Occipital Nerve Stimulation

Policy # 00253
Original Effective Date: 03/19/2010
Current Effective Date: 06/21/2017

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers occipital nerve stimulation (ONS) for all indications to be investigational.*

Background/Overview
Occipital nerve stimulation 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.

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 4 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 consecutive months. An estimated 45 million Americans experience chronic headaches. For at least half of these people, the problem is severe and sometimes disabling. There are several types of primary headaches, including vascular. Herein, we will only discuss types of vascular headache, including migraine, hemicrania continua, and cluster.

Migraine
Migraine is the most common type of vascular headache. Migraine headaches are usually characterized by severe pain on 1 or both sides of the head, an upset stomach, and, at times, disturbed vision. One-year prevalence of migraine ranges from 6% to 15% in adult men and from 14% to 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 amitriptyline, propranolol and other β-blockers, topiramate and other antiepileptic drugs, and verapamil.

Hemicrania Continua
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 women, and its true prevalence...
Occipital Nerve Stimulation

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Original Effective Date: 03/19/2010
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is not known. Indomethacin usually provides rapid relief of symptoms. Other nonsteroidal anti-inflammatory drugs, including ibuprofen, celecoxib, and naproxen, can provide some relief from symptoms. Amitriptyline and other tricyclic antidepressants are effective in some patients.

Cluster Headache
Cluster headache 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 1 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 person to person, but most people have 1 or 2 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 women. One-year prevalence is estimated to be 0.5 to 1.0 in 1000. 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.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
To date, the U.S. 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.

Centers for Medicare and Medicaid Services (CMS)
There is no national coverage determination.

Rationale/Source
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 also 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 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 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 most common complications were lead migration (21% of patients) and infection (7% of patients).

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 refractory to medical management. The trial evaluated study design and had no primary endpoint. 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 FDA, randomized 157 patients in a 2:1 ratio to active or sham stimulation. 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...
Occipital Nerve Stimulation

Policy # 00253
Original Effective Date: 03/19/2010
Current Effective Date: 06/21/2017

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.

Section Summary: Migraine

Two systematic reviews (2015, 2016) each identified 5 sham-controlled randomized trials. One of the systematic reviews also identified 5 case series. Findings from pooled analyses of RCTs were mixed. For example, compared to sham stimulation, response rates (ie, ≥50% reduction in VAS score) for ONS did not differ significantly, but the number of days with prolonged moderate-to-severe headache was reduced. ONS was also associated with a substantial number of minor and serious adverse events.

Non-Migraine Headaches

Hemicrania Continua

The evidence consists of a small crossover study of hemicrania continua by Burns et al (2008) who reported on the efficacy of continuous unilateral ONS in 6 patients. 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 (range, 80%-95% less), 1 reported 30% less pain, and 1 reported 20% worse pain. Adverse events were mild and associated with transient overstimulation.

Cluster Headache

Several case series assessing cluster headache were identified, with sample sizes ranging from 10 to 67 patients. In 2016, Fontaine et al published a prospective case series of 67 patients with chronic cluster headache (CCH). Data were taken from a French database on ONS for treating refractory headache disorders. Sixty-seven patients with CCH were included in the database; data were available for 52 (78%) patients at 3 months and 44 (66%) patients at 12 months. The primary outcome was a composite score that incorporated patient’s global impression of change, reduction in the frequency of headache attacks, and changes in prophylactic medications. For patients with available data, at 3 months, 34 (65.4%) of 52 were considered to be excellent responders, 9 (17.3%) of 52 were mild responders, and 9 (17.3%) of 52 were nonresponders. At 12 months, 22 (48%) of 44 were excellent responders, 10 (21.7%) of 44 were mild responders, and 15 (32.6%) of 44 were nonresponders. The series had a large amount of missing data at follow-up.

In 2016, Leone et al published a case series of ONS in 35 patients with CCH. This series had the longest follow-up (median, 6.1 years; range, 1.6-10.7 years). Selection criteria included daily or almost daily cluster headache attacks in the past year and resistance of prophylactic drugs. Twenty (66.7%) of the 30 patients in the per-protocol analysis had 50% or more reduction in headache number per day and were considered responders. In 12 (40%) patients, improvement was considered stable (ie, ≤3 headache attacks per month). Limitations of the series reporting on cluster headaches included lack of blinding and comparison groups.
Occipital Nerve Stimulation

Policy # 00253
Original Effective Date: 03/19/2010
Current Effective Date: 06/21/2017

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 of the 15 patients (87%) reported pain relief of greater than 50%. Device-related complications requiring additional surgeries (lead migration, uncomfortable position of generator, wound infection) occurring in 40% of patients 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.

Section Summary: Non-Migraine Headaches
The evidence on ONS for treatment of non-migraine headaches consists of case series; no RCTs or nonrandomized comparative studies were identified. Many of the case series had small sample sizes; series with over 25 patients were available only for treatment of cluster headache. Although case series tended to find that a substantial number of patients improved after ONS, the studies lacked blinding and comparison groups. Randomized controlled trials are needed to compare outcomes between ONS and comparators (eg, to control for a potential placebo effect).

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

Table 1. Summary of Key Trials

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<th>Trial Name</th>
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<th>Completion Date</th>
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<td>French Database of Occipital Nerves Stimulation in the Treatment of Refractory Chronic Headache Disorders (NGO)</td>
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<td>NCT01775735</td>
<td>Occipital Nerve Stimulation (ONS) for Migraine OPTIMISE</td>
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<td>Jun 2017</td>
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NCT: national clinical trial.
* Denotes industry-sponsored or cosponsored trial.

Summary
The evidence for occipital nerve stimulation in individuals who have migraine headaches includes 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.
Occipital Nerve Stimulation

Policy # 00253
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The evidence for occipital nerve stimulation in individuals who have non-migraine headache (e.g., hemicrania continua, cluster) includes case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Many of the case series had small sample sizes; series with over 25 patients were available only for treatment of cluster headache. Although the case series tended to find that a substantial number of patients improved after occipital nerve stimulation, these studies lacked blinding and comparison groups. RCTs are needed to compare outcomes between occipital nerve stimulation and comparators (e.g., to control for a potential placebo effect). The evidence is insufficient to determine the effects of the technology on health outcomes.

References

Policy History
Original Effective Date: 03/19/2010
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03/05/2010 Medical Policy Committee approval
03/19/2010 Medical Policy Implementation Committee approval. New Policy.
12/31/2010 Coding updated
02/03/2011 Medical Policy Committee approval

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Occipital Nerve Stimulation

Policy # 00253
Original Effective Date: 03/19/2010
Current Effective Date: 06/21/2017

02/16/2011 Medical Policy Implementation Committee approval. No change to coverage.
02/02/2012 Medical Policy Committee approval
02/15/2012 Medical Policy Implementation Committee approval. No change to coverage.
02/07/2013 Medical Policy Committee approval
02/20/2013 Medical Policy Implementation Committee approval. No change to coverage.
02/06/2014 Medical Policy Committee approval
02/19/2014 Medical Policy Implementation Committee approval. No change to coverage.
03/05/2015 Medical Policy Committee approval
03/20/2015 Medical Policy Implementation Committee approval. No change to coverage.
08/03/2015 Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
06/02/2016 Medical Policy Committee approval
06/20/2016 Medical Policy Implementation Committee approval. No change to coverage.
09/08/2016 Coding update
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
06/01/2017 Medical Policy Committee approval
06/21/2017 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 06/2018

Coding

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:
Occipital Nerve Stimulation

Policy # 00253
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A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
   1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
   2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
   3. Reference to federal regulations.

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