Occipital Nerve Stimulation

Policy Number: 7.01.125  Last Review: 5/2017

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for occipital nerve stimulation. This is considered investigational.

When Policy Topic is covered
Not Applicable

When Policy Topic is not covered
Occipital nerve stimulation is considered investigational for all indications.

Description of Procedure or Service

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Individuals:  
  - With migraine headache | Interventions of interest are:  
  - Occipital nerve stimulation | Comparators of interest are:  
  - Conservative treatment  
  - Medical management | Relevant outcomes include:  
  - Symptoms  
  - Functional outcomes  
  - Quality of life  
  - Treatment-related morbidity |

| Individuals:  
  - With non-migraine headache (e.g., hemicrania continua, cluster) | Interventions of interest are:  
  - Occipital nerve stimulation | Comparators of interest are:  
  - Conservative treatment  
  - Medical management | Relevant outcomes include:  
  - Symptoms  
  - Functional outcomes  
  - Quality of life  
  - Treatment-related morbidity |

Occipital nerve stimulation (ONS) delivers a small electrical charge to the occipital nerve in an attempt to prevent migraines and other headaches in patients who have not responded to medications. The device consists of a subcutaneously implanted pulse generator (in the chest wall or abdomen) attached to extension leads that are tunneled to join electrodes placed across one or both occipital nerves at the base of the skull. Continuous or intermittent stimulation may be used.

The evidence for occipital nerve stimulation in individuals who have migraine headaches includes randomized controlled trials (RCTs), systematic reviews of RCTs, and observational studies. Relevant outcomes are symptoms, functional
outcomes, quality of life, and treatment-related morbidity. Systematic reviews identified 5 RCTs; one was judged to be at low risk of bias. Findings from pooled analyses of RCTs were mixed. For example, compared to placebo, response rates to occipital nerve stimulation did not differ significantly but did reduce the number of days with prolonged moderate-to-severe headache. Moreover, occipital nerve stimulation was associated with a substantial number of minor and serious adverse events. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for occipital nerve stimulation in individuals who have non-migraine headache (eg, hemicrania continua, cluster) includes case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Most case series were small; many had 15 or fewer patients, with the largest having 22 patients. Moreover, RCTs are needed to compare outcomes between occipital nerve stimulation and controls to assess for the placebo effect. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Background**

Implanted peripheral nerve stimulators have been used for treatment of refractory pain for many years but only recently proposed for management of craniofacial pain. Occipital, supraorbital, and infraorbital stimulation have been reported in the literature.

There are four types of headache: vascular, muscle contraction (tension), traction, and inflammatory.

Primary (not the result of another condition) chronic headache is defined as headache occurring more than 15 days of the month for at least 3 months. An estimated 45 million Americans experience chronic headaches. For at least half of these people, the problem is severe and sometimes disabling.

Migraine is the most common type of vascular headache. Migraine headaches are usually characterized by severe pain on one or both sides of the head, an upset stomach, and, at times, disturbed vision. One-year prevalence of migraine ranges from 6%–15% in adult men and from 14%–35% in adult women. Migraine headaches may last a day or more and can strike as often as several times a week or as rarely as once every few years. Drug therapy for migraine is often combined with biofeedback and relaxation training. Sumatriptan is commonly used for relief of symptoms. Drugs used to prevent migraine include methysergide maleate, propranolol hydrochloride, ergotamine tartrate; amitriptyline, valproic acid, and verapamil.

Hemicrania continua, also a vascular headache, causes moderate pain with occasional severe pain on only one side of the head. At least one of the following symptoms must also occur; conjunctival injection and/or lacrimation, nasal congestion and/or rhinorrhea, or ptosis and/or miosis. Headache occurs daily and is continuous with no pain-free periods. Hemicrania continua occurs mainly in
woman, and its true prevalence is not known. Indomethacin usually provides rapid relief of symptoms. Other NSAIDs, including ibuprofen, celecoxib, and naproxen, can provide some relief from symptoms. Amitriptyline and other tricyclic antidepressants are effective in some patients.

