VHA Office of Integrated Veteran Care

Clinical Determination and Indication

Hypoglossal Nerve Stimulation for Obstructive Sleep Apnea

CDI Number: 00001

Original Effective Date: January 1, 2023

Last Review Date: September 01, 2024

I. Disclaimer

This document is currently in draft and is intended to be used as a reference for non-VA providers and not intended to replace clinical judgment when determining care pathways. These guidelines do not guarantee benefits or constitute medical advice.

II. Clinical Determinations and Indications

a. Indications for Hypoglossal Nerve Stimulation

Hypoglossal nerve stimulation (HNS) is indicated for the treatment of moderate to severe obstructive sleep apnea (OSA) and will be considered **medically necessary** when **ALL** the following criteria are met:

- Veteran is at least 18 years of age
- Body mass index (BMI) is less than 40 kg/m^2
- Documentation of an overnight polysomnography (PSG) performed in a sleep laboratory within 24 months of first consultation for HNS implant
    - Lab test is preferred, but Type III Home Sleep Apnea Tests (HSATs) are allowed with a recommendation for more than one night of HSATs when competing sleep disorders are present (e.g., insomnia)
- Veteran has predominantly obstructive events
    - Defined as central and mixed apneas less than 25% of the total apnea-hypopnea index (AHI)
- AHI is 15 to 100 events/hr.
- Documentation that demonstrates continuous positive airway pressure (CPAP) failure or intolerance, including shared decision making of intolerance despite consultation with a sleep expert

b. Limitations/Exclusions

Conditions/indications for which HNS is **not medically necessary** include, but are not limited to, the following:

- Central and mixed apneas that make up more than 25% of the total AHI

- Concentric palatal collapse at the soft palate level as seen on a drug-induced sleep endoscopy (DISE) procedure
- Veterans who are or who plan to become pregnant
- Veterans who are unable or do not have the necessary assistance to operate the sleep remote
- Any condition or procedure that has compromised neurological control of the upper airway

c. Description of Treatment

Obstructive sleep apnea is caused by the relaxation of muscles in the mouth and throat when a person is asleep, causing partial or complete blockage of airflow. Stimulation of these muscles can reduce the frequency and severity of these airflow blockages. Hypoglossal nerve stimulation is a treatment that uses a surgical implant to stimulate the hypoglossal nerve, preventing the tongue from blocking the airway. The hypoglossal nerve is the twelfth cranial nerve and innervates all the extrinsic and intrinsic muscles of the tongue, except for the palatoglossus which is innervated by the vagus nerve. The hypoglossal nerve stems from the hypoglossal nucleus in the brain stem, as a number of small rootlets, and passes through the hypoglossal canal, down through the neck, branching and innervating the tongue. There are two hypoglossal nerves, one on the left, and one on the right.

The only FDA-approved hypoglossal nerve stimulation system is available through Inspire Medical and has three implantable components: a stimulation lead that delivers mild stimulation to maintain multilevel airway patency during sleep, a breathing sensor lead identifying breathing patterns, and a generator that monitors breathing patterns. The two external components are a patient sleep remote that provides a noninvasive means for a patient to activate the generator and a physician programmer that allows the physician to noninvasively interrogate and configure the generator settings. The system battery life for the implantable components is 7 to 10 years.

To implant a hypoglossal nerve stimulation device, a surgeon will perform a two-to-three-hour surgery conducted under general anesthesia. A surgeon implants the system containing a neurostimulator subcutaneously in the patient's chest, with one lead attached to the patient's hypoglossal nerve (cranial nerve XII) at the base of the tongue and one lead implanted in the patient's chest. The lead in the chest consists of a pressure sensor that detects breathing. Information about respiration rate is relayed to the device, which stimulates the hypoglossal nerve in the tongue. When stimulated, the tongue moves forward, opening the airway. The patient can operate the device by remote control, which the patient activates before going to sleep. The device turns on after 30 minutes to minimize disrupting the patient's

sleep onset; the device must be manually turned off via remote when the patient wakes.

III. Background and Supporting Information

The following information is for reference purposes only in accordance with the medical benefits package outlined in 38 C.F.R. § 17.38 (b). Each subsection supports VA's determinations for medical necessity and alignment with generally accepted standards of medical practice.

a. Background of Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is a sleep disorder that involves cessation (stopping) or a significant decrease in airflow in the presence of breathing effort. It is the most common type of sleep disordered breathing and is characterized by recurring episodes of upper airway collapse during sleep. These episodes are associated with oxyhemoglobin desaturations, or low levels of oxygen in the blood, and arousals from sleep. The frequency of these episodes, or events, are utilized to categorize OSA by severity: mild OSA is defined as ≥5 to <15 events per hour; moderate OSA is defined as ≥15 to <30 events per hour; and severe OSA is defined as ≥30 events per hour.

