Medical Coverage Policy

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Obstructive Sleep Apnea Treatment Services

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Coverage Policy

In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Coverage of the treatment of obstructive sleep apnea and other sleep disorders varies across plans. Refer to the customer's benefit plan document for coverage details.

NONSURGICAL TREATMENT

Coverage for Durable Medical Equipment (DME) including continuous positive airway pressure (**CPAP**), **auto-titrating positive airway pressure (APAP), and bi-level positive airway pressure (BPAP) devices varies across plans. Refer to the customer's benefit plan document for coverage details.**

If coverage for positive airway pressure (PAP) devices is available, the following conditions of coverage apply.

CPAP (CPT code E0601) or auto-titrating PAP (APAP) (HCPCS code E0601) with or without a humidifier (HCPCS codes E0561, E0562) for an initial 90 day period is considered medically necessary for the treatment of OSA in an adult (18 years or older) when EITHER of the following criteria is met:

- apnea/hypopnea index (AHI) or respiratory disturbance index (RDI) or respiratory event index (REI) ≥ 15 as documented by polysomnography (PSG) or home sleep apnea test (HSAT)
- AHI/RDI/REI ≥ 5 and < 15 as documented by PSG or HSAT, when accompanied by symptoms of OSA (e.g., excessive daytime sleepiness, impaired cognition, mood disorders or insomnia) or when the individual has hypertension, ischemic heart disease or history of stroke

CPAP (HCPCS code E0601) or auto-titrating PAP (APAP) (HCPCS code E0601) with or without a humidifier (HCPCS codes E0561, E0562) for an initial 90 day period is considered medically necessary for the treatment of OSA in a <u>child</u> when ALL of the following criteria are met:

- OSA diagnosis established by diagnostic sleep test
- child weighs 30 kilograms (66 pounds) or more
- adenotonsillectomy has been unsuccessful or is contraindicated, or when definitive surgery is indicated but must await complete dental and facial development

Home titration using auto-titrating PAP (APAP) to determine a fixed CPAP pressure for ongoing treatment is considered medically necessary when ALL of the following criteria are met:

- individual meets the criteria for PAP (detailed in PAP section above)
- individual does not have a comorbid condition that would be expected to degrade the accuracy of auto-titration, such as any of the following:
  - congestive heart failure NYHA Class III or IV (LVEF ≤ 45%)
  - moderate to severe pulmonary disease, such as chronic obstructive pulmonary disease (COPD), documented on pulmonary function studies (PFTs)
  - prior diagnosis of central sleep apnea
  - pulmonary hypertension
  - no evidence of nocturnal oxygen desaturation* caused by a condition other than OSA (e.g. obesity hypoventilation syndrome [defined as pCO_2 > 45 mmHg and pO_2 < 60 mmHg on arterial blood gas])

Follow-up home titration using APAP is considered medically necessary when ALL of the following criteria are met:

- no comorbid condition that would be expected to degrade the accuracy of auto-titration
- no evidence of nocturnal oxygen desaturation* caused by a condition other than OSA (as described below)
- procedure to be performed for ANY of the following:
  - to determine whether pressure adjustment is needed when clinical response is insufficient or symptoms return despite a good initial response to PAP
  - substantial weight loss (e.g., 10% of body weight) to determine if adjustment of PAP pressure is indicated
  - substantial weight gain (e.g., 10% of body weight) with return of symptoms despite continued use of CPAP, to determine if adjustment of PAP pressure is indicated

* Significant oxygen desaturation:
- individual does not have evidence of significant oxygen desaturation defined as oxygen saturation < 80% for > 1% of sleep time or < 90% for > 30% of sleep time during prior diagnostic facility-based study or recording time during prior home sleep apnea test (HSAT)

Bi-level positive airway pressure (BPAP) without a back-up respiratory rate (HCPCS code E0470), with or without a humidifier (HCPCS codes E0561, E0562) for an initial 90 day period is considered medically necessary for the treatment of OSA for an individual with coexisting central hypoventilation or for an individual who requires, but proves intolerant to, high pressures of CPAP or APAP.

BPAP with a back-up respiratory rate (HCPCS codes E0471, E0472) for an initial 90 day period is considered medically necessary for the treatment of treatment-emergent central sleep apnea when ALL of the following criteria are met:

- diagnostic PSG shows five or more predominantly obstructive respiratory events (obstructive or mixed apneas, hypopneas or respiratory effort related arousals [RERAs]) per hour of sleep
- PSG during use of positive airway pressure without a backup rate shows significant resolution of obstructive events and emergence or persistence of central apnea or central hypopnea with all of the following:
  - central apneas and central hypopneas ≥ 5/hour
  - number of central apneas and central hypopneas >50% of total number of apneas and hypopneas.
- the central sleep apnea (CSA) is not better explained by another CSA disorder (e.g., CSA with Cheyne Stokes breathing or CSA due to a medication or substance)

A home trial of Auto Bi-level therapy (HCPCS code E0470) is considered medically necessary in an individual who is documented to have tried and failed CPAP or APAP.

Adaptive servo-ventilation (ASV) (HCPCS codes E0471, E0472) for an initial 90 day period is considered medically necessary for the treatment of treatment-emergent central sleep apnea when ALL of the following criteria are met:

- individual does not have symptomatic chronic heart failure (i.e., NYHA Class II-IV) and reduced left ventricular ejection fraction ≤ 45% and moderate to severe predominant central sleep apnea, as determined by cardiac assessment conducted prior to initiation of treatment
- diagnostic PSG shows five or more predominantly obstructive respiratory events (obstructive or mixed apneas, hypopneas or respiratory effort related arousals [RERAs]) per hour of sleep
- PSG during use of positive airway pressure without a backup rate shows significant resolution of obstructive events and emergence or persistence of central apnea or central hypopnea with all of the following:
  - central apneas and central hypopneas ≥ 5/hour
  - the number of central apneas and central hypopnea is >50% of total number of apneas and hypopneas.
- central sleep apnea (CSA) is not better explained by another CSA disorder (e.g., CSA with Cheyne Stokes breathing or CSA due to a medication or substance).

PAP Adherence

Continued Coverage Beyond the First Three Months (90 days) of Therapy

A medically necessary PAP device (E0470/E0471 or E0601) beyond the first three months of therapy when, no sooner than the 31st day but no later than the 91st day after initiating therapy, there is objective evidence documenting the member is adhering to PAP therapy.

Note: Objective evidence of adherence to PAP therapy, is defined as use of PAP ≥ 4 hours per 24 hour period for 70% of use during a consecutive 30 day period anytime during the first three months of initial usage.

If the above criterion is not met, continued coverage of a PAP device and related accessories will be considered not medically necessary.

CPAP, APAP, or BPAP loaner rental for up to 30 days is considered medically necessary when BOTH of the following criteria are met:

- demonstrated compliant use of the device
- description of malfunction and documentation that equipment has been sent for repair/assessment

PAP treatment (i.e., CPAP, APAP, BPAP) for any other indication is considered experimental, investigational or unproven.

Oral pressure therapy (e.g., Winx® Sleep Therapy System) is considered experimental, investigational or unproven.

ANY ONE of the following interfaces for use with CPAP, APAP, or BPAP is considered medically necessary:

- nasal mask (HCPCS code A7027)
- nasal pillows/prongs (HCPCS code A7034)
- full face mask (HCPCS code A7030)
- Oracle™ Oral Mask (Fisher & Paykel Healthcare, Irvine, CA) (HCPCS code A7044)

A replacement of any of the above interfaces for use with CPAP, APAP, or BPAP is considered medically necessary at a frequency of no more often than every three months.

An interface consisting of a boil and bite mouthpiece connected to nasal inserts (e.g., CPAP PRO® [Stevenson Industries, Inc., Simi Valley, CA]) is considered experimental, investigational or unproven.

In general, duplicate equipment (e.g., travel PAP) is considered a convenience item and not medically necessary. Replacement of a medically necessary PAP device is considered medically necessary only when reasonable wear and tear renders the item nonfunctioning and not repairable and the item is no longer under warranty.

Oral Appliance Therapy

Coverage for oral appliances varies across plans. Refer to the customer's benefit plan document for coverage details.

If coverage for oral appliances is available, the following conditions of coverage apply.

