Protocol

Deep Brain Stimulation

(70163)

Medical Benefit		**Effective Date**: 07/01/18	**Next Review Date**: 05/21
Preauthorization	No	**Review Dates**: 09/07, 11/08, 09/09, 09/10, 09/11, 07/12, 05/13, 05/14, 05/15, 05/16, 05/17, 05/18, 05/19, 05/20	

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With essential tremor or tremor in Parkinson disease	Interventions of interest are: • Deep brain stimulation of the thalamus	Comparators of interest are: • Pharmacologic therapy • Permanent neuroablative procedure (e.g., thalamotomy, pallidotomy)	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With symptoms associated with Parkinson disease	Interventions of interest are: • Deep brain stimulation of the globus pallidus interna or subthalamic nucleus	Comparators of interest are: • Pharmacologic therapy • Physical and speech therapy	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With primary dystonia	Interventions of interest are: • Deep brain stimulation of the globus pallidus interna or subthalamic nucleus	Comparators of interest are: • Pharmacologic therapy • Permanent neuroablative procedure (e.g., thalamotomy, pallidotomy)	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With tardive dyskinesia or tardive dystonia	Interventions of interest are: • Deep brain stimulation	Comparators of interest are: • Pharmacologic therapy	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With drug-refractory epilepsy	Interventions of interest are: • Deep brain stimulation	Comparators of interest are: • Pharmacologic therapy • Vagus nerve stimulation	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With multiple sclerosis	Interventions of interest are: • Deep brain stimulation	Comparators of interest are: • Pharmacologic therapy	Relevant outcomes include: • Symptoms • Functional outcomes

Populations	Interventions	Comparators	Outcomes
			• Quality of life • Treatment-related morbidity
Individuals: • With Tourette syndrome	Interventions of interest are: • Deep brain stimulation	Comparators of interest are: • Pharmacologic therapy • Cognitive-behavioral therapy	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With cluster headaches or facial pain	Interventions of interest are: • Deep brain stimulation	Comparators of interest are: • Pharmacologic therapy • Botulinum toxin • Conservative therapy (e.g., diet, exercise)	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With treatment-resistant depression	Interventions of interest are: • Deep brain stimulation	Comparators of interest are: • Pharmacologic therapy • Behavioral therapy • Psychotherapy	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With obsessive-compulsive disorder	Interventions of interest are: • Deep brain stimulation	Comparators of interest are: • Pharmacologic therapy • Behavioral therapy • Psychotherapy	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With anorexia nervosa, alcohol addiction, Alzheimer disease, Huntington disease, or chronic pain	Interventions of interest are: • Deep brain stimulation	Comparators of interest are: • Pharmacologic therapy • Behavioral therapy • Psychotherapy	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity

DESCRIPTION

Deep brain stimulation (DBS) involves the stereotactic placement of an electrode into a central nervous system nucleus (e.g., hypothalamus, thalamus, globus pallidus, subthalamic nucleus). DBS is used as an alternative to permanent neuroablative procedures for control of essential tremor and Parkinson disease. DBS is also being evaluated for the treatment of a variety of other neurologic and psychiatric disorders.

SUMMARY OF EVIDENCE

For individuals who have essential tremor or tremor in Parkinson disease who receive DBS of the thalamus, the evidence includes a systematic review and case series. Relevant outcomes are symptoms, functional outcomes, quality of life (QOL), and treatment-related morbidity. The systematic review (a TEC Assessment) concluded that there was sufficient evidence that DBS of the thalamus results in clinically significant tremor suppression and that outcomes after DBS were at least as good as thalamotomy. Subsequent studies reporting long-term follow-up have supported the conclusions of the TEC Assessment and found that tremors were effectively controlled

