Clinical Review Criteria
Deep Brain Stimulation

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Criteria
For Medicare Members

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<td>CMS Coverage Manuals</td>
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<td>National Coverage Determinations (NCD)</td>
<td>Deep Brain Stimulation for Essential Tremor and Parkinson's Disease (160.24)</td>
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<td>Local Coverage Determinations (LCD)</td>
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For Non-Medicare Members
Kaiser Permanente has elected to use the Deep Brain Stimulation (KP-0403) MCG* for medical necessity determinations.

*MCG Manuals are proprietary and cannot be published and/or distributed. However, on an individual member basis, Kaiser Permanente can share a copy of the specific criteria document used to make a utilization management decision. If one of your patients is being reviewed using these criteria, you may request a copy of the criteria by calling the Kaiser Permanente Clinical Review staff at 1-800-289-1363.

If requesting this service, please send the following documentation to support medical necessity:
- Last 6 months of clinical notes from requesting provider &/or specialist (neurology, neuro surgeon)

There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies:
- Refractory Obsessive - Compulsive Disorder
- Primary Headache
- Neuropathic Pain (see KP-0403)

(See also Occipital Nerve Stimulation for Primary Headache)

The following information was used in the development of this document and is provided as background only. It is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

Background
Deep-brain stimulation (DBS) was first developed in the late 1980’s. DBS involves ongoing electrical stimulation of a particular target in the brain and is designed to block the abnormal firing of neurons. The exact mechanism of action of DBS is not known. DBS has been used since the early 1990s to treat movement disorders such as Parkinson's disease, and, in 1999, the first report was published applying DBS to the treatment of refractory obsessive-compulsive disorder.

DBS consists of an insulated wire lead with four electrodes at its end that are surgically implanted into the affected area of the brain. A wire runs under the skin to a battery-operated pulse generator implanted near the collarbone or in abdomen. The generator is programmed to send continuous low voltage electrical pulses to the brain. It can be turned on or off when the patient swipes a special magnet over the generator. (Movement disorders patients...
typically turn off the device at night, because tremors usually stop during sleep.) The voltage can be adjusted in relation to the symptoms being treated.

To implant the electrodes, a neurosurgeon uses a stereotactic head frame and magnetic resonance or computed tomography imaging to map the brain and pinpoint the problem area. The patient's scalp is anesthetized before the procedure, but the patient is awake to report side effects while the electrodes are placed. This allows the lead to be placed for maximum effectiveness and minimum side effects.

**Evidence and Source Documents**

- *Electrical Stimulation of the Thalamus for Essential and Parkinsonian Tremor*
- *Globus Pallidus and Subthalamic Nucleus Stimulator Implant- Parkinson’s Refractory Obsessive-Compulsive Disorder*
- *Primary Headache*

**Medical Technology Assessment Committee (MTAC)**

**Electrical Stimulation of the Thalamus for Essential and Parkinsonian Tremor**

**BACKGROUND**

Essential tremor is the most common form of tremor that affects more than 1 million patients in the US. It is defined as tremor which is postural, usually involving the upper limbs, absent at rest, not exacerbated by movement and not of cerebellar or extrapyramidal origin. One of the symptoms of Parkinson's Disease is tremor. Treatment for mild cases of tremor involves pharmacologic therapy with propanalol or L-dopa for Parkinsonian tremor. Severe debilitating tremor is usually treated with stereotactic surgical thalamic ablation (thalmotomy). However, thalmotomy can result in clinically significant neurologic side effects and once lesioned, no further tremor control is possible. The beneficial effects of thalamic stimulation on tremor were first identified when stimulation was used to localize the electrode prior to making a lesion in the thalamus for tremor control.

Electrical tremor control systems consist of an electrode implanted in the thalamus connected to an implanted radio-frequency pulse generator. The stimulator is programmed for optimal tremor control by a Neurologist and can be turned on or off by the patient using a magnet.

