Hypoglossal nerve stimulation

Clinical Policy ID: CCP.1270

Recent review date: 8/2021

Next review date: 12/2022

Policy contains: Down syndrome; hypoglossal nerve stimulation; Inspire®; obstructive sleep apnea; upper airway stimulation.

This policy is a Sandhills Center Clinical Coverage Policy adopted from AmeriHealth Caritas of North Carolina. These clinical policies are used to assist with making coverage determinations. Sandhills Center'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 Sandhills Center 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. Sandhills Center 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. Sandhills Center's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Sandhills Center will update its clinical policies as necessary. Sandhills Center clinical policies are not guarantees of payment.

Coverage policy

Hypoglossal nerve stimulation is clinically proven and, therefore, medically necessary for members age 22 years or older with persistent obstructive sleep apnea who meet all of the following criteria (American Academy of Otolaryngology-Head and Neck Surgery, 2019; Woodson, 2018; Stimulation Therapy for Apnea Reduction trial; clinicaltrials.gov identifier NCT01161420):

- Body mass index ≤ 32 kg/m^2.
- Apnea-hypopnea index 15 to 65.
- Positive airway pressure failure defined as either:
    - An apnea-hypopnea index > 15 despite positive airway pressure usage.
    - Inability to use positive airway pressure (more than four hours of use per night for more than five nights per week) or unwilling to use positive airway pressure.
- Anatomy amenable to implantation and likelihood of high success (i.e., no complete concentric collapse at the soft palate level).

Hypoglossal nerve stimulation is clinically proven and, therefore, medically necessary for members with Down syndrome ages 10 to 21 years with persistent obstructive sleep apnea who meet all of the following criteria (Diercks, 2017):

- Prior adenotonsillectomy.

- Body mass index < 95th percentile for age.
- Moderate to severe obstructive sleep apnea (apnea-hypopnea index > 10 but < 50).
- Tracheotomy or positive airway pressure failure defined as either:
- Noncompliance, discomfort, or undesirable side effects.
- An apnea-hypopnea index > 10 despite compliant positive airway pressure usage.
- Unwilling to use positive airway pressure.

Limitations

Contraindications to hypoglossal nerve stimulation include (Inspire Medical Systems, 2020):

- Sleep study showing greater than 25% central or mixed apneas.
- Concentric palatal collapse seen on drug-induced sleep endoscopy.
- Inability to operate the therapy.
- Pregnancy (existing or planned).
- Pre-existing anatomic alterations or neurologic disorders that would affect device function.
- Members who require magnetic resonance imaging if Inspire® Model 3024 (Inspire Medical Systems, Inc. Golden Valley, Minnesota) is to be implanted, because it may cause tissue damage and/or damage to the device.
    - Members implanted with Inspire Model 3028 can undergo magnetic resonance imaging on the head and extremities if certain conditions and precautions are met.
- If diathermy (primarily used in physical therapy) is planned.
- Potential for electromagnetic incompatibility and interference from electrocautery, irradiation, lithotripsy, radiofrequency ablation, radiograph, fluoroscopy, ultrasonic devices, defibrillation, or radiation.
- Other implanted devices that may be susceptible to unintended interaction with the Inspire system.

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 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 of 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 for 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 retroglossal region of 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) granted premarket approval to the Inspire II Upper Airway Stimulator as a class III device. 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 (more than five nights per week of usage; usage defined as more than 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 premarket approval, the manufacturer is required to conduct two postapproval studies (U.S. Food and Drug Administration, 2014):

- Extended Follow-up of the Premarket Cohort (Stimulation Therapy for Apnea Reduction, ClinicalTrials.gov identifier: NCT01161420).
- Inspire Post-Approval Study Protocol Number 2014-001. New enrollment multi-center, prospective, single-arm cohort study to evaluate long-term device safety and effectiveness. The estimated completion date is September 2021. (ClinicalTrials.gov identifier: NCT02413970).

Findings

We identified one systematic review (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 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.

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 (2016) 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. 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. The policy ID was changed from CP# 09.02.04 to CCP.1270.