five to six years after DBS. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have symptoms (e.g., speech, motor fluctuations) associated with Parkinson disease (advanced or more than four years in duration with early motor symptoms) who receive DBS of the globus pallidus interna (GPi) or subthalamic nucleus (STN), the evidence includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are symptoms, functional outcomes, QOL, and treatment-related morbidity. One of the systematic reviews (a TEC Assessment) concluded that studies evaluating DBS of the GPi or STN have consistently demonstrated clinically significant improvements in outcomes (e.g., neurologic function). Other systematic reviews have also found significantly better outcomes after DBS than after a control intervention. An RCT in patients with levodopa-responsive Parkinson disease of at least four years in duration and uncontrolled motor symptoms found that QOL at two years was significantly higher when DBS was provided in addition to medical therapy. Meta-analyses of RCTs comparing DBS of the GPi with DBS of the STN have reported mixed findings and have not shown that one type of stimulation is clearly superior to the other. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have primary dystonia who receive DBS of the GPi or STN, the evidence includes systematic reviews, RCTs, and case series. Relevant outcomes are symptoms, functional outcomes, QOL, and treatment-related morbidity. A pooled analysis of 24 studies, mainly uncontrolled, found improvements in motor scores and disability scores after six months and at last follow-up (mean, 32 months). Both double-blind RCTs found that severity scores improved more after active than after sham stimulation. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have tardive dyskinesia or tardive dystonia who receive DBS, the evidence includes an RCT and case series. Relevant outcomes are symptoms, functional outcomes, QOL, and treatment-related morbidity. Few studies were identified and they had small sample sizes (range, nine to 19 patients). The RCT did not report statistically significant improvement in the dystonia severity outcomes or the secondary outcomes related to disability and QOL but may have been under-powered Additional studies, especially RCTs or other controlled studies, are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have epilepsy who receive DBS, the evidence includes systematic reviews, RCTs and many observational studies. Relevant outcomes are symptoms, functional outcomes, QOL, and treatment-related morbidity. Two RCTs with more than 15 patients were identified. The larger RCT evaluated anterior thalamic nucleus DBS and reported that DBS had a positive impact on seizure frequency during some parts of the blinded trial phase but not others, and a substantial number of adverse events (in >30% of patients). There were no differences between groups in 50% responder rates, Liverpool Seizure Severity Scale, or Quality of Life in Epilepsy scores. A seven year open-label follow-up of the RCT included 66% of implanted patients; reasons for missing data were primarily related to adverse events or dissatisfaction with the device. Reduction in seizure frequency continued to improve during follow-up among the patients who continued follow-up. The smaller RCT (n=16) showed a benefit with DBS. Many small observational studies reported fewer seizures compared with baseline, however, without control groups, interpretation of these results is limited. Additional trials are required to determine the impact of DBS on patient outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have Tourette syndrome who receive DBS, the evidence includes observational studies, RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, QOL, and treatment-related morbidity. Two RCTs with 15 or more patients have been reported. One RCT found differences in severity of Tourette syndrome for active vs. sham at three months while the other RCT did not. Neither study demonstrated improvements in comorbid symptoms of obsessive-compulsive disorder or depression. Both studies reported high rates of serious adverse events. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have cluster headaches or facial pain who receive DBS, the evidence includes a randomized crossover study and case series. Relevant outcomes are symptoms, functional outcomes, QOL, and treatment-related morbidity. In the randomized study, the between-group difference in response rates did not differ significantly between active and sham stimulation phases. Additional RCTs or controlled studies are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have treatment-resistant depression who receive DBS, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, QOL, and treatment-related morbidity. The only double-blind, parallel-group RCT in patients with depression did not find that DBS significantly increased the response rate compared with sham; two other RCTs were stopped due to futility. A crossover controlled trial randomized patients to active or to sham stimulation after a year of open-label stimulation. There was a greater reduction in symptom scores after active stimulation but only in patients who were responders in the open-label phase; these findings might not be generalizable. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have obsessive-compulsive disorder who receive DBS, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, QOL, and treatment-related morbidity. Among the RCTs on DBS for obsessive-compulsive disorder, only one has reported the outcome of greatest clinical interest (therapeutic response rate), and that trial did not find a statistically significant benefit for DBS compared with sham treatment. The evidence is insufficient to determine the effects of the technology on health.

For individuals who have multiple sclerosis who receive DBS, the evidence includes an RCT. Relevant outcomes are symptoms, functional outcomes, QOL, and treatment-related morbidity. One RCT with ten multiple sclerosis patients is insufficient evidence on which to draw conclusions about the efficacy of DBS in this population. Additional trials are required. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have anorexia nervosa, alcohol addiction, Alzheimer disease, Huntington disease, or chronic pain who receive DBS, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, QOL, and treatment-related morbidity. RCTs are needed to evaluate the efficacy of DBS for these conditions. The evidence is insufficient to determine the effects of the technology on health outcomes.

POLICY

Unilateral deep brain stimulation of the thalamus may be considered **medically necessary** in patients with disabling, medically unresponsive tremor due to essential tremor or Parkinson disease.

