



BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

Occipital Nerve Stimulation

Policy # 00253

Original Effective Date: 03/19/2010

Current Effective Date: 02/19/2014

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 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 three 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,



BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

Occipital Nerve Stimulation

Policy # 00253

Original Effective Date: 03/19/2010

Current Effective Date: 02/19/2014

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 eight 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.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

As of September 2013, the U.S. FDA has not cleared any ONS device for treatment of headache. The Synergy™[†] IPG (implantable pulse generator) device from Medtronic received marketing clearance in 1999 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) is 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. Medtronic and Boston Scientific Neuromodulation Systems (Precision™)[‡] are currently conducting clinical trials of devices.

Centers for Medicare and Medicaid Services (CMS)

There is no national coverage determination.

Rationale/Source

Controlled Trials

Migraine

A report of the Occipital Nerve Stimulation for the Treatment of Intractable Chronic Migraine Headache (ONSTIM) trial, a multicenter, randomized feasibility study of ONS for treatment of intractable chronic migraine headache, was published in 2011. The trial was designed to evaluate the study design and not powered for a single 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 (AS), 17 to preset stimulation (PS) of 1 minute per day, and 17 to medical management (MM). At the end of the 3-month trial, 28 patients remained in the AS group, 16 in the PS group and 17 in the MM group. A number of outcome measures were used including responder rate (percentage of patients who



BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

Occipital Nerve Stimulation

Policy # 00253
Original Effective Date: 03/19/2010
Current Effective Date: 02/19/2014

achieve 50% or greater reduction in number of headache days per month or a 3-point or greater reduction in average overall pain intensity compared to baseline). At the 3-month evaluation, the responder rate was 39% in the AS group, 6% in the PS group, and 0% in the MM group. Lead migration occurred in 12 of 51 (24%) of subjects. Three subjects required hospitalization for adverse events (infection, lead migration, and nausea). Limitations of the study include a short observation period and the inability to effectively blind subjects and investigators to treatment group.

This report was followed in 2012 by an industry-sponsored FDA-regulated double-blind trial that randomized 157 patients in a 2:1 ratio to active or sham stimulation. Intention-to-treat analysis revealed no significant difference between the groups in the percentage of patients who achieved 50% or greater reduction in visual analog scores (VAS) for pain at 12 weeks (active: 17.1%; control: 13.5%). More patients in the ONS group improved in the number of headache days, migraine-related disability, and direct reports of pain, although the benefits were modest. The most common adverse event was persistent implant site pain.

Serra and Marchioretto conducted a crossover study in which 30 patients with chronic migraine (100% of patients) and medication overuse headache (85% of patients) were implanted with an occipital nerve stimulator and randomized to "Stimulation On" or "Stimulation Off" arms. After 1 month, or if headaches worsened during the off period, patients were crossed over to the other arm. The mean number of days when patients randomized to the off condition turned on the generators was 4.65 days (range, 1-12 days). At baseline, the average frequency of migraines was 5.8 days per week and the median headache severity was 8 on an 11-point numerical rating scale. Headache intensity and/or frequency were significantly lower in the on arm compared to the off arm and decreased from baseline to each follow-up visit in all patients with Stimulation On. For example, the number of headaches decreased from a median of 6.3 days per week in the off phase to 2.1 days per week in the on phase. The median Migraine Disability Assessment (MIDAS) score decreased from 79 at baseline to 10 at 12-month follow-up. Quality of life measured by the SF-36 significantly improved from baseline throughout the follow-up period. Use of triptans decreased from a median of 20 to 3 doses/month and use of nonsteroidal anti-inflammatory drug (NSAIDs) use decreased from a median of 25.5 to 2 doses/month. There were 2 infections (6.7%) and 3 lead migrations (10%) during the study. This study is limited by the lack of a control group during follow-up and lack of blinding, although blinding of patients may be difficult due to paresthesia with this treatment.

Hemicrania Continua

Six patients with hemicrania continua received continuous unilateral ONS in a crossover study by Burns et al. in 2008. Pain on a 10-point scale was recorded hourly in patient diaries, and the MIDAS was administered at each follow-up visit. Four of 6 patients reported substantial improvement (80-95%), 1 reported a 30% improvement, and 1 reported that pain was worse by 20%. Adverse events were mild and associated with transient overstimulation.

Observational Studies

Aside from the 2 randomized studies and small crossover study discussed above, evidence on ONS for treatment of headache is limited to small case series.



BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

Occipital Nerve Stimulation

Policy # 00253

Original Effective Date: 03/19/2010

Current Effective Date: 02/19/2014

For example, in 2007, Schwedt et al. published a retrospective analysis of pre- and postimplant data from 15 patients with chronic, intractable headache implanted with the Synergy implantable pulse generator. Eight patients had chronic migraine, 3 chronic cluster, 2 hemicrania continua, and 2 posttraumatic headache. Eight patients had bilateral and 7 had unilateral lead placement. Nine patients reported at least a 50% reduction in headache pain, and none reported worsening of pain. Sixty percent of patients required lead revision within 1 year. The same authors conducted a retrospective review of the patients in the study reported above to determine if response to occipital nerve block (ONB) predicts response to ONS. Ten of 13 patients who had ONB had significant relief of pain (50% or more reduction in frequency or severity), and 3 were ONB nonresponders. Of the 3 ONB nonresponders, 2 were ONS responders. Thus, ONB may not be predictive of the therapeutic effect of ONS.

In 2009 Trentman et al. reported outcome measures at 1 year postimplant in 9 patients who participated in a feasibility trial of the Bion microstimulator. One patient stopped using the device before 1 year because of the time required to recharge the device. At 1 year, 7 of the 8 remaining patients had fair or better results in terms of reduction of disability, with 5 having greater than 90% reduction in disability.

Cluster Headache

Burns et al. reported on 14 patients with cluster headache in 2009. At a median follow-up of 17.5 months (range, 4-35 months), 10 of 14 patients reported improvement. Three reported improvement of 90% or better, 3 reported moderate improvement (30-60%), and 4 reported mild improvement (20-30%). Four patients required new electrode leads. A wide range of stimulation was used. Six patients required battery replacement. In 2011, Mueller et al. reported a prospective study of 10 patients with refractory chronic cluster headache who had been treated with bilateral ONS. At a mean follow-up of 12 months (range, 3-18 months), the frequency of the attacks were reduced by a mean of 44% (range, 20-90%) in 90% of the patients. The daily frequency of the attacks dropped from a mean of 6 to 3. Seventy percent of the patients required less medication during attacks. There was a nonsignificant tendency for improvement on the SF-36 in this small study.

Another publication from 2011 reported mean 37-month follow-up (range, 11-64 months) on 15 patients with intractable chronic cluster headache. The mean duration of cluster headache was 7 years, with a mean 2.5 attacks per day. One patient had an immediate postoperative infection and was explanted. For the remaining 14 patients, the mean attack frequency decreased from 2.24 to 0.12 per day. Twelve patients reported total or partial relief and 2 had no or minimal improvement. Two patients found the ONS-related paresthesias to be unbearable. In some patients contralateral attacks occurred. Technical problems included battery depletion (64%) and infection (20%). Five patients (33%) had the stimulators removed due to discomfort or infection, and 9 patients (60%) were reported to be 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 of the 15 patients (87%) reported pain relief of greater than 50%. Device-related complications requiring additional surgeries (lead



BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

Occipital Nerve Stimulation

Policy # 00253

Original Effective Date: 03/19/2010

Current Effective Date: 02/19/2014

migration, uncomfortable position of generator, wound infection) occurring in 40% of patients during the follow-up period.

Combined Occipital and Supraorbital Stimulation

Combined occipital and supraorbital neurostimulation was evaluated in 7 patients with chronic migraine by Reed et al. Responses to 2 stimulation programs were evaluated: one that stimulated only the occipital leads and one that stimulated both the occipital and supraorbital leads together. With follow-up ranging from 1 to 35 months, all patients reported a full therapeutic response but only to combined supraorbital-occipital neurostimulation.

Ongoing Clinical Trials

A search of online site ClinicalTrials.gov in September 2013 identified a number of clinical trials that are currently underway. Of particular note are the following:

- NCT01151631 is a randomized double-blind multicenter trial sponsored by Leiden University Medical Center that will compare low (30%) and high (100%) stimulation parameters in patients with medically intractable chronic cluster headache. Enrollment of 144 patients is anticipated with an expected completion date in January 2014.
- Recruitment (n=179) has been completed for an industry-sponsored Phase III trial from Boston Scientific titled Precision Implantable Stimulator for Migraine (PRISM) Study: ONS for Migraine (NCT00286078). The estimated study completion date is listed as January 2015. However, the posting for NCT00747812 (PRISM UK) states that Boston Scientific closed enrollment for PRISM UK early based on interim data from the PRISM US Pivotal Study, while the background section of a recent publication reports no significant difference in the PRISM trial between active treatment and sham controls for the number of migraine days/month.
- Boston Scientific began a randomized trial (OPTIMIZE) in 2013 to evaluate the Precision system for occipital nerve stimulation for migraine (NCT01775735). The study lists an estimated enrollment of 180 patients with completion expected June 2016.
- NCT01151631 is a study of occipital nerve stimulation in medically intractable chronic cluster headache sponsored by Leiden University Medical Center. The study has an estimated enrollment of 144 patients with completion expected January 2014.
- NCT01842763 is a French database of patients suffering from refractory chronic headache disorders (chronic migraine, cluster headache, chronic paroxysmal hemicranias, SUNCT syndrome, hemicrania continua, cervicogenic headache disorders), and treated by occipital nerve stimulation. The study began January 2013.
- Occipital nerve stimulation is also being studied for the treatment of fibromyalgia (NCT01298609).

