Occipital Nerve Stimulation

Policy # 00253
Original Effective Date: 03/19/2010
Current Effective Date: 06/20/2018

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.

Note: Percutaneous Electrical Nerve Stimulation (PENS) and Percutaneous Neuromodulation Therapy (PNT) is addressed separately in medical policy 00144.

Note: Spinal Cord Stimulation is addressed separately in medical policy 00260.

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

HEADACHE
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. Herein, we 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 one 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.

Treatment
Drug therapy for migraine is often combined with biofeedback and relaxation training. Sumatriptan and other triptans are 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 causes moderate and occasionally 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 is not known.

Treatment
Indomethacin usually provides rapid relief of symptoms. Other nonsteroidal anti-inflammatory drugs, including ibuprofen, celecoxib, and naproxen, can provide some relief of 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, conjunctival injection, lacrimation, rhinorrhea, and, less commonly, facial blushing, swelling, or sweating. Bouts of 1 headache every other day up 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 by 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 woman. One-year prevalence is estimated to be 0.5 to 1.0 in 1000.

Treatment
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.

Peripheral Nerve Stimulators
Implanted peripheral nerve stimulators have been used to treat refractory pain for many years, but have only recently been proposed to manage craniofacial pain. Occipital, supraorbital, and infraorbital stimulation have been reported in the literature.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
The U.S. FDA has not cleared or approved any ONS device for treatment of headache. In 1999, the Synergy™‡ IPG device (Medtronic), an implantable pulse generator, was approved by the 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 the 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. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Rationale/Source

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

MIGRAINE HEADACHE

Two systematic reviews of the literature on ONS have been published, both including RCTs and observational studies. The review by Chen et al (2015) identified 5 RCTs and 7 case series with at least 10 patients. Three of the RCTs were industry-sponsored, multicenter, parallel-group trials and two were single-center crossover trials. All five included a sham control group and one 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 trials did not find a significant difference in response rates between active and sham stimulation (relative risk [RR], 2.07; 95% confidence interval [CI], 0.50 to 8.55; p=0.31) and a pooled analysis of 3 trials 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 (2016) identified the same 5 RCTs as Chen. The Yang review only included studies conducted with patients who had migraines for 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% in each, and response rates in the other 2 series were 50% and 89%, respectively. Complication rates in the series ranged from 40% to 100%. Reviewers noted that the case series were subject to biases (e.g., 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 detailed next. The Occipital Nerve Stimulation for the Treatment of Intractable Chronic Migraine Headache trial, was a multicenter, randomized

feasibility study of ONS for treatment of intractable chronic migraine headache refractory to preventive medical management. The trial, reported by Saper et al (2011), 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 achieved ≥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 (6%) of the 51 subjects were hospitalized for adverse events (infection, lead migration, nausea). Trial limitations included a short observation period and ineffective blinding of subjects and investigators to treatment groups.

An industry-sponsored, double-blind trial, regulated by U.S. FDA and reported by Silberstein et al (2012), randomized 157 patients with chronic migraine refractory to preventive medical management in a 2:1 ratio to active or sham stimulation. Intention-to-treat (ITT) analysis revealed no significant differences 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 trial were published in 2015. 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.

Section Summary: Migraine Headache
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 with sham stimulation, response rates (i.e., ≥50% reduction in visual analogue scale [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 evaluating the use of ONS for hemicrania continua consists of a small crossover study 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), one reported 30% less pain, and one 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. Fontaine et al (2017) published a prospective case series of 67 patients with chronic cluster headache. Data were taken from a French ONS database on treatment of refractory headache disorders. Sixty-seven patients with chronic cluster headache 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.

Leone et al (2017) published a case series on use of ONS in 35 patients with chronic cluster headache. 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 number of headaches per day and were considered responders. In 12 (40%) patients, improvement was considered stable (i.e., ≤3 headache attacks per month).

Limitations of the series reporting on cluster headaches included lack of blinding and comparison groups.

Headache Associated With Chiari Malformation
Vadivelu et al (2012) 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 follow-up.

Occipital Neuralgia
A systematic review by Sweet et al (2015) identified 9 small case series (<15 patients each) assessing the efficacy of ONS for treating medically refractory occipital neuralgia. Reviewers did not pool study findings. Conclusions cannot be drawn on the impact of ONS on occipital neuralgia due to the lack of RCTs or other controlled studies.

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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 were small; 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. RCTs are needed to assess outcomes between ONS and comparators (e.g., to control for a potential placebo effect).

SUMMARY OF EVIDENCE
For individuals who have migraine headaches refractory to preventive medical management who receive ONS, the evidence 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 sham-controlled randomized trials. Findings from pooled analyses of these RCTs were mixed. For example, compared with placebo, response rates to ONS did not differ significantly but did reduce the number of days with prolonged moderate-to-severe headache. ONS was also 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.

For individuals who have non–migraine headaches (e.g., hemicrania continua, cluster headaches) who receive ONS, the evidence 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 ONS, these studies lacked blinding and comparison groups. RCTs are needed to compare outcomes between ONS 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.

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Policy History

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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
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
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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.
06/07/2018	Medical Policy Committee review
06/20/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 06/2019

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Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2017 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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

Code Type	Code
CPT	61885, 61886, 61888, 63650, 64553, 64555, 64568, 64569, 64570, 64575, 64999
HCPCS	L8680, L8681, L8682, L8683, L8685, L8686, L8687, L8688, L8689
ICD-10 Diagnosis	G43.001-G43.D1, G44.001-G44.89, M53.81-M53.83, M54.81, R51

*****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:

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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