Bilateral deep brain stimulation of the thalamus may be considered **medically necessary** in patients with disabling, medically unresponsive tremor in both upper limbs due to essential tremor or Parkinson disease.

Unilateral or bilateral deep brain stimulation of the globus pallidus or subthalamic nucleus may be considered **medically necessary** in the following patients:

- Those with Parkinson disease and ALL of the following:
  - a good response to levodopa; AND
  - motor complications not controlled by pharmacologic therapy; AND
  - one of the following:
    - a minimum score of 30 points on the motor portion of the Unified Parkinson Disease Rating Scale when the patient has been without medication for approximately 12 hours; OR

  - Parkinson disease for at least four years

- Patients older than seven years with chronic, intractable (drug refractory) primary dystonia, including generalized and/or segmental dystonia, hemidystonia, and cervical dystonia (torticollis).

Deep brain stimulation for other movement disorders, including but not limited to tardive dyskinesia, multiple sclerosis, and post-traumatic dyskinesia, is considered **investigational**.

Deep brain stimulation for the treatment of chronic cluster headaches is considered **investigational**.

Deep brain stimulation for the treatment of other psychiatric or neurologic disorders, including but not limited to epilepsy, Tourette syndrome, depression, obsessive-compulsive disorder, anorexia nervosa, alcohol addiction, Alzheimer disease, and chronic pain, is considered **investigational**.

POLICY GUIDELINES

Disabling, medically unresponsive tremor is defined as all of the following:

- tremor causing significant limitation in daily activities
- inadequate control by maximal dosage of medication for at least three months before implant.

Contraindications to DBS include:

- patients who are not good surgical risks because of unstable medical problems or because of the presence of a cardiac pacemaker
- patients who have medical conditions that require repeated magnetic resonance imaging (MRI)
- patients who have dementia that may interfere with the ability to cooperate
- patients who have had botulinum toxin injections within the last six months.

MEDICARE ADVANTAGE

Medicare Advantage will consider unilateral or bilateral thalamic ventralis intermedius nucleus (VIM) deep brain stimulation (DBS) **medically necessary** 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) only under the following conditions:

1. The devices are (FDA) approved devices for DBS or devices used in accordance with FDA approved protocols governing Category B Investigational Device Exemption (IDE) DBS clinical trials.
2. For thalamic VIM DBS to be considered reasonable and necessary, members must meet all of the following criteria:
   a. Diagnosis of ET based on postural or kinetic tremors of hand(s) without other neurologic signs, or diagnosis of idiopathic PD (presence of at least two cardinal PD features [tremor, rigidity or bradykinesia]) which is of a tremor-dominant form.
   b. Marked disabling tremor of at least level three or four on the Fahn-Tolosa-Marin Clinical Tremor Rating Scale (or equivalent scale) in the extremity intended for treatment, causing significant limitation in daily activities despite optimal medical therapy.
   c. Willingness and ability to cooperate during conscious operative procedure, as well as during post-surgical evaluations, adjustments of medications and stimulator settings.

3. For STN or GPi DBS to be considered reasonable and necessary, patients must meet all of the following criteria:
   a. Diagnosis of PD based on the presence of at least two cardinal PD features (tremor, rigidity or bradykinesia).
   b. Advanced idiopathic PD as determined by the use of Hoehn and Yahr stage or Unified Parkinson's Disease Rating Scale (UPDRS) part III motor subscale.
   c. L-dopa responsive with clearly defined "on" periods.
   d. Persistent disabling Parkinson's symptoms or drug side effects (e.g., dyskinesias, motor fluctuations, or disabling "off" periods) despite optimal medical therapy.
   e. Willingness and ability to cooperate during conscious operative procedure, as well as during post-surgical evaluations, adjustments of medications and stimulator settings.

DBS is **not medically necessary** for ET or PD members with any of the following:

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

MEDICARE ADVANTAGE POLICY GUIDELINES

Members who undergo DBS implantation should not be exposed to diathermy (deep heat treatment including shortwave diathermy, microwave diathermy and ultrasound diathermy) or any type of MRI, which may adversely affect the DBS system or adversely affect the brain around the implanted electrodes.

DBS should be performed with extreme caution in members with cardiac pacemakers or other electronically controlled implants, which may adversely affect or be affected by the DBS system.

