Clinical Policy Title: Hypoglossal nerve stimulation

Clinical Policy Number: 09.02.04

Effective Date: January 1, 2017
Initial Review Date: October 19, 2016
Most Recent Review Date: October 19, 2016
Next Review Date: October 2017

Related policies:

CP# 07.01.01  Treatment for obstructive sleep apnea in adults
CP# 07.01.05  Diagnosing obstructive sleep apnea in adults
CP# 10.03.05  Uvulopalatopharyngoplasty (UPPP)

ABOUT THIS POLICY: Keystone First has developed clinical policies to assist with making coverage determinations. Keystone First’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Keystone First when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First will update its clinical policies as necessary. Keystone First’s clinical policies are not guarantees of payment.

Coverage policy

Keystone First considers the use of hypoglossal nerve stimulation (HNS) to be investigational and, therefore, not medically necessary.

Limitations:

Note: The following CPT/HCPCS code is not listed in the Pennsylvania Medicaid fee schedule:

64999 - Unlisted procedure, nervous system

Alternative covered services:

- Weight management programs.
- Mandibular advancement devices (oral appliances).
- Positive airway pressure (PAP) therapy.
- Surgery (e.g., uvulopalatopharyngoplasty, maxillomandibular advancement, tracheostomy, palatal implants, correction of discrete anatomic abnormalities of the upper airway that significantly contribute to obstructive sleep apnea [OSA], such as enlarged tonsils or tongue.).

**Background**

Sleep apnea is a type of sleep disorder characterized by pauses in breathing (apnea) or instances of shallow or infrequent breathing during sleep. Obstructive sleep apnea (OSA) is the most common type of sleep apnea, caused by an obstruction of the upper airway during sleep. OSA is characterized by repetitive pauses in breathing during sleep, despite the effort to breathe, and is usually associated with a reduction in blood oxygen saturation (Balk 2011).

Untreated OSA is associated with symptoms of sleep deprivation and excessive sleepiness, cognitive dysfunction, diminished quality of life and productivity, sexual dysfunction, mood changes, increased accident risk, hypertension, non-insulin-dependent diabetes and other metabolic abnormalities, cardiac disease, and stroke. OSA affects persons in all age groups, especially middle-aged and elderly persons. OSA rates are increasing, likely due to escalating obesity rates (Balk 2011).

Polysomnography performed at a sleep lab is the standard diagnostic test for OSA, but diagnosis can be performed at home. Results are reported as the apnea-hypopnea index (AHI) and the respiratory disturbance index (RDI). According to the American Academy of Sleep Medicine, severity of OSA is defined as mild (AHI between five and 14 events per hour), moderate (AHI between 15 and 30 events per hour), and severe (AHI > 30 events per hour) (Qaseem 2013). There is no current established threshold level for the AHI that would indicate the need for treatment, but generally, people with relatively few apnea or hypopnea events per hour (often < 5 or < 15) are not formally diagnosed with OSA (Balk 2011).

The goals of OSA treatment are to alleviate airway obstruction during sleep, normalize sleep quality and improve AHI and oxyhemoglobin saturation levels. Treatment may improve comorbidities associated with untreated sleep apnea, primarily cardiovascular disease, non-insulin-dependent diabetes and associated mortality (Balk 2011, Randerath 2011). Treatment of OSA includes behavioral therapy (e.g., weight loss), drug therapy, positive airway pressure (PAP), dental or mandibular advancement devices (MADs), palatal implants, and surgery (upper airway or bariatric).

**HNS:**

HNS uses an implantable device that resembles a cardiac pacemaker. The surgeon implants a neurostimulator subcutaneously beneath the clavicle in the upper chest with one lead attached to the patient’s hypoglossal nerve at the base of the tongue and one pressure sensor lead implanted in the patient’s chest to detect breathing. Stimulation of the hypoglossal nerve occurs during sleep in parallel with a patient’s breathing. HNS contracts the genioglossus muscle, shifting the tongue forward and
opening the airway. The patient can turn the device on or off by remote control. There is delayed activation of the device to minimize disrupting the patient’s sleep onset.

One HNS system is available for commercial use in the United States (FDA 2016a). The Food and Drug Administration (FDA) has granted premarket approval (PMA) to the Inspire® II Upper Airway Stimulator (Inspire Medical Systems, Maple Grove, Minnesota) (FDA 2014). FDA classifies Inspire II as a class III device (PMA P130008, Product code MNQ). This first-in-class device is intended to treat a subset of adult patients at least 22 years of age with moderate to severe OSA (AHI 20 to 65) who have failed or cannot tolerate PAP treatments and who do not have a complete concentric collapse at the soft palate level. PAP intolerance is defined as either the inability to use PAP (> five nights per week of usage; usage defined as > four hours of use per night), or the unwillingness to use PAP (for example, a patient returns the PAP system after attempting to use it).

As a condition of PMA, the manufacturer is required to conduct two post-approval studies (FDA 2014):

- Extended Follow-up of the Premarket Cohort (Stimulation Therapy for Apnea Reduction [www.theSTARtrial.com], ClinicalTrials.gov identifier: NCT01161420).

**Searches**

Keystone First searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on August 24, 2016. Search terms were: "Hypoglossal Nerve Diseases/surgery"(MeSH), "Hypoglossal Nerve Diseases/therapy"(MeSH), and "hypoglossal nerve stimulation."

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews.**
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.
Findings

We identified two systematic reviews (Hayes 2016, Certal 2015), two evidence-based guidelines (Epstein 2009, Qaseem 2013) and no economic analyses for this policy. The evidence consists of six unique, low-to-very low quality pre-post studies that produced multiple publications with overlapping patient populations. The evidence suggests consistent short-term improvements in symptoms of OSA but inconsistent improvement in sleep quality or quality of life (QOL) in persons with moderate-to-severe OSA in whom continuous positive airway pressure (CPAP) had failed.