**04/19/1999: MTAC REVIEW**

**Electrical Stimulation of the Thalamus for Essential and Parkinsonian Tremor**

**Evidence Conclusion:** Several case series have been published examining the role of thalamic stimulation in essential tremor and in Parkinson's disease. It is clear that stimulation reduces contralateral upper limb tremor to a clinically significant extent. In essential tremor improvement was noted when performing activities such as writing, drinking and eating. Although quality of life was not formally assessed the degree of change is likely to be clinically important. In Parkinson's disease the utility of reducing tremor is less clear, with no change in ability to write, dress, cut food, or speak. Perioperative complications occur in approximately 10%, and at 12 months neurologic complications related to stimulus intensity are common, each of the following occurring in 2-4%: dystonia, dysarthria, paraesthesia, and disequilibrium.


Members noted that patients who had debilitating non-tremor symptoms of Parkinson’s disease such as rigidity and cogwheel movements would probably not show clinically significant improvements in their ability to eat, write or drink and therefore the benefits of thalamic stimulation would probably not outweigh the harms of this invasive surgical procedure in this population.

Electrical stimulation of the thalamus for the treatment of essential tremor meets GHC Medical Technology Assessment Criteria 1-5 for effectiveness and 6 for appropriateness and is therefore considered to be medically appropriate for patients who have failed maximal medical therapy for controlling their tremor.

Thalamic stimulation for treatment of Parkinsonian tremor also meets GHC Medical Technology Assessment Criteria 1-6 only for patients whose primary functional disability is tremor despite maximal medical therapy.

**10/03/2006: MTAC REVIEW**
Electrical Stimulation of the Thalamus for Essential and Parkinsonian Tremor

**Evidence Conclusion:** The evidence on deep brain stimulation for treating Parkinson’s disease consists of two randomized controlled trials. Both studies had results favoring deep brain stimulation. The stronger study methodologically found a statistically significant reduction in motor symptom scores in the group assigned to deep brain stimulation in a double-blind comparison to no stimulation (Deep Brain Stimulation Study Group, 2001). However, Medtronic, the device manufacturer funded the study and was responsible for data collection and analysis. The other randomized controlled trial found more improvement in quality of life and symptom severity scores in patients assigned to neurostimulation compared to medical management (Deutschl et al., 2006). Limitations of the latter study are the study was not blinded and study participants had already failed medical management. The Deutschl study was not funded by Medtronic, but several authors had financial links with the company.


Evidence updated but not brought to MTAC as no change from previous review outcome.

Globus Pallidus and Subthalamic Nucleus Stimulator Implant

**BACKGROUND**

Deep brain stimulation (DBS) is a technique that is being used to treat symptoms of Parkinson’s disease (PD). The main pharmacotherapy for PD is levodopa. Although levodopa is generally initially effective at reducing symptoms of PD, it eventually leads to side effects such as dyskinesias in many patients. Surgeries such as thalamotomy, pallidotomy are other possible treatments. An advantage of DBS is that, unlike other surgeries, it does not create lesions or destroy brain tissue.

Deep brain stimulation involves implanting an electrode into a specific region of the brain using stereotactic neurosurgical techniques. The electrode is connected to a programmable pulse generator that generates high frequency stimulation (>100 Hz) in a target nucleus. The pulse generator is implanted below the clavicle.

Thalamic stimulation, used to treat tremor, is the most well established application of DBS with Parkinson’s patients (thalamic stimulation for tremor met MTAC evaluation criteria in April, 1999). Other targets are the internal globus pallidus and subthalamic nucleus which are believed to be effective for treating a wider range of PD symptoms, including bradykinesia, rigidity dystonia and gait disorder, as well as tremor.

Medtronic, Inc. manufactures the device that provides deep brain stimulation (the Activa System). The FDA approved a version of this device in 1997 for stimulation of the thalamus to control Parkinson’s tremor and essential tremor. In March 2000, an FDA panel gave a premarket approval with conditions for bilateral DBS for the treatment of other Parkinson's symptoms.

10/10/2001: MTAC REVIEW

Globus Pallidus and Subthalamic Nucleus Stimulator Implant

**Evidence Conclusion:** The highest quality evidence consisted of one study that had a double-blind randomized component. In the double-blind randomized assessment, the study found a statistically significant reduction in motor symptom scores during deep-brain stimulation of the subthalamic nucleus or pars interna of the globus pallidus compared to no stimulation. The case series portion of the study found that symptoms improved significantly with stimulation 3 and 6 months post-implantation compared to pre-implantation. There were a substantial number of adverse effects but no comparison with adverse effects with other treatments or no treatment. A limitation of the study was that Medtronic, the device manufacturer, not only funded the study but also was responsible for data collection and analysis.

