonia**
On April 15, 2003, the Activa® Dystonia Therapy System (Medtronic) received a Humanitarian Device Exemption (HDE) from the FDA for unilateral and bilateral stimulation of the internal globus pallidus or the subthalamic nucleus and is indicated as an aid in the treatment of chronic, intractable (drug refractory), primary dystonia, including generalized and segmental dystonia, hemidystonia and cervical dystonia. Activa Dystonia Therapy is limited to use in implanting centers that receive Institutional Review Board (IRB) approval for the procedure. The safety and effectiveness of Activa Dystonia Therapy have not been established through a full PMA study. The therapy is approved for patients who are seven years of age and older. Available at: [http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cftopic/pma/pma.cfm?num=H020007](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cftopic/pma/pma.cfm?num=H020007). Accessed October 2013.

**Obsessive Compulsive Disorder**
On March 28, 2005, the Activa® Deep Brain Stimulation Therapy System was designated as a Humanitarian Use Device (HUD) for the treatment of chronic, treatment-resistant obsessive compulsive disorder (OCD) in a subset of patients. However, the FDA does not list a Humanitarian Device Exemption (HDE) approval for authorization to market the device.

On February 19, 2009, the Reclaim™ Deep Brain Stimulation Therapy device was designated as an HUD for the treatment of obsessive compulsive disorder (OCD). This device is indicated for bilateral stimulation of the anterior limb of the internal capsule (AIC) as an adjunct to medications and as an alternative to anterior capsulotomy for treatment of chronic, severe, treatment-resistant OCD in adult patients who have failed at least three selective serotonin reuptake inhibitors (SSRIs). See the following Web site for more information: [http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cftopic/pma/pma.cfm?num=H050003](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cftopic/pma/pma.cfm?num=H050003). Accessed October 2013.
Epilepsy

The Medtronic DBS therapy for refractory epilepsy (also known as the Intercept™ Epilepsy Control System) is under review by the FDA. On March 12, 2010, the FDA Neurological Devices Panel voted seven to five to recommend approval with conditions for the Medtronic DBS System for Epilepsy, and a final decision from FDA is pending. Medtronic submitted a premarket approval application (PMA) supplement in July 2009 for the Medtronic DBS System for Epilepsy as adjunctive treatment for partial-onset seizures in adults with medically refractory (i.e., treatment-resistant) epilepsy. Results from the Stimulation of the Anterior Nucleus of the Thalamus for Epilepsy (SANTE) trial supported Medtronic’s PMA. With the exception of the Intercept Patient Programmer, all components of the Medtronic system currently have U.S. marketing approval for other DBS indications as part of the Medtronic Activa PC Neurostimulation System for Tremor Control and Parkinson’s disease. The panel recommended the following conditions of approval for epilepsy:

- Labeling changes to address the increased risk of adverse events, including suicidal thoughts and actions, depression, memory problems, anxiety, and stimulation-related increased seizure frequency
- A five-year post-approval study that is hypothesis-driven, that has a control group, and targets various subgroups not well-defined in previous trials and that includes input from psychiatric experts to create an appropriate screening tool for suicidal tendencies

See the following Web sites for more information:

On May 10, 2005, the FDA issued a Public Health Notification regarding MRI-caused injuries in patients with implanted neurostimulators. Available at:

Additional Products

- Activa® Tremor Control Therapy (Medtronic, Inc.)
- Activa® Parkinson's Control Therapy (Medtronic, Inc.)
- Activa® Dystonia Therapy (Medtronic, Inc.)
- Intercept™ Epilepsy Control System
- Kinetra® neurostimulator (Medtronic, Inc.)
- Soletra® neurostimulator (Medtronic, Inc.)

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare covers unilateral or bilateral thalamic ventralis intermedia nucleus (VIM) 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) when specific criteria are met. Refer to the National Coverage Determination (NCD) for Deep Brain Stimulation for Essential Tremor and Parkinson's Disease (160.24).

Local Coverage Determinations (LCDs) do exist. Refer to the LCDs for Vagus Nerve Stimulation and Vagal Nerve Stimulation (VNS) for Intractable Depression.

(Accessed September 30, 2013)

APPLICABLE CODES

The codes listed in this policy are for reference purposes only. Listing of a service or device code in this policy does not imply that the service described by this code is a covered or non-covered

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health service. Coverage is determined by the benefit document. This list of codes may not be all inclusive.

<table>
<thead>
<tr>
<th>CPT® Code</th>
<th>Description</th>
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<tr>
<td>61863</td>
<td>Twist drill, burr hole, craniotomy, or craniectomy with stereotactic implantation of neurostimulator electrode array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), without use of intraoperative microelectrode recording; first array</td>
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<td>Twist drill, burr hole, craniotomy, or craniectomy with stereotactic implantation of neurostimulator electrode array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), with use of intraoperative microelectrode recording; first array</td>
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<td>61880</td>
<td>Revision or removal of intracranial neurostimulator electrodes</td>
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<td>61885</td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array</td>
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<tr>
<td>61886</td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to two or more electrode arrays</td>
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<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse 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, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming</td>
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<td>L8681</td>
<td>Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only</td>
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<td>L8682</td>
<td>Implantable neurostimulator radiofrequency receiver</td>
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<td>L8683</td>
<td>Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver</td>
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### HCPCS Code

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<td>L8687</td>
<td>Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension</td>
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<tr>
<td>L8689</td>
<td>External recharging system for battery (internal) for use with implantable neurostimulator, replacement only</td>
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### REFERENCES


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2013.


## POLICY HISTORY/REVISION INFORMATION

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<td>02/01/2014</td>
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