Adverse events reported in the reviewed studies included device malfunction, lead dislodgement, pain, numbness, swelling and discomfort. Nine adverse events voluntarily reported to the FDA Manufacturer and User Facility Device Experience (MAUDE) database related to inadequate device settings, granulation and infection at surgical site, and hematoma at the neck that required either explanation, setting adjustments or topical treatment (FDA 2016b). No device-related deaths have been reported.

Neither evidence-based guideline from the American College of Physicians or American Academy of Sleep Medicine mentions HNS as a treatment option. Both systematic reviews underscore the need for better-quality studies to define optimal patient selection and device performance and to demonstrate long-term effectiveness.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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<tbody>
<tr>
<td>Hayes (2016)</td>
<td><strong>Key points:</strong></td>
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<tr>
<td>HNS for OSA</td>
<td>• Systematic review of six pretest/posttest studies that had nine associated subsequent reports with follow-up data, additional outcomes, overlapping samples, and/or subgroup analyses. Sample sizes ranged eight to 126 patients with moderate-to-severe OSA in whom CPAP had failed.</td>
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<tr>
<td></td>
<td>• Overall quality: Low with high risk of bias.</td>
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<td></td>
<td>• Evidence reported consistent improvements in the AHI, oxygen desaturation index (ODI), and airflow mechanics with HNS, but inconsistent improvement in sleep quality and QOL.</td>
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<td></td>
<td>• Higher-quality research, with comparative study designs and larger sample sizes is needed to define the potential benefits of HNS for OSA and optimal patient selection criteria.</td>
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<tr>
<td>Certal (2015)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td>HNS for OSA</td>
<td>• Systematic review and meta-analysis of six prospective case series (200 total patients).</td>
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<tr>
<td></td>
<td>• Overall quality: low with high risk of bias and short-term follow up. No significant heterogeneity in devices used.</td>
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<td>• At 12 months, statistically significant reductions (mean difference, 95% confidence interval): AHI (-17.51, -20.69 to -14.34); ODI (-13.73, -16.87 to -10.58); Epworth Sleepiness Scale (-4.42, -5.39 to -3.44). Overall, the AHI and ODI were reduced by approximately 50%.</td>
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<td>• Similar significant reductions observed at three and six months.</td>
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<td>• Despite limitations, authors concluded that HNS may be considered in selected patients with OSA who fail medical treatment. Further studies comparing HNS with conventional</td>
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therapies are needed to definitively evaluate long-term outcomes.

**Glossary**

**Apnea** — An absence of breathing (respirations).

**Apnea-hypopnea index (AHI)** — The number of apneic episodes (obstructive, central and mixed) plus hypopneas (partial reduction in breathing) per hour of sleep.

**Continuous positive airway pressure (CPAP)** — Device that delivers a steady, gentle flow of air through a soft, pliable face or nasal mask. Used to ‘splint’ open a person’s airway during sleep.

**Genioglossus muscle** — Muscle that runs from the chin to the tongue. It is the major muscle responsible for protruding (or sticking out) the tongue.

**Hypoglossal nerve** — The twelfth cranial nerve that controls tongue movement.

**Obstructive sleep apnea (OSA)** — A life-threatening and life-altering condition that causes a person to stop breathing repeatedly during sleep due to obstruction of the airway by excess tissue in the upper airway, such as a semi-collapsed trachea, tongue relaxed to the back of the throat or a large amount of tissue in the uvula area.

**Polysomnography or overnight sleep study (PSG)** — Standard method of detecting sleep disorders and evaluating treatments in children and adults while sleeping. PSG measures information such as airflow, brain activity, respiratory effort, eye movements, leg movements, blood oxygen saturation and unusual behavior.

**Positive airway pressure (PAP)** — Provides a stream of air through a mask worn during sleep. This airflow keeps the airway open, preventing pauses in breathing and restoring normal blood oxygen saturation. PAP can be continuous (CPAP), bilevel (BPAP) or autotitrating (APAP).

**Respiratory disturbance index (RDI)** — The number of apneas (obstructive, central, or mixed) plus hypopneas per hour of total sleep time as determined by all-night PSG.

**References**

**Professional society guidelines/other:**


**Peer-reviewed references:**


FDA Manufacturer and User Facility Device Experience (MAUDE) database search using product code MNQ reported from 01/01/2014 to 07/31/2016 FDA website.  


FDA Premarket Approval (PMA) database searched using product code MNQ. FDA website.  


**Clinical trials:**

Searched clinicaltrials.gov on August 24, 2016 using terms obstructive sleep apnea | STAR | hypoglossal nerve. Three studies found, three relevant.

Stimulation Therapy for Apnea Reduction (www.theSTARtrial.Com). ClinicalTrials.gov website. 

A Pilot Study to Evaluate the Safety and Efficacy of the Hypoglossal Nerve Stimulator in Adolescents 
With Down Syndrome and Obstructive Sleep Apnea. ClinicalTrials.gov website. 

**CMS National Coverage Determinations (NCDs):**

No NCDs identified as of the writing of this policy.

**Local Coverage Determinations (LCDs):**

No LCDs identified as of the writing of this policy.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is 
not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and 
bill accordingly.

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<thead>
<tr>
<th>CPT Codes</th>
<th>Description</th>
<th>Comments</th>
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<tbody>
<tr>
<td>64999</td>
<td>Unlisted procedure, nervous system</td>
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<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
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<tbody>
<tr>
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<thead>
<tr>
<th>HCPCS Code</th>
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