**Articles:** The search yielded 146 articles, many of which were review articles, opinion pieces, dealt with technical aspects of the procedures or addressed other, similar treatments. There were a number of small studies (n=25 or less), mainly case series; one was an RCT with n=10. The strongest study was published after the formal search was conducted. This study included a randomized double-blind assessment of outcomes and the sample size was over 100. This partially randomized study was critically appraised: Deep-brain stimulation for Parkinson’s disease study group. Deep-brain stimulation of the subthalamic nucleus or the pars interna of the globus pallidus in Parkinson's disease. N Engl J Med 2001;345: 956-63. See Evidence Table.

The use of Globus Pallidus and Subthalamic Nucleus Stimulator Implant in treatment of Parkinson's Symptoms does meet the Kaiser Permanente Medical Technology Assessment Criteria.
Obsessive-compulsive disorder is a common psychiatric diagnosis, affecting approximately 3% of people worldwide (Burdick et al., 2009). For initial treatment of OCD, the American Psychiatric Association (APA) recommends cognitive behavioral therapy (CBT), pharmacotherapy with SSRIs, or a combination of the two. For patients who do not respond to monotherapy, the next step is either switching medications, augmenting with another medication, or adding CBT if not already initiated (Harvard Medical Letter, 2009).

Approximately 20-40% of patients have worsening symptoms despite conventional treatment. Surgery is an option for patients who experience severe and incapacitating symptoms in spite of multiple medication trials and/or medication and CBT. Primary surgical approaches are subcaudate tractotomy (creating a lesion beneath the head of the caudate nucleus in the substantial innominata), cingulotomy (radiofrequency ablation of the anterior cingulum), limbic leucotomy (combination of previous two procedures), and anterior capsulotomy (interrupting fibers between the thalamus and the anterior frontal lobe) (Burdwick et al., 2009).

Another potential alternative therapy for treatment-resistant patients is deep brain stimulation (DBS). DBS involves chronic electrical stimulation of a particular target in the brain and is designed to modulate transmission of the neural circuit. The exact mechanism of action of DBS is not known and this is an area of active research. DBS has been used since the early 1990s to treat movement disorders such as Parkinson’s disease, and, in 1999, the first report was published applying DBS to the treatment of refractory OCD. The optimal target for DBS in OCD patients is still being determined (Burdwick et al., 2009).

In February, 2009, the FDA approved a humanitarian device exemption for a deep brain stimulator for severe OCD by Medtronic (Reclaim device). The humanitarian device exemption is an FDA classification signifying that the technology is used to treat conditions that affect fewer than 4,000 new patients per year. The FDA reviews the safety of the device, but does not require that efficacy is established before approval. The FDA decision stipulates that deep brain stimulation is indicated for treatment of OCT in adult patients who have failed at least three SSRIs, and it can be used as an adjunct to medication. DBS is contraindicated in patients exposed to diathermy or MRIs, or who are unable to properly operate the brain stimulator. Medtronic plans to release the product commercially in the United States in mid-2009 (Medtronic website; FDA documents).

The Reclaim device by Medtronic includes a neurostimulator that is implanted subcutaneously in the upper abdominal region. The neurostimulator produces electrical stimulation pulses that are carried to an implanted set of leads via a lead extension. The leads are stereotactically introduced into the target area of the brain, and are fixed at the skull with a burr hole cap and ring. The neurostimulator is battery-powered. There are sparse clinical data on battery life. According to Medtronic, the battery is expected to last 6-16 months, or longer depending on the neurostimulator setting used. When the battery is depleted, it can be replaced surgically. The primary clinical data submitted by Medtronic for FDA approval was a case series of 26 patients treated at 3 centers in the US and one in Europe (FDA and Medtronic documents).