The cardinal symptoms of sleep apnea include the "3 S's": snoring, sleepiness, and significant-other report of sleep apnea episodes. Often, individuals are unaware that they have OSA and the associated daytime sleepiness risks, as well as the association with other debilitating medical conditions, including hypertension, cardiovascular disease, and coronary artery disease. In the United States, it has been reported that 25-30% of men and 9-17% of women meet the criteria for OSA. Anyone can develop OSA, though certain factors place individuals at an increased risk, including excessive weight, older age, naturally narrowed airway, and the presence of comorbidities, such as hypertension. Prevalence also increases with age, and it has been reported that there may be a genetic component, as obesity and upper airway soft tissue structure are both genetically inherited.

Nighttime in-laboratory level 1 polysomnography (PSG) is the gold standard test to diagnose OSA. During the test, electroencephalogram (EEG) leads, pulse oximeters, and other devices are used to monitor nasal and oral airflow, chest and abdomen movement, and muscle contractions in the chin, chest, and legs. Home sleep tests (HST) or portable monitoring (PM) have gained popularity in diagnosing OSA due to their relative accessibility and lower cost compared to other diagnostic tests. However, these options should only be used with specific rules and procedures in place to ensure an accurate diagnosis.

Treatment of OSA is a multi-pronged approach and should be individualized to each patient in collaboration with a clinical team. Important lifestyle changes should be emphasized, such as proper weight management and the avoidance of alcohol and smoking. Continuous positive airway pressure (CPAP) is the most effective treatment of OSA for adults. CPAP therapy prevents respiratory events by maintaining a positive airway pressure during sleep. If a patient has failed CPAP therapy, despite counseling and correction of common CPAP issues, or if a patient has anatomical features or narrowing that may be favorable for surgical intervention, surgical treatments may be indicated for OSA. Surgical treatments are rarely indicated as a primary therapy in adults. Surgical treatments for OSA include uvulopalatopharyngoplasty (UPPP), maxillomandibular advancement (MMA) and hypoglossal nerve stimulation (HNS).

b. Research, Clinical Trials, and Evidence Summaries

The concept of stimulating the tongue musculature to increase upper airway size and limit the pathophysiologic obstruction leading to obstructive sleep apnea was introduced in the late 1980s. A variety of strategies were utilized, including transcutaneous stimulation with placement of electrodes in the submental region, sublingual mucosa, and soft palate. However, these studies were limited by their lack of selective stimulation of the primary protrusion of the tongue, the genioglossus muscle. The following research studies provide recent evidence on hypoglossal nerve stimulation:

Schwartz et al. (2023) conducted a randomized clinical trial evaluating targeted hypoglossal nerve (THN) stimulation for the treatment of obstructive sleep apnea (OSA). The study was conducted at 20 different centers and included 138 patients with moderate to severe OSA who were randomly assigned to receive THN stimulation starting at one month (treatment group) or four months (control group). The THN stimulation was conducted on the proximal hypoglossal nerve and researchers evaluated AHI and oxygen desaturation index (ODI) responder rates as primary end points. All participants received 11 months of THN, with follow up at 12 months for the treatment group and 15 months for the control group. The researchers found that at four months the treatment group responded with strong and moderate effect sizes for AHI and ODI responder rates when compared to the control group. Additionally, in the treatment group, the drop in AHI and ODI was greater. At 12 and 15 months, the combined groups demonstrated AHI and ODI rates of 42.5% and 60.4%, respectively, meeting prespecified ODI but not AHI responder rates. Clinically meaningful improvements in secondary outcomes were also detected, including quality of life indices. Finally, patient satisfaction measures showed that 83% of participants were satisfied or very satisfied with their outcome and 88% expressed willingness to undergo the treatment again. Overall, THN yielded durable decreases in apnea severity

and OSA burden on quality of life, with a favorable safety profile after 11 months of active treatment, demonstrating superiority of THN versus a concurrent control group.

Costantino et al. (2019) performed a systematic review and meta-analysis evaluating HNS clinical outcomes in the treatment of moderate to severe OSA. The researchers included 12 peer-reviewed, prospective studies in the review, totaling 350 adult patients. Studies included compared baseline and post-implementation clinical outcomes, with no restrictions according to follow-up length. The researchers found that HNS represents an effective and safe surgical procedure for adult patients suffering from moderate to severe OSA. All primary outcomes, including apnea-hypopnea index, oxygen desaturation index, and Epworth Sleepiness Scale, showed a significant improvement. A surgical success rate was identified as 72.4% (Inspire), 76.9% (ImThera), 55% (Apnex) at 12 months, and 75% (Inspire) at 60-month follow-up. Further, the researchers found that only 6% of patients required surgical repositioning or replacement of the neurostimulator or implanted leads after five years.