A tongue-retaining device or a mandibular repositioning appliance (HCPCS codes E0485, E0486), also referred to as mandibular advancement appliance or mandibular advancement splint, is considered medically necessary for an individual with mild or moderate OSA when EITHER of the following criteria is met:

- AHI or RDI or REI ≥ 15 and < 30, as documented by polysomnography (PSG) or home sleep apnea test (HSAT)
- AHI or RDI or REI ≥ 5 and < 15 as documented by PSG or HSAT, when accompanied by symptoms of OSA (e.g., excessive daytime sleepiness, impaired cognition, mood disorders or insomnia) or when individual has hypertension, ischemic heart disease or history of stroke

A tongue-retaining device or a mandibular repositioning appliance (HCPCS codes E0485, E0486) is considered medically necessary for an individual with severe OSA (i.e., AHI or RDI or REI ≥ 30) who is unwilling or unable to comply with PAP treatment.

Follow-up sleep testing to improve or confirm oral appliance treatment efficacy and follow-up with their qualified healthcare professional to survey for dental-related side effects or occlusal changes and reduce their incidence is considered medically necessary.

Remote-controlled titration of an oral appliance (e.g., the MATRx oral appliance titration study [CPT code 95999]) to determine appropriateness of oral appliance therapy and/or parameters for fabrication of an oral appliance for OSA is considered experimental, investigational or unproven.

Replacement of a medically necessary oral appliance when the item has reached the end of its five year reasonable use lifetime, or when wear and tear renders the item nonfunctioning and not repairable and the item is no longer under warranty is considered medically necessary.

Over-the-counter (OTC) oral appliances that can be obtained without a prescription are excluded under many benefit plans and therefore are generally not covered. In addition, OTC oral appliances are considered not medically necessary.

SURGICAL TREATMENT

Tonsillectomy and/or adenoidectomy is considered medically necessary for the treatment of OSA as diagnosed by polysomnography (PSG) or HSAT.

Uvulopalatopharyngoplasty (UPPP) is considered medically necessary for the treatment of OSA when ALL of the following criteria are met:

- demonstrated narrowing or collapse of the retropalatal region (soft palate, uvula, tonsils, posterior pharyngeal wall) as a source of airway obstruction
- criteria for PAP met and individual has proved intolerant to or failed a trial of PAP
- for mild or moderate OSA in an adult, consideration has also been given to use of mandibular repositioning appliance (MRA) or tongue-retaining appliance

Uvulectomy as a stand-alone procedure for the treatment of OSA is considered experimental, investigational or unproven. (Note: this Coverage Policy is not intended to address uvulectomy performed for other indications (e.g., acute inflammation/angioedema of the uvula).

Multi-level or stepwise surgery (MLS) (e.g., UPPP and/or genioglossus advancement and hyoid myotomy (GAHM), maxillary and mandibular advancement osteotomy [MMO]) as a combined procedure or as stepwise multiple procedures is considered medically necessary for the treatment of OSA when ALL of the following criteria are met:

- narrowing of multiple sites in the upper airway
- criteria for PAP met and individual has proved intolerant to or failed a trial of PAP
- in an adult, a mandibular repositioning appliance (MRA) or tongue-retaining appliance has been considered and found to be ineffective or undesirable

Maxillo-mandibular advancement is considered medically necessary for the treatment of severe OSA when ALL of the following criteria are met:

- criteria for PAP met and individual has proved intolerant to or failed a trial of PAP
- in an adult, a mandibular repositioning appliance (MRA) or tongue-retaining appliance has been considered and found to be ineffective or undesirable
- individual has craniofacial disproportion or deformities

Tracheostomy is considered medically necessary for the treatment of OSA when other medical and surgical options do not exist, have failed or are refused, or when deemed necessary by clinical urgency.

ADDITIONAL PROCEDURES/SERVICES

The following procedures or services for the treatment of OSA are considered experimental, investigational or unproven:

- atrial overdrive pacing
- cautery-assisted palatal stiffening operation (CAPSO)
- electrical devices (e.g., Night Shift™ Sleep Positioner) as therapy for positional obstructive sleep apnea
- electrosleep therapy
- implanted upper airway hypoglossal nerve stimulation devices (e.g., Inspire® II Upper Airway Stimulation)
- injection Snoreplasty
- laser-assisted uvulopalatoplasty (LAUP)
- Pillar™ Palatal Implant System
- Provent™ Professional Sleep Apnea Therapy Device
- radiofrequency volumetric tissue reduction (RFVTR) of the soft palate, uvula, or tongue base (e.g., Coblation®, Somnoplasty®)
- tongue-base suspension (e.g., AIRVance System)
- tongue implant (e.g., ReVent System)
- transpalatal advancement pharyngoplasty

The treatment of snoring alone by any method is considered not medically necessary.

Overview

This Coverage Policy addresses treatments for obstructive sleep apnea (OSA).

General Background

Treatment of Obstructive Sleep Apnea (OSA)
Patients diagnosed with OSA receive education regarding the pathophysiology of OSA and the impact of lifestyle modifications, including weight loss, reduced alcohol consumption, especially at bedtime, and lateral sleeping position (vs. supine). While such noninvasive measures are encouraged, particularly in the obese or those with very poor sleep hygiene, OSA does not usually resolve with these measures alone. Potential treatment options for OSA include treatment with positive airway pressure (PAP), the use of oral appliances, and surgical interventions. Treatment decisions are based on condition severity, the presence of comorbidities and complicating factors, and the patient's tolerance and response to treatment.

Non-Surgical Treatment

Agency for Healthcare Research and Quality (AHRQ)
The 2011 AHRQ Comparative Effectiveness Review, Diagnosis and Treatment of Obstructive Sleep Apnea in Adults (discussed in the diagnosis section above) included the following key questions and conclusions regarding treatment with PAP and mandibular advancement devices (MAD):

Key Question: What is the comparative effect of different treatments for obstructive sleep apnea in adults?

- Despite no evidence or weak evidence on clinical outcomes, given the large magnitude of effect on the important intermediate outcomes AHI, ESS and other sleep study measures, the strength of evidence is moderate that CPAP is an effective treatment for OSA. However, the strength of evidence is insufficient to determine which patients might benefit most from treatment.
- Despite no or weak evidence on clinical outcomes, overall there is moderate strength of evidence that auto CPAP and fixed CPAP result in similar compliance and treatment effects for patients with OSA.

- The strength of evidence is low of no substantial difference in compliance or other outcomes between C-Flex and CPAP.
- The strength of evidence is insufficient regarding comparisons of different CPAP devices or modifications
- Despite no evidence or weak evidence on clinical outcomes, given the large magnitude of effect on the important intermediate outcomes AHI, ESS and other sleep study measures, overall the strength of evidence is moderate that MAD is an effective treatment for OSA in patients without comorbidities (including periodontal disease) or excessive sleepiness. However, the strength of evidence is insufficient to address which patients might benefit most from treatment.
- The strength of evidence is insufficient regarding comparisons of different oral devices.
- Despite no evidence or weak evidence on clinical outcomes, overall the strength of evidence is moderate that the use of CPAP is superior to MAD. However, the strength of evidence is insufficient to address which patients might benefit most from either treatment.

Positive Airway Pressure (PAP) Treatment
PAP is the most effective and widespread treatment of OSA. A flow generator delivers pressurized air into the nose and/or mouth, providing a pneumatic splint to the airway, preventing development of subatmospheric collapsing pressure. The flow generator is connected to the patient via connecting tubing and an interface attached to the patient's face. PAP may be provided using continuous positive airway pressure (CPAP), auto-titrating PAP (APAP), or bi-level positive airway pressure (BPAP).

For information on the usual maximum amount of PAP accessories see Appendix A (CGS Administrators, 2017).

Continuous Positive Airway Pressure (CPAP): CPAP is the most commonly used method of positive airway pressure. It is the simplest and most extensively studied mode of PAP, with the greatest amount of clinical experience. During CPAP titration, the minimum amount of positive pressure required eliminating or nearly eliminating respiratory events in REM and NREM sleep, including REM sleep with the patient in the supine position, is determined. Traditional CPAP maintains this effective fixed pressure at all times.