06/01/2009: MTAC REVIEW
Deep brain stimulation for the treatment of refractory obsessive-compulsive disorder

Evidence Conclusion: There is insufficient evidence to draw conclusions about the safety and effectiveness of deep brain stimulation for patients with refractory obsessive-compulsive disorder. The empirical literature consists of case series with 10 or fewer patients.

Articles: The Medline search limited to a range of clinical trials yielded 10 articles. No additional articles were identified on the manufacturer’s Web site. There were no randomized controlled trials or non-randomized comparative studies. The empirical literature consisted of small case series, with sample sizes ranging from 4 to 10. The studies do not meet MTAC criteria for reviewable evidence which requires that studies are published and, for case series, has a minimum sample size of 25.

The use of Deep brain stimulation for the treatment of refractory obsessive-compulsive disorder does not meet the Kaiser Permanente Medical Technology Assessment Criteria.

Primary Headache
BACKGROUND
Headache is a major worldwide health problem disabling millions of people and resulting in considerable economic burden. Up to 40% of patients seen in major headache clinics suffer from chronic daily headache. Chronic headache disorders include migraine, cluster headache, cervicogenic headache, occipital neuralgia, and others types of primary headache (Maizels 1998, Jasper 2008).

Cluster headache (CH), an excruciating headache syndrome, is the most common type of trigeminal autonomic cephalalgias, and is thought to be the most severe primary headache disorder. 10-20% of CH patients develop a
chronic form in which the attacks persist for more than one year without remissions, or with remissions lasting less than a month. Acute treatment for the attacks includes injectable or intranasal triptans or oxygen inhalation. About one percent will become refractory to medical treatment and fulfill the criteria of intractable headaches. These patients may get some relief with attack treatments, but the disorder could be disabling and may be associated with depression and suicidality (Magis 2007, Leroux 2008).

Migraine headache is a chronic headache that affects about 15% of the population and is one of the most common problems seen in emergency departments and doctors' offices. Migraine is believed to result from changes in the brain and surrounding blood vessels. The attacks typically last from 4-72 hours and vary in frequency from daily to less than one per year. Transformed migraines are chronic daily or almost daily headaches (>15/month) that lasts more than 4 hours. There is no cure for migraine, and medications can only help reduce the frequency and severity of disorder (Bigal 2008).

Cervicogenic headache is a chronic hemicranial pain that usually occurs daily. It usually begins at the suboccipital region and spreads anteriorly to the ipsilateral orbital, frontal, and temporal areas. It is typically unilateral, but occasionally affects the two sides. It is believed to be due to convergence of upper cervical and trigeminal sensory pathways allowing pain signals to refer from the neck to the trigeminal sensory fields of the head and face. Treatments with pain medication, physical therapy, manipulative treatment, and surgical interventions may provide only some inconsistent temporary relief of pain (Naja 2006).

Various ablative surgical procedures targeting the trigeminal nerve or the cranial parasympathetic outflow have been tried to treat these patients with intractable headaches. These include gamma knife surgery or root section of the trigeminal nerve, trigeminal tractotomy, microvascular decompression of the trigeminal nerve, glycerol injection of the Gasserian ganglion, and others. However, none of these procedures has a consistent effect, and many are associated with serious complications (Magis 2007).

Electrical stimulation of the brain was first attempted late in the 19th century, but its application for pain control began in the 1960s with spinal cord stimulation. The neurostimulator technique for ablating pain is based on the theory that peripheral nerve stimulation can produce specific focal analgesia and anesthesia. In addition, the technique may alter perception of pain by blocking cell membrane depolarization and axonal conduction with directly applied current (Shealy 1967, Lim 2007, Trentman 2008).

In the early 2000s, neurostimulation therapy emerged as a potential treatment option for a variety of different intractable primary headache disorders. This is an invasive device-based approach that has two broad types:

1. Peripheral therapy that involves branches of the occipital nerve: occipital nerve stimulation (ONS), and supraorbital nerve stimulation.

2. Central which refers to deep-brain stimulation (DBS) approaches e.g. hypothalamic deep brain stimulation used for chronic cluster headache (Schwedt 2009).