In 2019, we received a request for reconsideration of medical necessity criteria for the use of hypoglossal nerve stimulation in pediatric populations and added new findings of safety and efficacy in adult and pediatric populations. Long-term (five-year) results from the multicenter Stimulation Therapy for Apnea Reduction trial (Woodson, 2018; clinicaltrials.gov identifier NCT01161420) and new systematic review findings (Kompelli, 2019) support hypoglossal nerve stimulation as a second-line treatment for moderate to severe obstructive sleep apnea in selected adults who have failed positive airway pressure therapy. Hypoglossal nerve stimulation provides significant and durable improvements in outcome measures, such as quality of life, the Epworth Sleepiness Scale, snoring, and polysomnography. Common adverse events were pain (6.2%: 95% confidence interval 0.7 to 16.6), tongue abrasion (11.0%: 1.2 to 28.7), and internal (3.0%: 0.3 to 8.4)/external (5.8%: 0.3 to 17.4) device malfunction (Kompelli, 2019).

In pediatric populations (age 17 years or younger), the majority of cases of obstructive sleep apnea result from anatomical obstruction (e.g., adenotonsillar hypertrophy) for which hypoglossal nerve stimulation would not be indicated (Inspire, 2019). A systematic review previously included in this policy (Camacho, 2017) found that most children undergoing tongue surgeries were syndromic with craniofacial disorders, comorbidities, or other serious medical issues, and patients with Down syndrome had a higher incidence of obstructive sleep apnea than the general pediatric population. For adolescents and young adults with Down syndrome, obstructive sleep apnea often persists after adenotonsillectomy, and tongue-based obstruction is inadequately treated with positive airway pressure. Surgery may be indicated depending on the location and severity of the obstruction (Ishman, 2018).

A multicenter clinical trial (clinicaltrials.gov identifier: NCT02344108) is evaluating the safety and efficacy of hypoglossal nerve stimulation in participants (age 10 to 21 years) with Down syndrome and persistent severe obstructive sleep apnea (apnea-hypopnea index > 10 events/hour) after adenotonsillectomy and either tracheotomy or failed positive airway pressure therapy. Preliminary results (Diercks, 2017) from the first six participants suggest hypoglossal nerve stimulation was well-tolerated (mean use of 5.6 hours/night to 10.0

hours/night) with few adverse events. All experienced significant improvement in obstructive sleep apnea symptoms on polysomnography immediately following device activation and up to one year (n = 5), with a 56% to 85% reduction in the apnea-hypopnea index compared with their preoperative baseline. For the five children who completed a quality of life survey (OSA-18 questionnaire), all demonstrated a large improvement (change score ≥ 1.5) in sleep disturbance, caregiver concerns, and the mean OSA-18 score, and a moderate improvement (change score greater than 1.0 but less than 1.4) in daytime problems associated with obstructive sleep apnea from baseline to 12 months post-implantation.

As a result of these new findings, we changed the policy coverage for hypoglossal nerve stimulation from investigational to medically necessary for adults age 22 years or older and for members with Down syndrome ages 10 to 21 years. The coverage criteria are based on the inclusion criteria from the two clinical trials (Diercks, 2017; Woodson, 2018). We added contraindications from the device manufacturer.

In 2020, we added the results of one case series (Caloway, 2020), a substudy of a randomized controlled trial (Dedhia, 2019), and a systematic review of 12 prospective studies (Costantino, 2020). The new trial results warrant no coverage changes, but we modified the limitations to conform to the manufacturer's listed contraindications.

In 2021, we added several local coverage determinations to the policy (Centers for Medicare & Medicaid Services, 2020a, 2020b, 2020c, 2020d, 2020e). No policy changes are warranted.

References

On May 13, 2021, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "Hypoglossal Nerve Diseases/surgery" (MeSH), "Hypoglossal Nerve Diseases/therapy" (MeSH), "hypoglossal nerve stimulation," and "upper airway stimulation." We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

10/2016: initial review date and clinical policy effective date: 1/2017

10/2017: Policy references updated.

11/2018: Policy references updated. Policy ID changed.

9/2019: Policy references updated. Policy changed from investigational to medically necessary and limitations added.

8/2020: Policy references updated.

8/2021: Policy references updated.