Treatment-emergent central sleep apnea (CSA), also referred to as complex sleep apnea, is the emergence or increase in central apneas and hypopneas when treatment with CPAP or bilevel PAP without a backup rate feature is initiated. It is usually an incidental finding during the initial in-facility titration. The increase in central apneas and hypopneas prevents the apnea hypopnea index (AHI) from normalizing although obstructive apneas and hypopneas have been eliminated. The AHI is often higher during NREM than REM sleep. The prevalence of treatment-emergent CSA is not known, but one large prospective study reported an incidence of 12% during the first night with CPAP. The incidence is reported to be higher in split-night vs. full night PSG. Some patients develop treatment-emergent CSA during CPAP use even when it was not present initially. It is not clear whether treatment-emergent CSA and OSA are separate disorders. The fact that they respond differently to PAP therapy suggests that they result from separate pathophysiologic mechanisms. However, the presence of many potential mechanisms in which OSA treatment may induce central apneas suggests that they may not be separate disorders; the central apneas may merely be an effect of treating the OSA (Parthasarathy, 2017; AASM ICD 3rd ed., 2014; Kuzniar and Morgenthaler, 2012).

The natural history of treatment-emergent CSA is not well-defined. Observational studies have reported spontaneous resolution in 50-75% of patients, but these estimates cannot be relied upon due to the retrospective nature of most studies and significant number of patients lost to follow-up, which could overestimate the true rate of spontaneous improvement. Patients who continue the PAP treatment used when treatment-emergent CSA was detected may remain asymptomatic or they manifest symptoms and signs of disrupted sleep (e.g., excessive daytime sleepiness, poor subjective sleep quality, repetitive awakenings, and insomnia) due to the central apneas and related arousals. Symptoms related to recurrent oxyhemoglobin desaturation, including morning headaches and nocturnal angina, may also be reported. Optimal management of treatment-emergent CSA has not yet been defined. Continuation of CPAP, with follow-up sleep testing in two to three months to determine whether the condition has resolved spontaneously is one treatment option. Because the risks of even short-term central apneas and hypopneas are uncertain and haven't been well studied, however, changing the mode of pressure to either or bilevel positive airway pressure with a backup respiratory rate or adaptive servo-ventilation (ASV) has also been recommended. BPAP without a backup respiratory rate, however, does not

decrease the AHI in patients with treatment-emergent OSA, and may actually worsen the AHI (Parthasarathy, 2017).

AASM practice parameters for the use of continuous and bilevel positive airway pressure devices states that CPAP is indicated for the treatment of moderate to severe OSA, based on the fact that randomized controlled trials testing whether CPAP significantly reduces sleep related respiratory events compared to a controlled procedure had positive outcomes. The guideline also states that CPAP is recommended as an option for the treatment of mild OSA (Kushida, et al., 2006).

Currently available CPAP devices are FDA approved for home use for children who weigh more than 30 kilograms (66 pounds). Limited data is available on CPAP compliance in children. A small prospective study by Marcus et al. (2006) randomly assigned 29 children, ages two to 16, to six months of CPAP vs. BPAP. One third of the children dropped out before six months. Of the remaining 21 children for whom adherence data could be downloaded, the mean nightly use was 5.3 ± 2.5 hours. Parental assessment of adherence was considerably higher than actual use. PAP was highly effective, with a reduction of the AHI from 27 ± 32/hour to 3 ± 5/hour. Results were similar for children who received CPAP vs. BPAP. The authors concluded that PAP is effective in children with OSA, but adherence is an important issue. The authors suggested that additional research be conducted to develop methods to improve adherence and to develop other treatment alternatives for children who do not respond to tonsillectomy and adenoidectomy and are unable to tolerate CPAP.

Autotitrating Positive Airway Pressure (APAP): The pressure required to maintain airway patency changes during a night of sleep depending on body position, sleep stage, nasal obstruction, and ingestion of alcohol or hypnotic agents. Pressure requirements also change over time based on changes in body weight and upper airway properties. APAP devices deliver variable pressure according to the needs of the patient. When an obstructive event is detected, an APAP device will increase pressure until the event is eliminated. If no further events are detected during a set time period, the device will decrease pressure to a pre-set minimum. APAP devices may use combinations of physiologic signals to detect airflow obstruction, including snoring, flow, or impedance. Because the minimum pressure required to keep the airway open is used, the mean pressure applied throughout the night is reduced. This reduction in mean pressure may improve tolerance in some patients, resulting in improved adherence with the use of PAP (Ayas, et al., 2004; Nussbaumer, et al., 2006).

AASM practice parameters for the use of auto-titrating CPAP devices for titrating pressures and treating adult patients with OSA include the following recommendations (Morgenthaler, et al., 2007). Recommendations are classified as follows: Standard: a generally accepted patient care strategy that reflects a high degree of clinical certainty; Guideline: a patient care strategy that reflects a moderate degree of clinical certainty, and Option: a patient care strategy that reflects uncertain clinical use.

- APAP is not recommended to diagnose OSA (Standard)
- Patients with the following conditions are not currently candidates for APAP titration or treatment: (Standard)
  - Congestive heart failure
  - Lung disease, such as chronic obstructive pulmonary disease
  - Patients expected to have nocturnal arterial oxyhemoglobin desaturation due to conditions other than OSA (e.g., obesity, hypoventilation syndrome)
  - Patients who do not snore, either due to palate surgery or naturally
- APAP devices are not currently recommended for split-night titration (Standard)
- Certain APAP devices may be used during attended titration with PSG to identify a single pressure for use with standard CPAP for treatment of moderate to severe OSA. (Guideline)
- Certain APAP devices may be used in an unattended way to determine a fixed CPAP pressure for patients with moderate to severe OSA without significant comorbidities (CHF, COPD, central sleep apnea syndrome, or hypoventilation syndromes) (Option)
- Patients being treated with fixed CPAP on the basis of APAP titration or being treated with APAP must have close clinical follow-up to determine treatment effectiveness and safety. This is especially important during the first few weeks of PAP use. (Standard)

- A re-evaluation and, if necessary, a standard attended CPAP titration should be performed if symptoms do not resolve or the CPAP or if the APAP treatment otherwise appears to lack efficacy. (Standard)

Auto Bi-Level: Auto Bi-Level delivers a combination of Bi-Level technology and auto-CPAP. Instead of having one fixed inspiratory pressure and one fixed expiratory pressure, these two pressure settings auto adjust based on therapy need. A pressure support number is established to instruct the machine the differences in pressure between the inspiratory pressure and expiratory pressure. This pressure setting is typically between 3cm/H2O and 6cm/H2O. Much like auto CPAP machines, the Auto Bi-Level device can operate in two modes which are the standard Bi-Level mode or auto adjust mode. Individuals who require Auto Bi-Level therapy have the same determining factors as the standard Bi-Level candidates. Home Auto Bi-Level therapy is an alternative in an individual who has tried and failed CPAP and/or APAP therapy.

BPAP and Adaptive Servo-ventilation: BPAP delivers a higher fixed level of pressure during inspiration and a lower fixed pressure during expiration, unlike CPAP which delivers a level of positive airway pressure that remains constant during the respiratory cycle. BPAP is not considered a first-line treatment for OSA, but for those who require high levels of PAP, the lower pressure administered during expiration with BPAP can make treatment easier to tolerate. With most BPAP devices, it is possible to set a backup respiratory rate, which consists of the number of breaths initiated by the device per minute. When no backup rate is set, the device is said to be in spontaneous mode. BPAP with a backup respiratory rate is a treatment option for treatment-emergent central sleep apnea.

Adaptive servo-ventilation (ASV) provides a varying amount of inspiratory pressure superimposed on a low level of CPAP, with a backup respiratory rate. The degree of inspiratory pressure delivered is reciprocal to changes in peak flow, determined over a three to four minute window. ASV devices were introduced on the 1990s to treat central sleep apnea (CSA) syndromes, and have been used for patients with treatment-emergent CSA.

In 2016 the AASM published updated adaptive servo-ventilation (ASV) recommendations for the 2012 AASM Guideline: "The Treatment of Central Sleep Apnea Syndromes in Adults: Practice Parameters with an Evidence-Based Literature Review and Meta-Analyses". The AASM recommends a standard level against ASV targeted to normalize the apnea-hypopnea index (AHI) for the treatment of central sleep apnea syndromes related to congestive heart failure in adults with an ejection fraction ≤ 45% and moderate or severe central sleep apnea predominant, sleep-disordered breathing (Aurora, et al., 2016). ResMed identified a significant increase in the risk of cardiovascular death in patients with symptomatic, chronic heart failure (NYHA II–IV) with reduced ejection fraction (LVEF ≤ 45%) and moderate to severe predominant central sleep apnea (ResMed website, 2018).

