Clinical Policy Title: Hypoglossal nerve stimulation

Clinical Policy Number: CCP.1270

Effective Date: January 1, 2017
Initial Review Date: October 19, 2016
Most Recent Review Date: October 2, 2018
Next Review Date: October 2019

Related policies:
- CCP.1061 Treatment for obstructive sleep apnea in adults
- CCP.1147 Diagnosing obstructive sleep apnea in adults
- CCP.1172 Uvulopalatopharyngoplasty

ABOUT THIS POLICY: Select Health of South Carolina has developed clinical policies to assist with making coverage determinations. Select Health of South Carolina’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 Select Health of South Carolina 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. Select Health of South Carolina’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. Select Health of South Carolina’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Select Health of South Carolina will update its clinical policies as necessary. Select Health of South Carolina’s clinical policies are not guarantees of payment.

Coverage policy

Select Health of South Carolina considers the use of hypoglossal nerve stimulation to be investigational and, therefore, not medically necessary.

Limitations:

None.

Alternative covered services:

- Weight management programs.
- Mandibular advancement devices (oral appliances).
- Positive airway pressure 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, such as enlarged tonsils or tongue).

**Background**

Obstructive sleep apnea is a type of sleep disorder characterized by repetitive pauses in breathing (apnea) or instances of shallow or infrequent breathing, caused by an obstruction of the upper airway during sleep. Untreated obstructive sleep apnea is associated with a reduction in blood oxygen saturation and 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. It affects persons in all age groups, especially middle-aged and elderly persons, and rates of obstructive sleep apnea are increasing, likely due to escalating obesity rates (Balk, 2011).

The goals of obstructive sleep apnea treatment are to alleviate airway obstruction during sleep, normalize sleep quality, and improve the apnea-hypopnea index 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 obstructive sleep apnea includes behavioral therapy (e.g., weight loss), drug therapy, positive airway pressure, dental or mandibular advancement devices, palatal implants, and surgery (upper airway or bariatric).

**Hypoglossal nerve stimulation:**

Hypoglossal nerve stimulation 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. Hypoglossal nerve stimulation 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 hypoglossal nerve stimulation system is available for commercial use in the United States. The U.S. Food and Drug Administration (2014) has granted premarket approval to the Inspire® II Upper Airway Stimulator (Inspire Medical Systems, Maple Grove, Minnesota). They classify the Inspire II as a class III device (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 obstructive sleep apnea (apnea-hypopnea index 20 – 65) who have failed or cannot tolerate positive airway pressure treatments and who do not have a complete concentric collapse at the soft palate level. Positive airway pressure intolerance is defined as either the inability to use positive airway pressure (> five nights per week of usage; usage defined as > four hours of use per night), or the unwillingness to use positive airway pressure (for example, a patient returns the positive airway pressure system after attempting to use it).
As a condition of the pre-market approval, the manufacturer is required to conduct two post-approval studies (U.S. Food and Drug Administration, 2014):

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

**Searches**

Select Health of South Carolina searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality.
- The Centers for Medicare & Medicaid Services.

We conducted searches on August 21, 2018. Search terms were: “Hypoglossal Nerve Diseases/surgery” (MeSH), “Hypoglossal Nerve Diseases/therapy” (MeSH), and the free text terms “hypoglossal nerve stimulation” and “upper airway 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 one systematic review (Certal, 2015), two evidence-based guidelines (Qaseem, 2013; Epstein, 2009), 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 obstructive sleep apnea but inconsistent improvement in sleep quality or quality of life in persons with moderate-to-severe obstructive sleep apnea in whom continuous positive airway pressure 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 U.S. Food and Drug Administration Manufacturer and User Facility Device Experience database related to inadequate device
settings, granulation and infection at surgical site, and hematoma at the neck that required either explantation, setting adjustments or topical treatment (U.S. Food and Drug Administration, 2016). No device-related deaths have been reported.

Neither evidence-based guideline from the American College of Physicians (Qaseem, 2013) or American Academy of Sleep Medicine (Epstein, 2009) mentions hypoglossal nerve stimulation 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.