BACKGROUND

DEEP BRAIN STIMULATION

DBS involves the stereotactic placement of an electrode into the brain (i.e., hypothalamus, thalamus, globus pallidus, or subthalamic nucleus). The electrode is initially attached to a temporary transcutaneous cable for short-term stimulation to validate treatment effectiveness. Several days later, the patient returns for permanent subcutaneous surgical 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 most severe symptoms. However, use of bilateral stimulation using two electrode arrays has also been investigated 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 disease (PD), 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 adverse effects of neurostimulation, such as dysarthria, disequilibrium, or involuntary movements.

REGULATORY STATUS

In 1997, the Activa® Tremor Control System (Medtronic) was cleared for marketing by the U.S. Food and Drug Administration (FDA) for DBS. The Activa® Tremor Control System consists of an implantable neurostimulator, a deep brain stimulator lead, an extension that connects the lead to the power source, a console programmer, a software cartridge to set electrical parameters for stimulation, and a patient control magnet, which allows the patient to turn the neurostimulator on and off, or change between high and low settings.

The original FDA-labeled indications for Activa® were limited to unilateral implantation of the device for the treatment of tremor, but in 2002, the FDA-labeled indications were expanded to include bilateral implantation as a treatment to decrease the symptoms of advanced PD not controlled by medication. In 2003, the labeled indications were further expanded to include "…unilateral or bilateral stimulation of the internal globus pallidus or subthalamic nucleus to aid in the management of chronic, intractable (drug refractory) primary dystonia, including generalized and/or segmental dystonia, hemidystonia, and cervical dystonia (torticollis) in patients seven years of age or above." This latter indication was cleared for marketing by the FDA through the humanitarian device exemption process. In 2017, the indications for PD were modified to include "adjunctive therapy in reducing some of the symptoms in individuals with levodopa-responsive Parkinson's Disease of at least four years' duration that are not adequately controlled with medication."

In 2009, the Reclaim® device (Medtronic), a DBS device, was cleared for marketing by the FDA through the humanitarian device exemption process for the treatment of severe obsessive-compulsive disorder.

In 2014, the Brio Neurostimulation System (now called Infinity; St. Jude Medical Neuromodulation) was cleared for marketing by the FDA for the treatment of Parkinsonian tremor.

In 2016, the St. Jude Medical's Infinity DBS device with directional leads was approved by the FDA. 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.

In2017, a second system with directional leads, the Vercise Deep Brain Stimulation System (Boston Scientific), was approved by the 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.

In 2018, the FDA approved the Medtronic DBS System for Epilepsy (Medtronic, Inc) through the Premarket Approval process. The pivotal study was the Stimulation of the Anterior Nucleus of the Thalamus for Epilepsy. The intended use is bilateral stimulation of the anterior nucleus of the thalamus as an adjunctive therapy for reducing the frequency of seizures in individuals 18 years of age or older diagnosed with epilepsy characterized by partial-onset seizures, with or without secondary generalization, that are refractory to three or more antiepileptic medications.

FDA product code: MHY.