In 2014, the Stimulation Therapy for Apnea Reduction (STAR) Trial was published as the initial clinical trial using an INSPIRE Medical Systems upper airway stimulation (UAS) device as an alternative therapy to CPAP for treatment of OSA which led to FDA approval. This study evaluated the stability of improvement of 123/126 (98%) subjects using polysomnographic measures of sleep disordered breathing, patient reported outcomes, and the durability of hypoglossal nerve and safety at 18 months [Dedhia et al (2015)]. The median AHI was reduced by 67.4% and the median ODI was reduced by 67.5% at 18 months. The Functional Outcomes of Sleep Questionnaire (FOSQ) and Epworth Sleepiness Scale (ESS) improved at 18 months compared to baseline while the functional threshold was unchanged from baseline at 18 months. The research concluded that upper airway stimulation via the hypoglossal nerve maintained a durable effect of improving airway stability during sleep and improved patient reported outcomes without an increase of the stimulation thresholds or tongue injury at 18 months.

Soose et al. (2016) evaluated 111/126 (88%) of the STAR Trial participants at the 24-month interval, measuring self- and bedpartner-report of snoring intensity, ESS, and FOSQ. The study identified sustained improvement in mean FOSQ score from baseline (14.3) to 24 months (17.2). Similar sustained improvements were observed with all FOSQ subscales and FOSQ-10. Subjective daytime sleepiness, as measured by mean ESS, improved from baseline (11.6) to 24 months (7.1). Self-reported snoring severity showed an increased percentage of "no" or "soft" snoring from 22% at baseline to 91% at 24 months. Researchers concluded that HNS therapy can

provide improvement in sleep related quality-of-life outcomes and can be maintained throughout a 24-month period.

Woodson et al. (2016) evaluated 116/126 (92%) of the STAR clinical trial participants at the 36-month interval. Ninety-eight participants agreed to a voluntary 36-month polysomnography (PSG). Self-report daily device usage of 81%. In the PSG group, 74% reduced the AHI median value of 28.2/hr., at baseline to 8.7 and 6.2 at 36 months. Improved self-reported outcomes maintained at 36 months. Researchers concluded that treatment with hypoglossal nerve stimulation continued to show improvements in respiratory and quality-of-life outcomes throughout a 36-month period.

Gillespie et al. (2017) evaluated 91/126 (72%) of the STAR Trial participants at the 48-month interval. Subjective daytime sleepiness, as measured by ESS, and quality-of-life, as measured by FOSQ, maintained reduction compared to baseline. Soft to no snoring was reported by 85% of bed partners. Researchers concluded that UAS benefits had been maintained.

Woodson et al (2018) published the STAR investigators' 5-year patient outcomes for 97/126 (77%) participants, and 71 (56 %) consented to voluntary PSG. Improvement in sleepiness and quality of life were observed, with normalization of scores increasing from 33% to 78% and 15% to 67%, respectively. AHI response rate (AHI less than 20/hr. and greater than 50% reduction) was 75% (n equal to 71). Researchers concluded that improvements were maintained in sleepiness, quality of life, and respiratory outcomes observed with 5 years of UAS.

Finally, the 2019 VA/DoD Clinical Practice Guideline for the Management of Chronic Insomnia Disorder and Obstructive Sleep Apnea recommends patients with OSA (with apnea-hypopnea index of 15-65 per hour, a BMI <32 kg/m^2 and who cannot adhere to positive airway pressure therapy) seek an evaluation for surgical treatment with HNS therapy. The clinical practice guideline recognizes that not every patient is a good surgical candidate based on comorbid conditions and general health status and the consideration of this device and compatibility with magnetic resonance imaging (MRI) should be accounted for.

c. U.S. Food & Drug Administration (FDA) Information

VA generally only approves use of medical devices that have received at least FDA clearance for 510(k) Premarket Notification. The FDA has determined these Class II devices are substantially equivalent (SE) to legally marketed predicate devices and may be marketed in the U.S.

To search for devices that have received FDA 510(k) clearance or Premarket Approval (PMA), please visit the FDA Devices database.

Information	Description
Product Name	Inspire Upper Airway Stimulation
PMA Applicant	Inspire Medical Systems, Inc.
Address	5500 Wayzata Blvd. Suite 1600 Golden Valley, MN 55416 US
Approval Date	June 8, 2023
Approval Letter	Approval Letter

d. Medicare Coverage Determinations

Available Medicare coverage determinations are listed below as a resource. VA and Medicare are governed by separate laws and regulations; thus, VA coverage determinations may be different.