Summary

The literature to date on the use of ONS consists primarily of small case series, small randomized trials and two small crossover studies. While the case series report substantial benefit, treatment-related improvements in the randomized controlled trials were modest. Randomized controlled trials (to account for potential placebo effect) with greater numbers of patients and longer follow-up are needed. It is noted that a number of trials are in progress. At this time the available evidence is insufficient to permit conclusions



Blue Cross Blue Shield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

Occipital Nerve Stimulation

Policy # 00253

Original Effective Date: 03/19/2010

Current Effective Date: 02/19/2014

concerning the impact of ONS on net health outcome. In addition, no implanted occipital nerve stimulators have received U.S. FDA approval. Therefore, ONS is considered investigational.

References

1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual, "Occipital Nerve Stimulation", 7.01.125, 11:2013.
2. Saper JR, Dodick DW, Silberstein SD et al. Occipital nerve stimulation for the treatment of intractable chronic migraine headache: ONSTIM feasibility study. *Cephalalgia* 2011; 31(3):271-85.
3. Silberstein SD, Dodick DW, Saper J et al. Safety and efficacy of peripheral nerve stimulation of the occipital nerves for the management of chronic migraine: results from a randomized, multicenter, double-blinded, controlled study. *Cephalalgia* 2012; 32(16):1165-79.
4. Serra G, Marchioretto F. Occipital nerve stimulation for chronic migraine: a randomized trial. *Pain Physician* 2012; 15(3):245-53.
5. Burns B, Watkins L, Goadsby PJ. Treatment of hemicrania continua by occipital nerve stimulation with a bion device: long-term follow-up of a crossover study. *Lancet Neurol* 2008; 7(11):1001-12.
6. Schwedt TJ, Dodick DW, Hentz J et al. Occipital nerve stimulation for chronic headache--long-term safety and efficacy. *Cephalalgia* 2007; 27(2):153-7.
7. Schwedt TJ, Dodick DW, Trentman TL et al. Response to occipital nerve block is not useful in predicting efficacy of occipital nerve stimulation. *Cephalalgia* 2007; 27(3):271-4.
8. Trentman TL, Rosenfeld DM, Vargas BB et al. Greater occipital nerve stimulation via the Bion microstimulator: implantation technique and stimulation parameters. Clinical trial: NCT00205894. *Pain Physician* 2009; 12(3):621-8.
9. Burns B, Watkins L, Goadsby PJ. Treatment of intractable chronic cluster headache by occipital nerve stimulation in 14 patients. *Neurology* 2009; 72(4):341-5.
10. Mueller OM, Gaul C, Katsarava Z et al. Occipital nerve stimulation for the treatment of chronic cluster headache - lessons learned from 18 months experience. *Cen Eur Neurosurg* 2011; 72(2):84-9.
11. Magis D, Gerardy PY, Remacle JM et al. Sustained effectiveness of occipital nerve stimulation in drug-resistant chronic cluster headache. *Headache* 2011; 51(8):1191-201.
12. Vadivelu S, Bolognese P, Milhorat TH et al. Occipital nerve stimulation for refractory headache in the Chiari malformation population. *Neurosurgery* 2012; 70(6):1430-6; discussion 36-7.
13. Reed KL, Black SB, Banta CJ, 2nd et al. Combined occipital and supraorbital neurostimulation for the treatment of chronic migraine headaches: initial experience. *Cephalalgia* 2010; 30(3):260-71.
14. National Institute for Health and Care Excellence. IPG452 Occipital nerve stimulation for intractable chronic migraine. 2013. Available online at: <http://publications.nice.org.uk/occipital-nerve-stimulation-for-intractable-chronic-migraine-ipg452>. Last accessed September, 2013.

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 2013 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.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

©2014 Blue Cross and Blue Shield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

Occipital Nerve Stimulation

Policy # 00253
Original Effective Date: 03/19/2010
Current Effective Date: 02/19/2014

CPT is a registered trademark of the American Medical Association.

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, 64555, 64568, 64569, 64575
HCPCS	L8680, L8681, L8682, L8683, L8685, L8686, L8687, L8688, L8689
ICD-9 Diagnosis	339.0 thru 339.89, 346.00 thru 346.93, 723.8, 784.0
ICD-9 Procedure	04.92

Policy History

Original Effective Date: 03/19/2010
Current Effective Date: 02/19/2014

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
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.
Next Scheduled Review Date: 02/2015

*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.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.