RELATED PROTOCOL

Vagus Nerve Stimulation

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

1. Blue Cross and Blue Shield Technology Evaluation Center. Deep brain stimulation of the thalamus for tremor. TEC Assessment. 1997;Volume 12:Tab 20.
2. Schuurman PR, Bosch DA, Merkus MP, et al. Long-term follow-up of thalamic stimulation versus thalamotomy for tremor suppression. Mov Disord. Jun 15 2008;23(8):1146-1153. PMID 18442104.
3. Hariz MI, Krack P, Alesch F, et al. Multicentre European study of thalamic stimulation for parkinsonian tremor: a 6 year follow-up. J Neurol Neurosurg Psychiatry. Jun 2008;79(6):694-699. PMID 17898034.
4. Putzke JD, Uitti RJ, Obwegeser AA, et al. Bilateral thalamic deep brain stimulation: midline tremor control. J Neurol Neurosurg Psychiatry. May 2005;76(5):684-690. PMID 15834027.
5. Pahwa R, Lyons KE, Wilkinson SB, et al. Long-term evaluation of deep brain stimulation of the thalamus. J Neurosurg. Apr 2006;104(4):506-512. PMID 16619653.
6. Pollo C, Kaelin-Lang A, Oertel MF, et al. Directional deep brain stimulation: an intraoperative double-blind pilot study. Brain. Jul 2014;137(Pt 7):2015-2026. PMID 24844728.
7. Steigerwald F, Muller L, Johannes S, et al. Directional deep brain stimulation of the subthalamic nucleus: A pilot study using a novel neurostimulation device. Mov Disord. Aug 2016;31(8):1240-1243. PMID 27241197.
8. Rebelo P, Green AL, Aziz TZ, et al. Thalamic Directional Deep Brain Stimulation for tremor: Spend less, get more. Brain Stimul. Jan 6 2018. PMID 29373260.
9. Dembek TA, Reker P, Visser-Vandewalle V, et al. Directional DBS increases side-effect thresholds-A prospective, double-blind trial. Mov Disord. Oct 2017;32(10):1380-1388. PMID 28843009.
10. Blue Cross and Blue Shield Technology Evaluation Center. Bilateral deep brain stimulation of the subthalamic nucleus or the globus pallidus interna for treatment of advanced Parkinson's disease. TEC Assessment. 2001;Volume 16:Tab 16.
11. Perestelo-Perez L, Rivero-Santana A, Perez-Ramos J, et al. Deep brain stimulation in Parkinson's disease: meta-analysis of randomized controlled trials. J Neurol. Nov 2014;261(11):2051-2060. PMID 24487826.
12. Kleiner-Fisman G, Herzog J, Fisman DN, et al. Subthalamic nucleus deep brain stimulation: summary and meta- analysis of outcomes. Mov Disord. Jun 2006;21(Suppl 14):S290-304. PMID 16892449.
13. Appleby BS, Duggan PS, Regenberg A, et al. Psychiatric and neuropsychiatric adverse events associated with deep brain stimulation: A meta-analysis of ten years' experience. Mov Disord. Sep 15 2007;22(12):1722-1728. PMID 17721929.
14. Schuepbach WM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson's disease with early motor complications. N Engl J Med. Feb 14 2013;368(7):610-622. PMID 23406026.
15. Sako W, Miyazaki Y, Izumi Y, et al. Which target is best for patients with Parkinson's disease? A meta-analysis of pallidal and subthalamic stimulation. J Neurol Neurosurg Psychiatry. Sep 2014;85(9):982-986. PMID 24444854.