NCD Number	Name	Effective Date
None	N/A	N/A

LCD Number	Contractor	Original/Revision Effective Date
L38528	Wisconsin Physicians Service Insurance Corporation	04/25/2024
L38307	CGS Administrators, LLC	03/07/2024
L38276	Palmetto GBA	04/13/2023
L38387	National Government Services, Inc.	04/01/2020
L38398	First Coast Service Options, Inc.	03/15/2020
L38310	Noridian Healthcare Solutions, LLC	03/15/2020
L38312	Noridian Healthcare Solutions, LLC	03/15/2020
L38385	Novitas Solutions, Inc.	03/15/2020

- NCD: National Coverage Determination
- LCD: Local Coverage Determination

e. TRICARE Policy Manual

Available TRICARE coverage determinations are listed below as a resource. VA and TRICARE are governed by separate laws and regulations; thus, VA coverage determinations may be different.

TRICARE Policy Manual 6010.60-M, Chapter 4, Section 8.1

IV. Definitions

Term	Definition
Apnea	The cessation (interruption) of airflow for at least 10 seconds. Apnea may last for 30 seconds or longer
Apnea/Hypopnea Index (AHI)	The average number of apneas or hypopneas per hour of sleep
Hypopnea	Peak signal excursions drop by at least 30% of pre-event baseline using nasal pressure (diagnostic study), positive airway pressure device flow (titration study), or an alternative hypopnea sensor (diagnostic study); duration of the at least 30% drop in signal excursion is 10 or more seconds; and there is 3% or greater oxygen desaturation from pre-event baseline and/or the event is associated with an arousal
Central Sleep Apnea (CSA)	A sleep disorder in which the brain temporarily fails to signal the muscles that control breathing. As a result, one may experience repeated pauses in breathing or shallow breathing, which can lead to decreased oxygen levels and fragmented sleep
Genioglossus Muscle	Fan-shaped, extrinsic muscle that is involved in forming most of the tongue mass
Maxillomandibular advancement surgery	Detachment of both the upper and lower jaws to surgically advance anteriorly to increase space in the oropharynx
Mixed Sleep Apnea (MSA)	A condition when a patient experiences both Obstructive Sleep Apnea (OSA) and Central Sleep Apnea (CSA) at the same time. MSA is sometimes referred to as Complex Sleep Apnea
Obstructive Sleep Apnea (OSA)	Repetitive episodes of upper airway obstruction due to the collapse and obstruction of the upper airway during sleep Mild OSA: AHI of 5 to <15 Moderate OSA: AHI of 15 to <30 Severe OSA: AHI ≥30
Oxyhemoglobin	Represents the fraction of oxygenated hymoglobin in relation to the total hemoglobin present, including non-oxygen-binding hemoglobins
Patency	The quality or state of being open or unobstructed

Term	Definition
Positive Airway Pressure (PAP)	Positive airway pressure may be continuous (CPAP) or auto-adjusting (APAP) or Bi-level (Bi-PAP)
PAP Intolerance	PAP use for less than 4 hours per night for 5 nights or more per week, or refusal to use CPAP. CPAP intolerance may be observed in patients with mild, moderate, or severe OSA
Respiratory Disturbance Index (RDI)	The number of apneas, hypopneas, or respiratory event-related arousals per hour of sleep time. RDI is often used synonymously with the AHI
Respiratory Event Index (REI)	The number of events per hour of monitoring time. Used as an alternative to AHI or RDI in home sleep studies when actual sleep time from EEG is not available
Respiratory Event Related Arousal (RERA)	An event lasting at least 10 seconds associated with flattening of the nasal pressure waveform and/or evidence of increasing respiratory effort, terminating in an arousal but not otherwise meeting criteria for apnea or hypopnea
Soft Palate	Muscular roof of the mouth, sitting behind the hard palate
Sublingual Mucosa	The membrane of the ventral (under) surface of the tongue
Submental Region	Distinct anatomical area under the chin (mentum), between the chin and neck
Uvulopalatopharyngoplasty	Surgical removal of the uvula and tissue from the soft palate to create more space in the oropharynx

V. References

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VI. CDI History/Revision Information

- Explanation of changes to the CDI

Revision Type	Date of Revision	Update(s) Made to CDI
Content Updates	01/31/2024	Expanded indicators from June 2023 FDA approval: increased the upper limit baseline apnea-hypopnea index (AHI) and increased the upper limit body mass index (BMI) warning
Content Updates	01/31/2024	Added research/evidence summaries: • Costantino et al. (2019) • Schwartz et al. (2023)