The SERVE-HF study is a multinational, multicenter randomized parallel trial designed to assess the effects of addition of ASV to optimal medical management compared with medical management alone in patients with symptomatic chronic heart failure, left ventricular ejection fraction (LVEF) ≤ 45%, and predominant central sleep apnea (n=1325). The study began in 2008, with an estimated completion date of May 2015. On May 13, 2015, ResMed issued a press release and Urgent Field Safety Notice based on preliminary results of the trial. Although there were no significant differences between the two groups in the primary endpoint of all-cause mortality or unplanned hospitalization for worsening heart failure, there was a significant 2.5% absolute increased annual risk of cardiovascular mortality for those randomized to ASV therapy compared to those in the control group. Ten percent of those in the ASV group experiences a cardiovascular death each year compared to 7.5% of those in the control group; a 33.5% relative increased risk of cardiovascular mortality (p=0.010) (Cowie, et al., 2013, ResMed website, 2018).

According to the ResMed website, manuals for their ASV products are being updated to state that use of ASV is contraindicated in patients with symptomatic chronic heart failure with reduced ejection fraction (LVEF ≤ 45%). Although only ResMed ASV devices were used in the SERVE-HF study, Philips Respironics is actively evaluating the information provided by ResMed and until that investigation is complete, are strongly recommending that clinicians adhere to the recommendations published by ResMed (FDA website).

Adaptive servo-ventilation (ASV) is therefore considered to be contraindicated for an individual with predominantly central sleep apnea who has symptomatic chronic heart failure and reduced left ventricular

ejection fraction ≤ 45%. BPAP with a back-up rate, however, may be considered as a therapeutic option for such patients.

Note: This Coverage Policy is not intended to address the use of BPAP or adaptive servoventilation in the treatment of respiratory conditions other than OSA or treatment-emergent CSA (e.g. obesity hypoventilation syndrome, respiratory failure, chronic obstructive pulmonary disease, neuromuscular chest wall disease).

ResMed identified a significant increase in the risk of cardiovascular death in patients with symptomatic, chronic heart failure (NYHA II–IV) with reduced ejection fraction (LVEF ≤ 45%) enthaler et al. (2014) conducted a small randomized controlled trial to compare clinical and PSG outcomes over prolonged treatment of patients with complex sleep apnea syndrome with CPAP (n=33) vs. ASV (n=33). The device used was the ResMed VPAP Adapt SV flow generator, and devices were set in the ASV mode or CPAP mode, depending on the allocation arm. At baseline, the diagnostic AHI was 37.7 ± 27.8 (central apnea index [CAI] 3.2 ± 5.8) and best CPAP AHI was 37.0 ± 24.9 (CAI 29.7 ± 25.0). After second night treatment titration, the AHI was 4.7 ± 8.1 (CAI 1.1 ± 3.7) on ASV and 14.1 ± 20.7(CAI 8.8 ±16.3) on CPAP (p<0.0003). At 90 days the ASV vs. CPAP AHI was 4.4 ± 9.6 vs. 9.9 ±11.1 (p=0.0024) and CAI was 0.7 ± 3.4 vs. 4.8 ± 6.4 (p<0.0001), respectively. In the intention to treat analysis, success (i.e., AHI <10) at 90 days was achieved in 89.7% of patients in the ASV group compared to 64.5% of those in the CPAP group (p=0.0214). There were no significant differences in changes in compliance, Epworth Sleepiness Scale, or Sleep Apnea Quality of life index.

Dellweg et al. (2013) conducted a small randomized controlled trial to compare treatment with noninvasive positive pressure ventilation using bilevel positive airway pressure (BPAP) with a backup rate (n=19) vs. servoventilation (n=18) for the treatment of CPAP-induced central sleep apnea. Inclusion criteria consisted of AHI ≥ 15 during initial PSG with a predominance of obstructive events, or AHI ≥ 15 on CPAP therapy after six weeks of CPAP treatment during a follow-up PSG, with a predominance of central events. During initial titration, BPAP with a backup rate and servoventilation significantly improved the AHI (9.1 ± 4.3 vs. 9 ± 6.4 events/hour), apnea indices (2 ± 3.1 versus 3.5 ± 4.5 events/hour) central apnea index (2 ± 3.1 vs. 2.5 ± 3.9 events/hour) and oxygen desaturation indices (10.1 ± 4.5 vs. 8.9 ± 8.4 events/hour) when compared to CPAP treatment (all p < 0.05). After 6 weeks the following differences were observed: between BPAP with a backup rate and servoventilation, respectively: AHI (16.5 ± 8 versus 7.4 ± 4.2 events/hour, ,p = 0.027), apnea indices (10.4 ± 5.9 versus 1.7 ± 1.9 events/hour, p = 0.001), central apnea index (10.2 ± 5.1 vs. 1.5 ± 1.7 events/hour, p < 0.0001)) and oxygen desaturation indices (21.1 ± 9.2 versus 4.8 ± 3.4 events/hour, p < 0.0001). Sleep was not affected by either intervention. The authors stated that changes in carbon dioxide homeostasis inducted by BPAP with a backup rate but not by servoventilation might have accounted for the different results at six weeks.

Allam et al. (2007) conducted a retrospective review to evaluate the application and effectiveness of ASV in the treatment of complex and central sleep apnea (CSA) syndromes. The analysis was performed by a chart review of 100 consecutive patients who underwent PSG using ASV at the Mayo Clinic Sleep Center. ASV titration was performed for treatment emergent CSA (63%), CSA (22%) or CSA/Cheyne Stokes breathing patterns (15%). The median diagnostic AHI was 48 events per hour (range 24-62). With CPAP, obstructive apneas decreased, but the appearance of central apneas maintained the AHI at 31 events/hour (range 17-47; p=0.02). With BPAP in spontaneous mode, AHI trended toward worsening vs. baseline, with a median 75 event/hour (range 46-111; p=0.055). BPAP with a backup rate improved the AHI to 15 events per hour (range 11-31; p=0.002). Use of ASV dramatically improved the AHI to a mean of 5 events per hour (range 1-11) vs. baseline and vs. CPAP (p<0.0001). ASV also resulted in increased REM sleep (18%) vs. baseline (12%) and vs. CPAP (10%).

AASM practice parameters on the use of CPAP and BPAP (Kushida, et al. 2006) state that BPAP is an optional therapy in some cases where high pressure is needed and the patient experiences difficulty exhaling against a fixed pressure. BPAP may also be indicated when coexisting central hypoventilation is present. These practice parameters were published prior to publication of the AASM International Classification of Sleep Disorders (ICSD) 3rd edition, and do not specifically address treatment-emergent central sleep apnea. AASM practice parameters for the treatment of central sleep apnea (Aurora et al., 2011) were also published prior to publication of ICSD 3rd edition and therefore do not include recommendations for treatment-emergent CSA.

There is lack of high quality evidence to determine the appropriate mode of PAP for patients with treatment-emergent CSA. CSA resolves spontaneously in a significant percentage of patients who continue to be treated

with CPAP. It is not possible to identify any PSG or patient characteristics, however, that would predict resolution of treatment-emergent CSA. The condition may persist on CPAP, despite improvement in daytime sleepiness; Patients with treatment-emergent CSA treated with CPAP who remain symptomatic are likely to be less compliant than those whose treatment-emergent CSA resolves. Therefore, initial treatment with BPAP with a back-up respiratory rate or adaptive servoventilation rather than CPAP is reasonable as the initial mode of PAP therapy for patients with treatment-emergent CSA (Morgenthaler, 2014; Kuzniar, 2012).

C-Flex: C-Flex (Respironics, Inc., Murrysville, PA) received FDA 510(k) approval on Oct 10, 1999. C-Flex is a feature available on CPAP, APAP, and BPAP devices manufactured by Respironics. The C-Flex feature lowers the initial expiratory pressure in proportion to the patient's expiratory flow rate. The pressure is then increased to therapeutic levels near the end of exhalation when airway collapse is most likely. It has been proposed that C-Flex could result in increased comfort and may improve treatment adherence. C-Flex is a standard feature on PAP devices.