**Policy updates:**

In 2017, new results for the Stimulation Therapy for Apnea Reduction trial (Gillespie, 2017; Clinicaltrials.gov identifier NCT01161420) and a multicenter, single-arm trial in Germany (Hofauer, 2017; Steffen, 2017; Clinicaltrials.gov identifier NCT02293746, publication date updated to 2018) provide low-quality evidence of sustained benefit on patient-reported outcomes (Epworth Sleepiness Scale, Functional Outcomes of Sleep Questionnaire, and snoring levels) up to 48 months after implantation, and short-term improvement in sleep architecture in a small subset of participants in the German study (Heiser, 2017).

Reported adverse effects in the trials were rare and generally unrelated to the device or the procedure. Seventeen adverse events associated with hypoglossal nerve stimulation were reported between October 1, 2016 and July 31, 2017; most were related to device malfunction, lead migration, and surgical site complications (e.g., infection or hematoma), but one event of paralysis to the hypoglossal nerve was noted (U.S. Food and Drug Administration, 2017). A position statement from the American Academy of Otolaryngology-Head and Neck Surgery supports hypoglossal nerve stimulation as an effective second-line treatment of moderate-to-severe obstructive sleep apnea in carefully selected patients who are intolerant or unable to achieve benefit with positive pressure therapy (American Academy of Otolaryngology-Head and Neck Surgery, 2016). Nonetheless, the optimal patient selection criteria and the relative benefits and harms of hypoglossal nerve stimulation compared to established surgical procedures remain undefined, and higher quality studies are needed. No changes to the policy are warranted.

In 2018, we added one systematic review/meta-analysis of outcomes of tongue surgeries in pediatric patients with obstructive sleep apnea, which found evidence for hypoglossal nerve stimulation was limited to a case report (Camacho, 2017). No policy changes are warranted. Policy ID changed from CP# 09.02.04 to CCP.1270.

**Summary of clinical evidence:**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camacho (2017)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td>Tongue surgeries for pediatric obstructive sleep apnea</td>
<td>• Systematic review and meta-analysis of 11 studies (n = 116) who underwent base-of-tongue reduction (n = 114), tongue suspension (n = 1), and hypoglossal nerve stimulation (n = 1);</td>
</tr>
<tr>
<td>Citation</td>
<td>Content, Methods, Recommendations</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------------</td>
</tr>
</tbody>
</table>
| Gillespie (2017) | Most children were syndromic with craniofacial disorders, co-morbidities, or other serious medical issues.  
- Hypoglossal nerve stimulation and tongue-base suspension are limited to case reports.  
- The specific type of surgery must be tailored to the patient.  
- Patients with co-morbidities should undergo treatment in centers that are equipped to provide appropriate perioperative care. |

**Key points:**
- Multicenter, prospective phase 3 trial of 91 participants from 126 implanted participants.  
- Inclusion criteria:  
  - Pre-implant apnea-hypopnea index (based on in-laboratory polysomnography) 20 to 50 events per hour.  
  - Apnea-hypopnea index contribution from central or mixed sleep apnea < 25%.  
  - No primarily lateral obstructive sleep apnea (defined as limited sleep apnea [apnea-hypopnea index <10 events per hour] when lying on side).  
  - No complete concentric collapse at the level of the soft palate observed during a drug-induced sleep endoscopy.  
  - Difficulty accepting or adhering to continuous positive airway pressure.  
  - BMI ≤ 32 kg/m².  
  - No significant neuromuscular or cardiopulmonary disease.  
- Following the 12-month visit, 46 consecutive responding subjects were randomized 1:1 to either a therapy maintenance group (ON group) or a therapy withdrawal group (OFF group).  
- Safety and patient-reported outcomes at 48 months, including Epworth Sleepiness Scale, Functional Outcomes of Sleep Questionnaire, and snoring level compared with preimplantation baseline.  
- The majority of participants were white (97%), male (83%), and between the ages of 18 and 65 years (87.3%).  
- Safety: 107 total events recorded in 126 participants (85%) mostly related to pre-existing conditions, general anesthesia, or surgical procedures; 13 serious adverse events but unrelated to device; one revision procedure performed.  
- Significant reduction in Epworth Sleepiness Scale daytime sleepiness ($P = .01$) and improvement in Functional Outcomes of Sleep Questionnaire sleep-related quality of life ($P = .01$).  
- 85% of bed partners reported soft or no snoring.  
- Two patients required additional surgery without complication for lead malfunction. |