Cluster headache is a vascular headache that occurs in cyclical patterns or clusters of severe or very severe unilateral orbital or supraorbital and/or temporal pain. The headache is accompanied by at least one of the following autonomic symptoms: ptosis (drooping eyelid), conjunctival injection, lacrimation, rhinorrhea, and, less commonly, facial blushing, swelling, or sweating. Bouts of one headache every other day to 8 attacks per day may last from weeks to months, usually followed by remission periods when the headache attacks stop completely. The pattern varies from one person to another, but most people have one or two cluster periods a year. During remission, no headaches occur for months, and sometimes even years. The intense pain is caused by the dilation of blood vessels, which creates pressure on the trigeminal nerve. While this process is the immediate cause of the pain, the etiology is not fully understood. It is more common in men than in woman. One-year prevalence is estimated to be 0.5 to 1.0/1,000. Management of cluster headache consists of abortive and preventive treatment. Abortive treatments include subcutaneous injection of sumatriptan, topical anesthetics sprayed into the nasal cavity, and strong coffee. Some patients respond to rapidly inhaled pure oxygen. A variety of other pharmacologic and behavioral methods of aborting and preventing attacks have been reported with wide variation in patient response.

To date, the U.S. Food and Drug Administration (FDA) has not cleared or approved any occipital nerve stimulation device for treatment of headache. In 1999, the Synergy™ IPG device (Medtronic), an implantable pulse generator, was approved by FDA through the premarket approval process for management of chronic, intractable pain of the trunk or limbs, and off-label use for headache is described in the literature. The Genesis™ neuromodulation system (St. Jude Medical) was approved by FDA for spinal cord stimulation and the Eon™ stimulator has received CE mark approval in Europe for the treatment of chronic migraines.

**Rationale**

This evidence review was created in 2010 and has been updated periodically based on a literature search of the MEDLINE database. The most recent literature review was performed through February 12, 2016.

Assessment of efficacy for therapeutic interventions involves a determination of whether the intervention improves health outcomes. The optimal study design for a therapeutic intervention is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. It is recognized that RCTs are particularly important to assess treatments of painful conditions, due to the expected placebo effect and the subjective nature of pain assessment in general. Intermediate outcome measures, also known as surrogate outcome measures, may be adequate if there is an established link between the intermediate outcome
and true health outcomes. Nonrandomized comparative studies and uncontrolled studies can sometimes provide useful information on health outcomes but are prone to biases such as noncomparability of treatment groups, the placebo effect, and variable natural history of the condition.

Migraine
Two systematic reviews of the literature on occipital nerve stimulation (ONS) were published in 2015. Both included RCTs and observational studies. The study by Chen et al identified 5 RCTs and 7 case series with at least 10 patients. Three of the RCTs were industry-sponsored, multicenter, parallel-group trials and 2 were single-center crossover trials. All 5 included a sham control group and 1 trial also included a medication management group. Risk of bias was judged to be high or unclear for all trials. Meta-analyses were performed on 2 outcomes. A pooled analysis of 2 studies did not find a significant difference in response rate between active and sham stimulation (risk ratio [RR], 2.07; 95% confidence interval [CI], 0.50 to 8.55; p=0.31) and a pooled analysis of 3 studies showed a significantly greater reduction in the number of days with prolonged moderate-to-severe headache (mean difference, 2.59; 95% CI, 0.91 to 4.27; p=0.003).

In their systematic review, Yang et al(2) identified the same 5 RCTs as Chen. The Yang review only included studies conducted with patients with migraine of at least 6 months in duration who did not respond to oral medications. In addition to the RCTs, 5 case series met the inclusion criteria. Yang did not pool study findings. The definition of response rate varied across studies and could include frequency and/or severity of headaches. Response rates in 3 case series with self-reported efficacy were 100% each, and response rates in the other 2 series were 50% and 89%, respectively. Complication rates in the series ranged from 40% to 100%. The authors noted that the case series were subject to biases (eg, inability to control for the placebo effect), that RCT evidence was limited, and that complication rates were high.

The 2 parallel-group RCTs published as full-text journal articles are described in more detail below.

The Occipital Nerve Stimulation for the Treatment of Intractable Chronic Migraine Headache (ONSTIM) trial, was a multicenter, randomized feasibility study of ONS for treatment of intractable chronic migraine headache.(3) The trial evaluated study design and had no primary end point. One hundred ten patients were enrolled, and patients who had a positive response to a short-acting occipital nerve block were randomized as follows: 33 to adjustable stimulation, 17 to preset stimulation of 1 min/d, and 17 to medical management. At the 3-month evaluation, the response rate (percentage of patients who achieve ≥50% reduction in number of headache days per month or a ≥3-point reduction in average overall pain intensity vs baseline) was 39% in the adjustable stimulation group, 6% in the preset stimulation group, and 0% in the medical management group. Twelve (24%) of 51 subjects who had successful ONS device implantation experienced lead migration and 3 of the 51 subjects were hospitalized for adverse events (infection, lead migration, nausea). Study limitations included a short
observation period and ineffective blinding of subjects and investigators to treatment groups.