Oral Pressure Therapy
Oral pressure therapy has also been proposed for the treatment of OSA. The Winx® Sleep Therapy System (ApriCure, Inc., Redwood City CA) received FDA approval through the 510(k) process on May 22, 2013. An earlier version of the device was approved in 2012. The Winx Sleep Therapy System consists of a small electronic bedside console, a soft polymer mouthpiece, a flexible polymer tube that connects the mouthpiece to the console, and a physician's software application. The mouthpiece is an intraoral device that is worn during sleep. The system is designed to increase airway patency and decrease airway obstruction by delivering a gentle negative pressure into the oral cavity and holding the tongue and soft palate out of the airway. Published evidence evaluating the use of this device is limited to feasibility studies and a small case series (Colrain, et al., 2013). There is insufficient evidence to determine the safety and efficacy of this system for the treatment of OSA.

PAP Interfaces: PAP is most commonly applied using a nasal mask, or alternately, nasal pillows or prongs. An Oracle™ Oral Mask (Fisher & Paykel Healthcare, Irvine, CA) may be used as an alternative to nasal interfaces. The Oracle interface delivers pressure through the mouth rather than the nose. The type of interface used is likely to influence acceptance and adherence to PAP therapy; compliance is affected by the incidence of side effects, including claustrophobia, air leaks, pressure sores, nasal stuffiness, dry mouth and mask discomfort (Chai, et al, 2006)

In a Cochrane review, Chai et al. (2006, updated 2014) compared the efficacy of various CPAP delivery interfaces available for the treatment of OSA (n=132). Two studies compared nasal masks with the Oracle Oral Mask and showed no significant difference in compliance at one month. There were no significant differences in any of the physiological parameters (e.g., apnea-hypopnea index, arousal index, and minimum oxygen saturation), Epworth Sleepiness Scale (ESS) or symptoms of OSA. One study comparing a nasal mask to nasal pillows showed a significant difference in compliance in favor of nasal pillows (p=0.02), fewer overall adverse effects (p<0.001), and greater interface satisfaction (p=0.001). A study comparing nasal mask with face mask showed significantly greater compliance and lower ESS scores with use of a nasal mask. The nasal mask was the preferred interface in almost all patients. The authors concluded that due to the limited number of studies comparing various interface types, the optimum form of delivery interface remains unclear. Nasal pillows or the Oracle oral mask may be useful alternatives when a patient is unable to tolerate conventional nasal masks. A full-face mask, while not a first-line interface, may be used if nasal obstruction or dryness limits the use of a nasal interface.

CPAP PRO® (Stevenson Industries, Inc., Simi Valley, CA) has been proposed as an interface alternative without straps or headgear. CPAP PRO consists of a boil and bite dental appliance that is snapped in place on the upper teeth, with a small bracket extending beyond the lips to attach to a pair of nasal tubes. The paired nasal tubes combine to form a "Y"; the lower arm is attached to a CPAP machine, and the upper arms terminate in soft silicone nasal inserts. There are no published studies of CPAP PRO in the medical literature. It is not possible to determine how this device compares to standard and broadly used CPAP interfaces.

Home PAP Titration

As discussed in the PSG section above, PAP pressures may be titrated during the second portion of a split-night PSG when a diagnosis of OSA has been established during the initial diagnostic portion of the exam, or during a full-night PSG that follows a diagnostic PSG in which the diagnosis of OSA is established. In-facility PSG, rather than home/portable testing, is indicated only for patients who are not suitable candidates for home testing due to medical comorbidities, or when sleep disorders other than OSA are suspected. When a diagnosis of OSA is established following a home/portable study, home titration to determine a fixed CPAP pressure can be effectively completed using auto-titrating positive airway pressure. Evidence from several well-designed trials demonstrates that home PAP titration using APAP compared to in-facility titration results in similar outcomes in terms of improvement in AHI, Epworth Sleepiness scores, and CPAP acceptance and adherence (Gao, et al., 2012, Mulgrew, et al., 2007; Cross, et al., 2006).

The AASM practice parameters on the use of APAP for titrating pressures, discussed above (Morgenthaler, et al., 2007), state:

- Certain APAP devices may be used in an unattended way to determine a fixed CPAP pressure for patients with moderate to severe OSA without significant comorbidities (CHF, COPD, central sleep apnea syndrome, or hypoventilation syndromes). (Option).

The writing committee noted that the evidence was specific to each device, including the particular version of software and device version, and the pressure determination should be made by experienced sleep specialists after examining the raw pressure titration data for each patient. For these reasons, the authors did not find that the available evidence supported a guideline recommendation. The use of APAP for titrating pressures was considered an option, meaning that this is a patient care strategy that reflects uncertain clinical use and implies inconclusive or conflicting evidence, or conflicting expert opinion.

Although PSG-directed titration remains the standard method for determination of effective CPAP pressure, unattended titration using an APAP device may be a reasonable option for patients diagnosed with moderate or severe OSA without significant comorbidities.

Adherence to PAP Therapy
The ability of PAP to reverse the repetitive upper airway obstruction of sleep apnea is dramatic. PAP has been demonstrated to normalize sleep architecture, reduce daytime sleepiness, enhance daily functioning, elevate mood, reduce auto accidents, and decrease blood pressure and cardiovascular events. Despite the efficacy of CPAP, studies evaluating adherence report high rates of non-adherence. Adherence to PAP therapy is usually defined as ≥ four hours of CPAP usage for ≥ 70% of the nights monitored, based on a 1993 prospective study by Kribbs et al., evaluating patterns of CPAP use. Patient reports of the frequency and duration of CPAP use frequently overestimate actual use. The average duration of CPAP use is approximately five hours per night, as reported in numerous studies. The available evidence indicates that CPAP used for more than six hours per night results in normal levels of objectively measured and subjectively reported daytime sleepiness, and improved daily functioning (Kribbs, et al., 1993; Gay, et al., 2006; Weaver and Grundstein, 2008). CPAP adherence is measured objectively using downloaded information from an electronic chip or through a modem which transmits information.

As stated above, adherence to PAP therapy is usually defined as ≥ four hours of CPAP usage for ≥ 70% of the nights monitored. Patients with borderline adherence to PAP therapy (e.g., 55%-69% of nights for at least three hours but less than four hours per night, may require intervention to evaluate barriers to treatment. According to the AASM Clinical Guideline, Evaluation, Management, and Long-Term Care of Obstructive Sleep Apnea in Adults (Epstein, et al., 2009) CPAP usage should be objectively monitored with time meters to help assure utilization. The guidelines also recommend close follow-up for PAPA usage and problems by appropriately trained health care providers to establish effective utilization patterns and remediate problems, if needed. This is especially important during the first few weeks of PAP use.

Oral Appliances
Various oral appliances have been developed for the treatment of OSA. Most of these devices are designed based on the principal that advancing the mandible and holding it forward during sleep improves upper airway patency and/or decreases upper airway collapsibility. The appliance is attached to the upper and lower dental

arches and allows for incremental advancement of the mandible. Studies using cephalometry have shown that these mandibular repositioning appliances (MRAs) lower the tongue position, reduce the mandibular plane-to-hypoid distance, advance the mandible and widen the upper oropharynx (retropalatal and retroglossal) in some patients. An MRA, also referred to as mandibular advancement appliances (MAA) mandibular advancement device (MAD) or mandibular advancement splint (MAS) may be custom-made based on dental impressions or may consist of a prefabricated appliance adapted to the patient's dimensions. Side effects reported with the use of MRAs include discomfort in the temporomandibular joint (TMJ), tooth and facial musculature discomfort, bite change, excessive salivation, and mouth dryness. Contraindications to MRA therapy include moderate to severe TMJ disorders, an inadequate protrusive ability, and lack of an adequate number of healthy teeth in the upper and lower dental arch. Significant bruxism may also be a contraindication, since damage to the appliance or increased pain may result. Patients with full dentures are generally unable to use an MRA but may be treated with a tongue-retaining appliance (TRA).