The occipital nerve stimulators (ONS) are implanted surgically in a 3 phase procedure: Phase 1. An incision is made over the occipital region at the level of the first cervical vertebra for the subcutaneous implantation of bilateral electrodes. These are tunneled in a cephalad direction so that they come to lie across the path of the greater occipital nerve on each side of the head. Phase 2. Confirmation of the electrode position by testing each separately by an external stimulator. The operator gradually increases the amplitude delivered to the electrodes from 0 to 4 v, and the patient is asked to locate and describe any sensation he/she feels. Correct placement is confirmed by the patient describing a vibrating sensation that radiates at least 4 cm cephalad from the base of the skull, on the side of the tested electrode, and Phase 3. Implantation of the stimulator battery in the pectoral, abdominal, or gluteal region, and connecting it to the electrodes via subcutaneously tunneled leads. The procedure is performed under sedation or general anesthesia, however during the second phase the patients are required to be awake and to be able to identify the position of the occipital electrodes when the electric stimulus is applied. Potential complications of the procedure include lead migration, infection, localized pain, muscle spasm, and lack or loss of effect (Lim 2007, Trentman 2008).

The deep brain stimulation (DBS) of the posterior hypothalamus has been investigated in patients with chronic cluster headaches or SUNCT (short-lasting, unilateral, neuralgiform headache attacks with conjunctival injection and tearing). DBS involves MRI guided stereotactic placement of an electrode into the brain (e.g. thalamus, globus pallidus, or subthalamic nucleus). It is typically implanted unilaterally on the side corresponding to the most severe symptoms. The use of bilateral stimulation using two electrodes has been investigated in patients with bilateral, severe symptoms. Initially, the electrode(s) is/are attached to a temporary transtuminate cable to validate treatment effectiveness and, if effective, the patient returns to surgery several days later for permanent subcutaneous implantation of the cable and a radiofrequency-coupled or battery-powered programmable stimulator. After implantation, noninvasive programming of the neurostimulator can be adjusted to control the
patient’s symptoms. The procedures can be performed only by a highly experienced neurosurgeon and may be associated with a small risk of mortality due to intra-cerebral hemorrhage. Before implantation, all patients must undergo complete preoperative neuroimaging to exclude disorders associated with increased hemorrhagic risk (Leon 2006, Bartsch 2008).

Neither the occipital nerve stimulation nor the deep brain stimulators are approved to date by the U.S. Food and Drug Administration for the treatment or prevention of primary headaches.

08/03/2009: MTAC REVIEW
Deep Brain Stimulation for the Treatment of Primary Headache
Evidence Conclusion: The literature on brain stimulation for the treatment of chronic primary headache is limited and does not provide sufficient evidence to determine the efficacy or safety of either occipital or deep brain stimulation therapy for the prevention or treatment of chronic headache. There are no published randomized or nonrandomized controlled trials on the intervention to date. The empirical studies consist of a few very small case series with no comparison groups and a number of case reports. The outcome measures varied between studies as some reported change in pain and others reported on headache frequency intensity, disability and/or medication use. To date all published studies on hypothalamic deep brain stimulation are small case series and case reports with a combined total of 55 participants with refractory chronic cluster headache. Leone et al’s series had the largest size (N=16) and follow-up duration (mean 23 months). The results of this study and other case series indicate that this invasive procedure has potential serious complications, and is not always effective. Deep brain stimulation was not compared to another treatment or intervention to determine that the benefit observed was a placebo effect.

Articles: The search yielded almost four hundred articles. The majority was review articles, opinion pieces, or dealt with technical aspects the procedure. DBS: The search identified 12 small case series and reports with a total number of 57 patients on deep-brain stimulation for chronic cluster headache. Leone M, Franzini A, Broggi G, et al. Hypothalamic stimulation for intractable cluster headache; long-term experience. Neurology 2006:67:150-152. See Evidence Table.

The use of Deep brain stimulation for the treatment of primary headache does not meet the Kaiser Permanente Medical Technology Assessment Criteria.

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MDCRPC Medical Director Clinical Review and Policy Committee
MPC Medical Policy Committee

Revision History

Codes
CPT: 61850, 61860, 61863, 61864, 61867, 61868, 61870, 61875, 61880, 61885, 61886, 61888