16. Combs HL, Folley BS, Berry DT, et al. Cognition and depression following deep brain stimulation of the subthalamic nucleus and globus pallidus pars internus in Parkinson's disease: a meta-analysis. Neuropsychol Rev. Dec 2015;25(4):439-454. PMID 26459361.
17. Tan ZG, Zhou Q, Huang T, et al. Efficacies of globus pallidus stimulation and subthalamic nucleus stimulation for advanced Parkinson's disease: a meta-analysis of randomized controlled trials. Clin Interv Aging. Jul 2016;11:777-786. PMID 27382262.
18. Wang JW, Zhang YQ, Zhang XH, et al. Cognitive and psychiatric effects of STN versus GPi deep brain stimulation in Parkinson's disease: a meta-analysis of randomized controlled trials. PLoS One. Jun 2016;11(6): e0156721. PMID 27248139.
19. Xie CL, Shao B, Chen J, et al. Effects of neurostimulation for advanced Parkinson's disease patients on motor symptoms: A multiple-treatments meta-analysis of randomized controlled trials. Sci Rep. May 04 2016;6: 25285. PMID 27142183.
20. Xu F, Ma W, Huang Y, et al. Deep brain stimulation of pallidal versus subthalamic for patients with Parkinson's disease: a meta-analysis of controlled clinical trials. Neuropsychiatr Dis Treat. Jul 2016;12:1435-1444. PMID 27382286.
21. U.S. Food and Drug Administration. Summary of Safety and Probable Benefit. Medtronic Activa Dystonia Therapy. 2003; http://www.accessdata.fda.gov/cdrh_docs/pdf2/H020007b.pdf. Accessed February 22, 2018.
22. Moro E, LeReun C, Krauss JK, et al. Efficacy of pallidal stimulation in isolated dystonia: a systematic review and meta-analysis. Eur J Neurol. Apr 2017;24(4):552-560. PMID 28186378.
23. Rodrigues, FF, Duarte, GG, Prescott, DD, Ferreira, JJ, Costa, JJ. Deep brain stimulation for dystonia. Cochrane Database Syst Rev, 2019 Jan 11;1:CD012405. PMID 30629283.
24. Kupsch, AA, Benecke, RR, Müller, JJ, Trottenberg, TT, Schneider, GG, Poewe, WW, Eisner, WW, Wolters, AA, Müller, JJ, Deuschl, GG, Pinsker, MM, Skogseid, II, Roeste, GG, Vollmer-Haase, JJ, Brentrup, AA, Krause, MM, Tronnier, VV, Schnitzler, AA, Voges, JJ, Nikkhah, GG, Vesper, JJ, Naumann, MM, Volkmann, JJ. Pallidal deep-brain stimulation in primary generalized or segmental dystonia. N. Engl. J. Med., 2006 Nov 10;355(19). PMID 17093249.
25. Volkmann J, Mueller J, Deuschl G, et al. Pallidal neurostimulation in patients with medication-refractory cervical dystonia: a randomised, sham-controlled trial. Lancet Neurol. Sep 2014;13(9):875-884. PMID 25127231.
26. Gruber, DD, Südmeyer, MM, Deuschl, GG, Falk, DD, Krauss, JJ, Mueller, JJ, Müller, JJ, Poewe, WW, Schneider, GG, Schrader, CC, Vesper, JJ, Volkmann, JJ, Winter, CC, Kupsch, AA, Schnitzler, AA. Neurostimulation in tardive dystonia/dyskinesia: A delayed start, sham stimulation-controlled randomized trial. Brain Stimul, 2018 Sep 27;11(6). PMID 30249417.
27. Damier P, Thobois S, Witjas T, et al. Bilateral deep brain stimulation of the globus pallidus to treat tardive dyskinesia. Arch Gen Psychiatry. Feb 2007;64(2):170-176. PMID 17283284.
28. Gruber D, Trottenberg T, Kivi A, et al. Long-term effects of pallidal deep brain stimulation in tardive dystonia. Neurology. Jul 7 2009;73(1):53-58. PMID 19564584.
29. Pouclet-Courtemanche H, Rouaud T, Thobois S, et al. Long-term efficacy and tolerability of bilateral pallidal stimulation to treat tardive dyskinesia. Neurology. Feb 16 2016;86(7):651-659. PMID 26791148.
30. Kwan, PP, Arzimanoglou, AA, Berg, AA, Brodie, MM, Allen Hauser, WW, Mathern, GG, Moshé, SS, Perucca, EE, Wiebe, SS, French, JJ. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia, 2009 Nov 6;51(6). PMID 19889013.
31. Borghs, SS, de la Loge, CC, Cramer, JJ. Defining minimally important change in QOLIE-31 scores: estimates from three placebo-controlled lacosamide trials in patients with partial-onset seizures. Epilepsy Behav, 2012 Feb 22;23(3). PMID 22341962.
32. Sprengers, MM, Vonck, KK, Carrette, EE, Marson, AA, Boon, PP. Deep brain and cortical stimulation for epilepsy. Cochrane Database Syst Rev, 2017 Jul 19;7:CD008497. PMID 28718878.