TRAs, also referred to as tongue-retaining devices (TRD), hold the tongue forward and affect genioglossus muscle activity in patients with OSA. The effect on other upper airway muscles has not been evaluated, however. TRAs may be custom-made or fitted by the patient. There are few studies on the use of TRAs, and these devices are generally only used in patients with contraindications to the use of an MRA**.**

A randomized controlled crossover trial was conducted by Phillips et al. (2013) to evaluate the health outcomes of optimal CPAP therapy compared to use of a mandibular advancement device (MAD). A total of 126 patients with moderate to severe OSA were randomly assigned to a treatment order and 108 completed the trial with both devices. The reduction in AHI was greater with CPAP than with MAD (CPAP AHI, 4.5 ± 6.6/hour; MAD AHI 11.1 ± 12.1/hour, $p < 0.01$), but compliance was higher with MAD (6.50 ± 1.3 hours/night vs. 5.20 ± 2 hours/night, $p<0.00001$). The 24-hour mean arterial pressure was not inferior on treatment with MAD compared to CPAP. Neither treatment improved blood pressure. Sleepiness, driving simulator performance, and disease-specific quality of life improved on both treatments by similar amounts, but MAD was superior to CPAP for improving four general quality of life domains. The authors stated that the similar results in terms of important health outcomes may be explained by greater efficacy of CPAP being offset by inferior compliance compared to MAD.

Titration of an Oral Appliance: Titration of adjustable mandibular advancement devices, during sleep studies, involves slowly adjusting (titrating) the mandibular advancement device to move the lower jaw, or mandible, forward slightly to enlarge the upper airway and thus prevent it from collapsing during sleep. Various methods have been proposed to predict treatment outcome with mandibular repositioning appliances for obstructive sleep apnea. Titration can be guided by a combination of both subjective symptomatic improvement and objective monitoring by overnight oximetry to find the optimally effective advancement level. A newly available remotely controlled mandibular titration device provides an objective mechanism by which to determine the maximal therapeutic level of mandibular protrusion during sleep. Optimizing mandibular advancement in individual patients is important for successful treatment, although no standardized titration procedure currently exists (Sutherland, et al., 2014).

Per the manufacturer website, (Zephyr Sleep Technologies; Calgary, Alberta Canada) MATRx is a remote-controlled, oral appliance titration study performed in the sleep lab. The MATRx study is proposed to identify the target protrusive position that will provide effective oral appliance therapy. MATRx is widely compatible with all types of PSG systems and has been installed in sleep labs across the US and Canada.

There is insufficient evidence in the published peer-reviewed literature to demonstrate the efficacy, long-term outcomes, impact on health outcomes and clinical utility of single-night oral appliance titration (e.g., the MATRx oral appliance titration study) to determine appropriateness of oral appliance therapy or parameters for fabrication of an oral appliance for the treatment of OSA.

A prospective, blinded outcome study (n=67) was performed by Remmers et al. (2013). Study objectives were to address the need for a validated tool that prospectively identifies favorable candidates for oral appliance therapy in treatment of obstructive sleep apnea. Therapeutic outcome with a mandibular protruding oral appliance was predicted following a mandibular protrusive titration study in the PSG laboratory. The mandibular protrusion titration study was performed using the MATRx device during a standard PSG study. All participants were blindly treated with a MRA, at either the predicted effective target protrusive position (ETPP) or a sham position, and

therapeutic outcome was compared against prediction. At the final protrusive position, standard predictive parameters (sensitivity, specificity, positive and negative predictive values) showed statistically significant predictive accuracy (p< 0.05) in the range of 83% to 94%. The predicted ETPP provided an efficacious protrusive position in 87% of participants predicted to be therapeutically successful with MRA therapy (p<0.05). No long term outcomes were reported in this study.

Kastoer, et al. 2016 conducted a systematic review to evaluate the efficacy of remotely controlled mandibular positioner (RCMP) as a predictive selection tool in the treatment of obstructive sleep apnea (OSA) with oral appliances that protrude the mandible (OAm), exclusively relying on single-night RCMP titration. A total of 254 OSA patients from four full-text articles and five conference meeting abstracts were included in the review. Criteria for successful RCMP test and success with OAm differed between studies. Study populations were not fully comparable due to range-difference in baseline apnea hypopnea index (AHI). In all the studies elimination of airway obstruction events during sleep by RCMP titration predicted OAm therapy success by the determination of the most effective target protrusive position (ETPP). A statistically significant association is found between mean AHI predicted outcome with RCMP and treatment outcome with OAm on polysomnographic or portable sleep monitoring evaluation (p < 0.05). The authors concluded that existing evidence regarding the use of RCMP in patients with OSA indicates that it might be possible to protrude the mandible progressively during sleep under poly(somno)graphic observation by RCMP until respiratory events are eliminated without disturbing sleep or arousing the patient. ETPP as measured by the use of RCMP was significantly associated with success of OAm therapy in the reported studies.

In a 2017 UptoDate document on oral appliances in the treatment of obstructive sleep apnea in adults, the author reported that single-night titration is a promising approach whose practical application has begun to enter clinical practice. Single-night titration studies may be useful as a method for predicting which individuals will have a successful treatment outcome with an oral appliance (Cistulli, 2017).

American Academy of Sleep Medicine (AASM): The 2015 Clinical Practice Guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy replaces the 2006 Practice Parameter on the use of oral appliances in the treatment of obstructive sleep apnea and snoring (Ramar, et al., 2015).

Recommendations are classified as Standard, Guideline, or Option, in descending order based on the benefits vs. harms and the quality of evidence. Recommendations are included in the relevant sections below.

Standard
- Sleep physicians prescribe oral appliances, rather than no therapy, for adult patients who request treatment of primary snoring (without obstructive sleep apnea).
- Sleep physicians consider prescription of oral appliances, rather than no treatment, for adult patients with obstructive sleep apnea who are intolerant of CPAP therapy or prefer alternate therapy.

Guideline
- When oral appliance therapy is prescribed by a sleep physician for an adult patient with obstructive sleep apnea, a qualified dentist use a custom, titratable appliance over non-custom oral devices.
- Qualified dentists provide oversight—rather than no follow-up—of oral appliance therapy in adult patients with obstructive sleep apnea, to survey for dental related side effects or occlusal changes and reduce their incidence.
- Sleep physicians conduct follow-up sleep testing to improve or confirm treatment efficacy, rather than conduct follow-up without sleep testing, for patients fitted with oral appliances.
- Physicians and qualified dentists instruct adult patients treated with oral appliances for obstructive sleep apnea to return for periodic office visits—as opposed to no follow-up—with a qualified dentist and a sleep physician.

Surgical Treatment
Patients with obstructive sleep apnea (OSA) who fail or cannot comply with conservative treatment may be candidates for surgical interventions. The surgical techniques used to treat OSA specifically modify either the retropalatal or retrolingual region of the pharyngeal airway, or, in the case of tracheotomy, bypass the pharyngeal portion of the upper airway. The goals of surgical intervention in the treatment of OSA include

resolution of clinical signs and symptoms of OSA and normalization of sleep quality, AHI, and oxyhemoglobin saturation levels.

Numerous upper airway procedures have been developed that may be used alone or in combination with other procedures to treat OSA. Palatal surgery procedures include uvulopalatopharyngoplasty (UPPP) and laser-assisted uvulopalatoplasty (LAUP). Additional palatal stiffening procedures introduced recently include cautery-assisted palatal stiffening operation (CAPSO) and radiofrequency energy (Coblation®, Somnoplasty®).

Palatal surgical procedures alone are not successful in achieving adequate reductions in AHI in most patients. The following procedures may be performed either alone or following palatal surgery when an unacceptable AHI persists: tracheotomy; inferior sagittal mandibular osteotomy (ISO) and genioglossal advancement with hyoid myotomy and suspension (GAHN); and maxillomandibular osteotomy and advancement (MMO). Several additional tongue-base procedures have been proposed for the treatment of OSA, including tongue base suspension with the AIRVance System (Influence Corp; San Francisco, CA), and base-of-tongue Somnoplasty.

American Academy of Sleep Medicine (AASM): Practice Parameters for the Surgical Modification of the Upper Airway for Obstructive Sleep Apnea in Adults (Aurora et al., 2010), based on a systematic review of the literature (Caples et al, 2010) updated earlier practice parameters published in 1996.