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
</table>
| Heiser (2017) and Steffen (2018) | Multicenter, prospective single-arm study of 60 patients with moderate-to-severe obstructive sleep apnea who could not adhere to continuous positive airway pressure.  
- Key study exclusion criteria included body mass index > 35 kg/m², apnea-hypopnea index < 15 or > 65, or complete concentric collapse at the soft palate during sedated endoscopy.  
- Home sleep test and patient-reported outcomes at baseline and 6 and 12 months after implantation.  
- The average usage time of the system was 42.9 ± 11.9 hours per week.  
- Significant reduction in median apnea-hypopnea index from 28.6 per hour to 8.3 per hour at six months and 9.5 per hour at 12 months. No patient required surgical revision of the implant. |

**Key points:**
- Multicenter, prospective single-arm study of 60 patients with moderate-to-severe obstructive sleep apnea who could not adhere to continuous positive airway pressure.  
- Key study exclusion criteria included body mass index > 35 kg/m², apnea-hypopnea index < 15 or > 65, or complete concentric collapse at the soft palate during sedated endoscopy.  
- Home sleep test and patient-reported outcomes at baseline and 6 and 12 months after implantation.  
- The average usage time of the system was 42.9 ± 11.9 hours per week.  
- Significant reduction in median apnea-hypopnea index from 28.6 per hour to 8.3 per hour at six months and 9.5 per hour at 12 months. No patient required surgical revision of the implant. |
<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
</table>
| - Hofauer (2017)  
Effects of upper airway stimulation on sleep architecture in patients with obstructive sleep apnea  
Clinicaltrials.gov NCT02293746 | **Key points:**  
- Single-arm study of 26 patients who received an upper airway stimulation implant. Treatment outcome was evaluated two and three months after surgery.  
- Pre- and month 2 post-implantation apnea-hypopnea index were 33.9 per hour and 9.1 per hour, respectively ($P < .001$).  
- Time spent in N1-sleep was 23.2% at baseline and 16.0% at month 3.  
- The amount of time spent in N2- and N3-sleep did not change during the observation period.  
- There was a significant increase of the amount of rapid eye movement sleep at month 2 (15.7%) from baseline (9.5%; $P = .010$), and a reduction of the number of arousals and the arousal index. |
Position statement: hypoglossal nerve stimulation for obstructive sleep apnea | **Key points:**  
- Hypoglossal nerve stimulation is an effective second-line treatment of moderate-to-severe obstructive sleep apnea in patients who are intolerant or unable to achieve benefit with positive pressure therapy. Not all adult patients are candidates for upper airway stimulation therapy and appropriate polysomnographic, age, body mass index, and objective upper airway evaluation measures are required for proper patient selection. |
| - Certal (2015)  
Hypoglossal nerve stimulation for obstructive sleep apnea | **Key points:**  
- Systematic review and meta-analysis of six prospective case series (200 total patients).  
- Overall quality: low with high risk of bias and short-term follow up. No significant heterogeneity in devices used.  
- At 12 months, statistically significant reductions (mean difference, 95% confidence interval): apnea-hypopnea index (-17.51, -20.69 to -14.34); oxygen desaturation index (-13.73, -16.87 to -10.58); Epworth Sleepiness Scale (-4.42, -5.39 to -3.44). Overall, the apnea-hypopnea index and oxygen desaturation index were reduced by approximately 50%.  
- Similar significant reductions observed at three and six months.  
- Despite limitations, authors concluded that hypoglossal nerve stimulation may be considered in selected patients with obstructive sleep apnea who fail medical treatment. Further studies comparing hypoglossal nerve stimulation with conventional therapies are needed to definitively evaluate long-term outcomes. |

**References**

**Professional society guidelines/other:**


Peer-reviewed references:


Centers for Medicare & Medicaid Services National Coverage Determinations:

No National Coverage Determinations identified as of the writing of this policy.

Local Coverage Determinations:

A55834 Response to Comments: L33777 Noncovered Services First Coast Service Options, Inc.

A52928 Sources of Information and Basis for Decision Noncovered Services Local Coverage Determination.

L33777 Noncovered services.

**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.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>64999</td>
<td>Unlisted procedure, nervous system</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Category III codes</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0466T, 0467T, 0468T</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>G47.33</td>
<td>Obstructive sleep apnea</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS Level II Code</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td>Not Applicable</td>
<td></td>
</tr>
</tbody>
</table>