In 2012, an industry-sponsored, double-blind trial, regulated by U.S. Food and Drug Administration, randomized 157 patients in a 2:1 ratio to active or sham stimulation.(4) Intention-to-treat (ITT) analysis revealed no significant difference between groups in the percentage of patients who achieved 50% or greater reduction in visual analog scale scores for pain at 12 weeks (active, 17.1%; control, 13.5%). More patients in the ONS group had fewer days with headache, less migraine-related disability, and greater pain relief, although benefits were modest. The most common adverse event was persistent implant site pain. Results from the 52-week open-label extension of this study were published in 2015.(5) Results were reported for the ITT population and for the 125 patients who met selection criteria for intractable chronic migraine. Twenty-four patients were excluded from analysis due to explantation of the ONS system (n=18) or loss to follow-up. Mean headache days at baseline were 21.6 for the ITT population and 24.2 for the intractable chronic migraine group. In the ITT population, headache days were reduced by 6.7 days, and a reduction of 50% or more in the number of headache days and/or pain intensity was observed in 47.8% of this group. Seventy percent of patients experienced at least 1 of 183 device-related adverse events, of which 8.6% of events required hospitalization and 40.7% of events required surgical intervention. Eighteen percent of patients had persistent pain and/or numbness with the device.

**Non-Migraine Headaches**

**Hemicrania Continua**
The efficacy of continuous unilateral ONS was evaluated in a small (N=6) crossover study of hemicrania continua by Burns et al.(6) Pain on a 10-point scale was recorded hourly in patient diaries, and the Migraine Disability Assessment was administered at each follow-up visit. Four of 6 patients reported substantially less pain (80%-95%), 1 reported a 30% less pain, and 1 reported 20% worse pain. Adverse events were mild and associated with transient overstimulation.

**Cluster Headache**
Burns et al also reported on 14 patients treated for cluster headache with various stimulation devices.(7) At a median follow-up of 17.5 months (range, 4-35 months), 10 of 14 patients reported improvement in pain frequency, severity, or duration, with frequency the most common. Three reported improvement of 90% or better, 3 reported moderate improvement (30%-60%), and 4 reported mild improvement (20%-30%). Four patients experienced electrode failure and 6 required battery replacement. In 2011, Mueller et al reported a prospective study of 10 patients with refractory chronic cluster headache treated with bilateral ONS.(8) At a mean follow-up of 12 months (range, 3-18 months), mean cluster frequency was reduced by 44% (range, 20%-90%) in 90% of the patients. Mean daily frequency of the attacks dropped from 6 to 3. Seventy percent of the patients also required less medication during attacks.
Also in 2011, Magis et al reported mean 37-month follow-up (range, 11-64 months) on 15 patients with cluster headache. Mean cluster headache duration was 7 years, with a mean 2.5 attacks per day. For the 14 patients followed (1 patient developed a postoperative infection and required device explantation), mean attack frequency decreased from 2.24 to 0.12 attacks per day. Twelve patients reported total or partial elimination of headache and 2 had no or minimal improvement. Adverse events included ONS-related paresthesias, contralateral attacks, technical problems (battery depletion), site infection, and stimulators removal (due to discomfort or infection). Nine patients reported being pain-free for extended periods.

**Headache Associated With Chiari Malformation**

Vadivelu et al reported on a series of 22 patients with Chiari malformation and persistent occipital headaches. Of the 22, 15 (68%) had a successful occipital neurostimulator trial and underwent permanent implantation. At a mean follow-up of 18.9 months (range, 6-51 months), 13 (87%) of the 15 patients reported pain relief greater than 50%. Forty percent of patients reported device-related complications requiring additional surgery (lead migration, uncomfortable position of generator, wound infection) during the follow-up period.

**Occipital Neuralgia**

A 2015 systematic review by Sweet et al identified 9 small case series (<15 patients each) assessing the efficacy of ONS for treating medically refractory occipital neuralgia. The authors did not pool study findings. We could not draw conclusions about the impact of ONS on occipital neuralgia due to the lack of RCTs or other controlled studies.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 1.

### Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<tbody>
<tr>
<td>NCT01775735a</td>
<td>Occipital Nerve Stimulation (ONS) for Migraine OPTIMISE</td>
<td>180</td>
<td>Sep 2016</td>
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<tr>
<td>NCT01151631</td>
<td>Occipital Nerve Stimulation in Medically Intractable Chronic Cluster Headache</td>
<td>144</td>
<td>Dec 2016</td>
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<td>NCT01842763</td>
<td>French Database of Occipital Nerves Stimulation in the Treatment of Refractory Chronic Headache Disorders</td>
<td>50</td>
<td>Dec 2016</td>
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</table>

NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.

**Summary of Evidence**

The evidence for occipital nerve stimulation in individuals who have migraine headaches includes randomized controlled trials (RCTs), systematic reviews of RCTs, and observational studies. Relevant outcomes are symptoms, functional
outcomes, quality of life, and treatment-related morbidity. Systematic reviews identified 5 RCTs; one was judged to be at low risk of bias. Findings from pooled analyses of RCTs were mixed. For example, compared to placebo, response rates to occipital nerve stimulation did not differ significantly but did reduce the number of days with prolonged moderate-to-severe headache. Moreover, occipital nerve stimulation was associated with a substantial number of minor and serious adverse events. The evidence is insufficient to determine the effects of the technology on health outcomes.

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**Practice Guidelines and Position Statements**

**Congress of Neurological Surgeons**
A 2015 evidence-based guideline from the Congress of Neurological Surgeons states: “the use of occipital nerve stimulation is a treatment option for patients with medically refractory occipital neuralgia.”(11) The statement had a level III recommendation based on a systematic review of literature (see Rationale section) that only identified case series.

**National Institute for Health and Care Excellence**
A 2013 guidance from the U.K.’s National Institute for Health and Care Excellence (NICE) noted that the evidence on ONS for intractable chronic migraine shows some efficacy for short-term outcomes but very little evidence about long-term outcomes.12 With regard to safety, NICE indicated that there are risks of complications that need further surgery. Therefore, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research. NICE has recommended that clinicians wanting to undertake ONS for intractable chronic migraine should ensure that patients understand the uncertainty about the procedure’s safety and efficacy, and provide them with clear written information.

**U.S. Preventive Services Task Force Recommendations**
Not applicable.

**Medicare National Coverage**
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.
References

Billing Coding/Physician Documentation Information
61885 Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array
61886 Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to 2 or more electrode arrays
64553 Percutaneous implantation of neurostimulator electrodes; cranial nerve
64568 Incision for implantation of cranial nerve (eg, vagus nerve) neurostimulator electrode array and pulse generator
64569 Revision or replacement of cranial nerve (eg, vagus nerve) neurostimulator electrode array, including connection to existing pulse generator
64570 Removal of cranial nerve (eg, vagus nerve) neurostimulator electrode array and pulse generator
64999 Unlisted procedure, nervous system
C1787  Patient programmer, neurostimulator
C1820  Generator, neurostimulator (implantable), with rechargeable battery and charging system
C1897  Lead, neurostimulator test kit (implantable)
L8679  Implantable neurostimulator, pulse generator, any type
L8680  Implantable neurostimulator electrode, each
L8681  Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
L8682  Implantable neurostimulator radiofrequency receiver
L8683  Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver
L8684  Radiofrequency transmitter (external) for use with implantable sacral root neurostimulator receiver for bowel and bladder management, replacement
L8685  Implantable neurostimulator pulse generator, single array, rechargeable, includes extension
L8686  Implantable neurostimulator pulse generator, single array, nonrechargeable, includes extension
L8687  Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
L8688  Implantable neurostimulator pulse generator, dual array, nonrechargeable, includes extension
L8689  External recharging system for battery (internal) for use with implantable neurostimulator, replacement only

ICD10 Codes
G43.00-  Migraine code range
G43.89
G44.00-  Other headache syndromes code range
G44.919

There are no specific codes for this procedure.

Additional Policy Key Words
N/A

Policy Implementation/Update Information
5/1/06  New policy, considered investigational.
5/1/07  No policy statement changes.
5/1/08  No policy statement changes.
5/1/09  No policy statement changes.
5/1/10  No policy statement changes.  Title number changed from 7.01.500 to 7.01.125.  Coding updated.
5/1/11  No policy statement changes.  Coding updated.
5/1/12  No policy statement changes.
5/1/13  No policy statement changes.
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<tr>
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<tr>
<td>5/1/17</td>
<td>No policy statement changes.</td>
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State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.