Recommendations are classified as Standard, Guideline, or Option, in descending order based on the benefits vs. harms and the quality of evidence. Recommendations for individual procedures are included in the relevant sections below.

Standard:
- The presence and severity of obstructive sleep apnea (OSA) must be determined before initiating surgical therapy
- The patient should be advised about potential surgical success rates and complications, the availability of alternative treatment options such as nasal positive airway pressure and oral appliances, and the levels of effectiveness and success rates of these alternative treatments.
- The desired outcomes of treatment include resolution of the clinical signs and symptoms of OSA and the normalization of sleep quality, the apnea-hypopnea index, and oxyhemoglobin saturation levels.

Option
- Maxillo-mandibular advancement (MMA) is indicated for surgical treatment of severe OSA in patients who cannot tolerate or who are unwilling to adhere to positive airway pressure therapy, or in whom oral appliances, which are more often appropriate in mild and moderate OSA patients, have been considered and found ineffective or undesirable.
- Uvulopalatopharyngoplasty (UPPP) as a sole procedure, with or without tonsillectomy, does not reliably normalize the apnea hypopnea index (AHI) when treating moderate to severe OSA syndrome. Therefore, patients with severe OSA should initially be offered positive airway pressure (PAP) therapy, while those with moderate OSA should initially be offered either PAP therapy or oral appliances.
- Use of multi-level or stepwise surgery (MLS), as a combined procedure or as stepwise multiple operations, is acceptable in patients with narrowing of multiple sites in the upper airway, particularly if they have failed UPPP as a sole treatment.
- Laser-assisted uvulopalatoplasty (LAUP) is not routinely recommended as a treatment for obstructive sleep apnea syndrome.
- Radiofrequency ablation (RFA) can be considered as a treatment in patients with mild to moderate OSA who cannot tolerate or who are unwilling to adhere to PAP therapy, or in whom oral appliances have been considered and found ineffective or undesirable.
- Palatal implants may be effective in some patients with mild OSA who cannot tolerate or who are unwilling to adhere to PAP therapy, or in whom oral appliances have been considered and found ineffective or undesirable.

An AHRQ comparative effectiveness review was conducted in 2011 to systematically review the evidence on OSA diagnosis and treatment in adults (discussed above in the diagnosis section). The review provided the following conclusions regarding surgical treatment of OSA:

Key Question: What is the comparative effect of different treatments for OSA in adults?

- The strength of evidence is insufficient to determine the relative merits of surgical treatments versus CPAP.
- The strength of evidence is insufficient regarding the relative merit of mandibular advancement devices versus surgery in the treatment of OSA.

American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS): No evidence-based practice guidelines were found by the AAO-HNS that address the treatment of OSA. The AAO-HNS has published several position statements related to OSA treatment options; however, these documents are based on an informal process of expert or committee consensus (AAO-HNS website).

American Academy of Pediatrics (AAP): The 2012 AAP Clinical Practice Guideline, Diagnosis and Management of Childhood Obstructive sleep Apnea Syndrome key action statement for adenotonsillectomy states that if a child is determined to have OSA, has a clinical examination consistent with adenotonsillar hypertrophy, and does not have a contraindication to surgery, the clinician should recommend adenotonsillectomy as the first line of treatment. If the child has OSA but does not have adenotonsillar hypertrophy, other treatment should be considered. Clinical judgment is required to determine the benefits of adenotonsillectomy compared with other treatments in obese children with varying degrees of adenotonsillar hypertrophy. (Evidence Quality: Grade B, Recommendation Strength: Recommendation) (Marcus, et al., 2012).

Cautery-Assisted Palatal Stiffening Operation (CAPSO): CAPSO is an office-based procedure in which a midline strip of soft palate mucosa is removed, and the wound is left to heal by secondary intention. The procedure has been proposed as a treatment for OSA based on the premise that the resulting midline palatal scar stiffens the palate and eliminates palatal snoring.

Wassmuth et al. (2000) conducted a case series (n=25) to evaluate the ability of CAPSO to treat OSA. PSG was performed preoperatively and at three months following the procedure on all patients. Patients with a reduction in the AHI of 50% or more and an AHI of 10 or less were classified as responders. Based on these criteria, 40% of patients were considered to have responded to CAPSO. Mean AHI improved from 25.1 ± 12.9 to 16.6 ± 15.0. The ESS improved from 12.7 ± 5.6 to 8.8 ± 4.6. The authors concluded that CAPSO is as effective as other palatal surgeries in the management of OSA.

Although this case series reported promising results, there is insufficient evidence in the published medical literature to demonstrate the safety, efficacy, and long-term outcomes of CAPSO in the treatment of OSA. Data from well-designed trials with adequate numbers of patients that compare this procedure with other treatments of OSA are lacking.

Laser-Assisted Uvulopalatoplasty (LAUP)/Uvulectomy: LAUP differs from UPPP in that much less palatal tissue is removed, the tonsils and pharyngeal pillars are not altered, and a carbon dioxide laser is used rather than a scalpel. Vertical transpalatal laser incisions measuring approximately one cm are made bilaterally through the soft palate lateral to the base of the tongue, followed by partial vaporization of the uvula. Up to seven separate treatment sessions may be required. Well-designed trials evaluating the safety and efficacy of LAUP are lacking.

Camacho et al. (2017) conducted a meta-analysis and systematic review of 23 studies (n=717) to evaluate LAUP alone as a treatment for OSA in adults. Most of the published studies were case series with two randomized controlled trials. The authors concluded that LAUP reduced AHI by 32% among all patients; while the lowest oxygen saturation only changed minimally. The individual data demonstrated a 23% success rate and a cure rate of 8%. AHI worsened among 44% of the patients. The authors recommended that LAUP be performed with caution or not at all due to unfavorable results of the published studies.

AASM 2010 Practice Parameters for the Surgical Modification of the Upper Airway for OSA, as noted above, state that LAUP is not routinely recommended. The evidence was judged to be low quality LAUP does not generally normalize the AHI, and the literature does not demonstrate significant improvement in secondary outcomes. Two studies performed since the last review in 2001 actually reported worsening of the overall AHI.

Uvulectomy: Uvulectomy has been proposed as a surgical treatment for snoring and mild obstructive sleep apnea. There are no well-designed studies in the peer-reviewed medical literature that evaluate uvulectomy for the treatment of obstructive sleep apnea. Based on the available evidence, it is not possible to determine the safety and efficacy of this procedure compared to established medical and surgical treatment. Uvulectomy performed as a separate procedure is not addressed in relevant published specialty society guidelines.

(Note: This Coverage Policy is not intended to address uvulectomy when performed for other indications (e.g., acute inflammation/angioedema of the uvula).

Maxillomandibular Advancement (MMA): Maxillomandibular advancement is a surgical procedure that involves the simultaneous advancement of the maxilla and mandible through sagittal split osteotomies. The procedure provides enlargement of the retrolingual airway, and some advancement of the retropalatal airway (Aurora, et al., 2011).

Holty and Guilleminault (2010) conducted a systematic review and meta-analysis of 22 studies (n=627 patients) to evaluate the clinical efficacy and safety of maxillomandibular advancement for the treatment of OSA. The mean AHI decreased from 63.9/hour to 9.5/hour (p<0.001) following surgery. The pooled surgical success and cure (AHI<5) rates were 86.0% and 43.2%, respectively. Younger age, lower preoperative weight and AHI, and greater degree of maxillary advancement were predictive of increased surgical success. The major and minor complication rates were 1.0% and 31%, respectively. Long-term surgical success was maintained at a mean follow-up of 44 months. Statistically significant improvements in quality of life measures, OSA symptomatology (i.e., excessive daytime sleepiness) and blood pressure control were reported after MMA. The authors concluded that MMA appears to be a safe and highly effective treatment for OSA, but further research is needed to assess clinical outcomes of MMA more thoroughly in long-term cohort studies, and to identify which OSA patients would benefit most from MMA.

AASM Practice Parameters for the Surgical Modification of the Upper Airway for OSA (Aurora et al., 2010), discussed above, state that MMA is indicated for surgical treatment of severe OSA in patients who cannot tolerate or who are unwilling to adhere to positive airway pressure therapy, or in whom oral appliances, which are more often appropriate in mild and moderate OSA patients, have been considered and found ineffective or undesirable. The evidence was considered to be very low quality, consisting of nine case series, but did tend to demonstrate consistent effectiveness in severe OSA. In the published series, AHI was reduced to at least 10/hour in most patients, but PAP remains more effective in normalizing AHI, and improvement in other measures such as sleepiness and quality of life are well supported for PAP but are lacking for MMA. PAP or oral appliance therapy therefore should be suggested ahead of MMA in appropriate candidates.