33. Li MCH, Cook MJ. Deep brain stimulation for drug-resistant epilepsy. Epilepsia. Feb 2018;59(2):273-290. PMID 29218702.
34. Bouwens van der Vlis TAM, Schijns O, Schaper F, et al. Deep brain stimulation of the anterior nucleus of the thalamus for drug-resistant epilepsy. Neurosurg Rev. Jan 6 2018. PMID 29306976.
35. Fisher R, Salanova V, Witt T, et al. Electrical stimulation of the anterior nucleus of thalamus for treatment of refractory epilepsy. Epilepsia. May 2010;51(5):899-908. PMID 20331461.
36. Food and Drug Administration. Medtronic DBS System for Epilepsy, Summary of Safety and Effectiveness Data (SSED). Accessed March 8, 2019.
37. Troster AI, Meador KJ, Irwin CP, et al. Memory and mood outcomes after anterior thalamic stimulation for refractory partial epilepsy. Seizure. Feb 2017;45:133-141. PMID 28061418.
38. Cukiert A, Cukiert CM, Burattini JA, et al. Seizure outcome after hippocampal deep brain stimulation in patients with refractory temporal lobe epilepsy: A prospective, controlled, randomized, double-blind study. Epilepsia. Oct 2017;58(10):1728-1733. PMID 28744855.
39. Salanova V, Witt T, Worth R, et al. Long-term efficacy and safety of thalamic stimulation for drug-resistant partial epilepsy. Neurology. Mar 10 2015;84(10):1017-1025. PMID 25663221.
40. Kim SH, Lim SC, Kim J, et al. Long-term follow-up of anterior thalamic deep brain stimulation in epilepsy: A 11-year, single center experience. Seizure. Nov 2017;52:154-161. PMID 29040867.
41. Baldermann JC, Schuller T, Huys D, et al. Deep brain stimulation for Tourette-syndrome: a systematic review and meta-analysis. Brain Stimul. Mar-Apr 2016;9(2):296-304. PMID 26827109.
42. Fraint A, Pal G. Deep brain stimulation in Tourette's syndrome. Front Neurol. Aug 2015;6:170. PMID 26300844.
43. Schrock LE, Mink JW, Woods DW, et al. Tourette syndrome deep brain stimulation: a review and updated recommendations. Mov Disord. Apr 2015;30(4):448-471. PMID 25476818.
44. Servello D, Zekaj E, Saleh C, et al. Sixteen years of deep brain stimulation in Tourette's Syndrome: a critical review. J Neurosurg Sci. Jun 2016;60(2):218-229. PMID 26788742.
45. Piedad JC, Rickards HE, Cavanna AE. What patients with Gilles de la Tourette syndrome should be treated with deep brain stimulation and what is the best target? Neurosurgery. Jul 2012;71(1):173-192. PMID 22407075.
46. Kefalopoulou Z, Zrinzo L, Jahanshahi M, et al. Bilateral globus pallidus stimulation for severe Tourette's syndrome: a double-blind, randomised crossover trial. Lancet Neurol. Jun 2015;14(6):595-605. PMID 25882029.
47. Welter, MM, Houeto, JJ, Thobois, SS, Bataille, et al. Anterior pallidal deep brain stimulation for Tourette's syndrome: a randomised, double-blind, controlled trial. Lancet Neurol, 2017 Jun 25;16(8). PMID 28645853.
48. Martinez-Ramirez, DD, Jimenez-Shahed, JJ, Leckman, et al. Efficacy and Safety of Deep Brain Stimulation in Tourette Syndrome: The International Tourette Syndrome Deep Brain Stimulation Public Database and Registry. JAMA Neurol, 2018 Jan 18;75(3). PMID 29340590.
49. International Headache Society. International Classification of Headache Disorders. 2018; https://www.ichd-3.org. Accessed January 8, 2019.
50. Fontaine D, Lazorthes Y, Mertens P, et al. Safety and efficacy of deep brain stimulation in refractory cluster headache: a randomized placebo-controlled double-blind trial followed by a 1-year open extension. J Headache Pain. Feb 2010;11(1):23-31. PMID 19936616.
51. Bussone G, Franzini A, Proietti Cecchini A, et al. Deep brain stimulation in craniofacial pain: seven years' experience. Neurol Sci. May 2007;28(Suppl 2):S146-149. PMID 17508162.
52. Broggi G, Franzini A, Leone M, et al. Update on neurosurgical treatment of chronic trigeminal autonomic cephalalgias and atypical facial pain with deep brain stimulation of posterior hypothalamus: results and comments. Neurol Sci. May 2007;28(Suppl 2):S138-145. PMID 17508161.
53. Morishita T, Fayad SM, Higuchi MA, et al. Deep brain stimulation for treatment-resistant depression: systematic review of clinical outcomes. Neurotherapeutics. Jul 2014;11(3):475-484. PMID 24867326.
54. Mosley PE, Marsh R, Carter A. Deep brain stimulation for depression: Scientific issues and future directions. Aust N Z J Psychiatry. Nov 2015;49(11):967-978. PMID 26276049.

55. Dougherty DD, Rezai AR, Carpenter LL, et al. A randomized sham-controlled trial of deep brain stimulation of the ventral capsule/ventral striatum for chronic treatment-resistant depression. Biol Psychiatry. Aug 15 2015;78(4):240-248. PMID 25726497.
56. Bergfeld IO, Mantione M, Hoogendoorn ML, et al. Deep brain stimulation of the ventral anterior limb of the internal capsule for treatment-resistant depression: a randomized clinical trial. JAMA Psychiatry. May 01 2016;73(5):456-464. PMID 27049915.
57. de Koning PP, Figee M, van den Munckhof P, et al. Current status of deep brain stimulation for obsessive-compulsive disorder: a clinical review of different targets. Curr Psychiatry Rep. Aug 2011;13(4):274-282. PMID 21505875.
58. Hamani C, Pilitsis J, Rughani AI, et al. Deep brain stimulation for obsessive-compulsive disorder: systematic review and evidence-based guideline sponsored by the American Society for Stereotactic and Functional Neurosurgery and the Congress of Neurological Surgeons (CNS) and endorsed by the CNS and American Association of Neurological Surgeons. Neurosurgery. Oct 2014;75(4):327-333; quiz 333. PMID 25050579.
59. Alonso P, Cuadras D, Gabriels L, et al. Deep brain stimulation for obsessive-compulsive disorder: a meta-analysis of treatment outcome and predictors of response. PLoS One. Jul 2015;10(7):e0133591. PMID 26208305.
60. Kisely S, Hall K, Siskind D, et al. Deep brain stimulation for obsessive-compulsive disorder: a systematic review and meta-analysis. Psychol Med. Dec 2014;44(16):3533-3542. PMID 25066053.
61. Naesstrom M, Blomstedt P, Bodlund O. A systematic review of psychiatric indications for deep brain stimulation, with focus on major depressive and obsessive-compulsive disorder. Nord J Psychiatry. Oct 2016;70(7): 483-491. PMID 27103550.
62. Cruccu G, Garcia-Larrea L, Hansson P, et al. EAN guidelines on central neurostimulation therapy in chronic pain conditions. Eur J Neurol. Oct 2016;23(10):1489-1499. PMID 27511815.
63. Zesiewicz TA, Elble RJ, Louis ED, et al. Evidence-based guideline update: treatment of essential tremor: report of the Quality Standards subcommittee of the American Academy of Neurology. Neurology. Nov 8 2011;77(19):1752-1755. PMID 22013182.
64. Zesiewicz TA, Elble R, Louis ED, et al. Practice parameter: therapies for essential tremor: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. Jun 28 2005;64(12):2008-2020. PMID 15972843.
65. Pahwa R, Factor SA, Lyons KE, et al. Practice Parameter: treatment of Parkinson disease with motor fluctuations and dyskinesia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. Apr 11 2006;66(7):983-995. PMID 16606909.
66. Zesiewicz TA, Sullivan KL, Arnulf I, et al. Practice Parameter: treatment of nonmotor symptoms of Parkinson disease: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. Mar 16 2010;74(11):924-931. PMID 20231670.
67. Bhidayasiri R, Fahn S, Weiner WJ, et al. Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. Jul 30 2013; 81(5):463-469. PMID 23897874.
68. Bhidayasiri R, Jitkritsadakul O, Friedman JH, et al. Updating the recommendations for treatment of tardive syndromes: A systematic review of new evidence and practical treatment algorithm. J Neurol Sci. Feb 5 2018. PMID 29454493.
69. Muller-Vahl KR, Cath DC, Cavanna AE, et al. European clinical guidelines for Tourette syndrome and other tic disorders. Part IV: deep brain stimulation. Eur Child Adolesc Psychiatry. Apr 2011;20(4):209-217. PMID 21445726.
70. Kennedy SH, Milev R, Giacobbe P, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) Clinical guidelines for the management of major depressive disorder in adults. IV. Neurostimulation therapies. J Affect Disord. Oct 2009;117(Suppl 1):S44-53. PMID 19656575.

71. National Institute for Health and Care Excellence (NICE). Deep brain stimulation for tremor and dystonia (excluding Parkinson's disease) [IPG188]. 2006; https://www.nice.org.uk/guidance/ipg188. Accessed February 22, 2018.
72. National Institute for Health and Care Excellence (NICE). Deep brain stimulation for refractory chronic pain syndromes (excluding headache) [IPG382]. 2011; http://guidance.nice.org.uk/IPG382. Accessed February 22, 2018.
73. National Institute for Health and Care Excellence (NICE). Deep brain stimulation for intractable trigeminal autonomic cephalalgias [IPG381]. 2011; http://www.nice.org.uk/IPG381. Accessed February 22, 2018.
74. National Institute for Health and Care Excellence (NICE). Deep brain stimulation for refractory epilepsy [IPG416]. 2012; http://guidance.nice.org.uk/IPG416. Accessed February 22, 2018.
75. National Institute for Health and Care Excellence (NICE). Deep brain stimulation for Parkinson's disease [IPG19]. 2003; https://www.nice.org.uk/guidance/ipg19. Accessed February 22, 2018.
76. Centers for Medicare & Medicaid (CMS). National Coverage Determination (NCD) for Deep Brain Stimulation for Essential Tremor and Parkinson's Disease (160.24). 2003; https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=279&ncdver=1&DocID=160.24&bc=gAAAABAAAAAA&. Accessed February 22, 2018.
77. National Coverage Determination (NCD) for Deep BRAIN STIMULATION for Essential Tremor and Parkinson's Disease (160.24), Implementation Date 4/1/2003.