Traditional "stepped" care frequently utilizes MMA as a final approach for surgical treatment of OSA, but MMA may be considered as an initial or sole approach in treating OSA. The authors recommended multidisciplinary evaluation to identify which patients would benefit from MMA as initial or sole therapy. There is a need for further clarification regarding the relative risks and benefits of MMA compared with other treatment modalities.

Multi-Level or Stepwise surgery (MLS): This category includes a wide array of combined procedures that address narrowing of multiple upper airway sites. MLS often consists of phase I, utilizing UPPP and/or genioglossus advancement and hyoid myotomy (GAHM). Phase II procedures, consisting of maxillary and mandibular advancement osteotomy (MMO), may be considered for patients who fail phase I surgeries (Aurora, et al., 2011).

AASM Practice Parameters for the Surgical Modification of the Upper Airway for OSA (Aurora, et al, 2010) discussed above state that use of multi-level or stepwise surgery (MLS), as a combined procedure or as stepwise multiple operations, is acceptable in patients with narrowing of multiple sites in the upper airway, particularly if they have failed UPPP as a sole treatment. Although a large volume of literature addressing MLS

exists, the evidence is of low quality, consisting of observational case series or comparative studies without randomization. While a multilevel approach may eventually result in significant improvement in AHI, available data are heterogeneous, clinical outcomes such as cardiovascular events are not well studies, and multiple procedures could be associated with increased morbidity and mortality.

Pillar™ Palatal Implant System: The Pillar Palatal Implant System (Restore Medical, St. Paul, MN) received FDA 510(k) approval on December 18, 2002, for the treatment of snoring. On June 7, 2004, FDA approval of the Pillar System was expanded to include treatment of OSA. According to the FDA summary, the Pillar System consists of an implant and delivery tool, and is designed to stiffen the tissue of the soft palate to reduce the incidence of snoring in some patients and to reduce the incidence of airway obstruction in patients with mild to moderate OSA. The implant is a cylindrical-shaped segment of braided polyester filaments. The delivery tool consists of a handle and needle assembly that allows for positioning and placement of the implant in the submucosa of the soft palate.

A meta-analysis of the efficacy of the Pillar implant in the treatment of snoring and OSA was conducted by Choi et al. (2013). Efficacy for snoring (seven studies) and for mild to moderate OSA (seven studies) was analyzed separately. For patients with mild to moderate OSA, the Pillar implant significantly reduced the Epworth Sleepiness Scale ($p<.001$) and AHI ($p=.002$) compared to pre-procedure values. The authors noted that these results indicate that the Pillar implant has a moderate effect on snoring and mild to moderate OSA, but more studies with a high level of evidence are needed to arrive at a definite conclusion.

Friedman et al. (2007) conducted a retrospective review to assess subjective and objective improvement in 145 patients with mild to moderate OSA treated with a single-stage multilevel minimally invasive technique. All patients were treated with nasal surgery, palatal stiffening by Pillar implants, and radiofrequency volume reduction of the tongue base. Of 145 patients, 122 had a minimum follow-up of six months and complete data available for review. The primary outcome measure was change from baseline in AHI. The mean AHI decreased from 28.2 ± 7.6 preoperatively to 14.5 ± 10.2 postoperatively ($p<.0001$). Mean Epworth Sleepiness Scale (ESS) decreased from 9.7 ± 3.9 to 7.0 ± 3.3 ($p<.0001$). It is difficult to draw conclusions from this study due to its retrospective design, lack of long-term outcomes, and the inability to determine the individual impact of each procedure on short-term outcomes.

Nordgard et al. (2006) conducted a prospective nonrandomized study of 25 patients with untreated OSA with an AHI of 10–30, as determined by preoperative PSG, and BMI ≤ 30. Three permanent implants were placed in the soft palate of each patient in an office setting under local anesthesia. A repeat PSG showed a mean decrease in AHI from 16.2 to 12.1 for the study group. Twenty of 25 patients demonstrated a reduced AHI, and 12 of 25 patients demonstrated an AHI of 10 or less 90 days post-implant. The mean ESS score decreased from 9.7 to 5.5. The authors concluded that palatal implants can significantly improve AHI and other sleep-related parameters in patients with mild to moderate OSA and BMI ≤ 30, with short-term results comparable to those reported for UPPP. The authors acknowledged the lack of long-term outcomes in this study and the limited number of patients. As with other palatal procedures, reduction in effectiveness over time may be expected. The authors further concluded that while short-term durability and effectiveness have been established, longer-term research needs to be conducted.

A multicenter non-comparative study was conducted by Walker et al. (2006) to evaluate the safety and effectiveness of the Pillar Palatal Implant System (n=53). Primary inclusion criteria were primary palatal contribution to OSA as determined by the investigator, an AHI of 10–30 events per hour, BMI ≤ 32 kg/m^2, age 18 or greater, and soft palate length adequate to accommodate a 28-mm implant. Each patient had three implants placed in the soft palate in an office procedure under local anesthesia. The primary outcome measure was AHI. PSG was performed prior to and 90 days following Pillar implantation. The AHI decreased from 25.0 ± 13.9 to 22.0 ± 14.8 events/hour ($p=0.05$). ESS scores, a secondary outcome measure, decreased from 11.0 ± 5.1 to 6.9 ± 4.5 ($p=<0.001$). The AHI was reduced to below 10 in 12 patients (23%), and the AHI increased in 18 patients (34%). There were no serious complications. The most common adverse event was partial extrusion. Of 202 implants, 20 became partially exposed through the mucosa of the soft palate. All were removed and, in most cases, the implant was replaced.

AASM Practice Parameters for the Surgical Modification of the Upper Airway for OSA (Aurora, et al., 2010) discussed above, state that palatal implants may be effective in some patients with mild obstructive sleep apnea who cannot tolerate or are unwilling to adhere to PAP therapy, or in whom oral appliances have been considered and found ineffective or undesirable. Evidence is of very low quality, and while this procedure may be an alternate mode of therapy for mild OSA, it is difficult to predict if it will ultimately be found to be a reliably effective intervention.

There is insufficient evidence in the published medical literature to demonstrate the safety, efficacy, and long-term outcomes of the Pillar System in the treatment of OSA.

Radiofrequency Volumetric Tissue Reduction (RFVTR): RFVTR (e.g., Coblation®, Somnoplasty®) is a procedure used to remove redundant tissue in the upper airway. Although the procedure has been used to remove tissue from the turbinates and tonsils, recent studies of RFA in the treatment of OSA have limited the procedure to the soft palate, uvula and tongue base.

The ENTec™ ReFlex™ Wand (ArthroCare Corp., Sunnyvale, CA) received FDA approval through the 510(k) process on February 4, 2000, for ablation and coagulation of soft tissue in otolarygological (ENT) surgery, including tissue in the uvula/soft palate for the treatment of snoring and submucosal palatal shrinkage. The ReFlex Wand is used to perform Coblation® treatment using radiofrequency energy. In 2002, the ENTec Plasma Wand received 510(k) approval for ablation, resection, and coagulation of soft tissue and hemostasis of blood vessels in ENT surgery, including tissue of the uvula/soft palate for the treatment of snoring.

The Somnoplasty system (Somnus Medical Technologies, Sunnyvale, CA) received FDA 510(k) approval on July 17, 1997, for coagulation of soft tissue, including the uvula/soft palate. The 510(k) summary states that the Somnoplasty system may reduce the severity of snoring in some individuals. An expanded approval on November 2, 1998, states that the system is intended for the reduction of the incidence of airway obstruction in patients with upper airway resistance syndrome and OSA. The Somnoplasty system is comprised of an RF generator and tissue coagulating electrodes. The procedure is usually performed on an outpatient basis with local anesthesia.

AASM practice parameters discussed above (Aurora, et al., 2010) state that RFA can be considered in patients with mild to moderate OSA who cannot tolerate or are unwilling to adhere to PAP therapy, or in whom oral appliances have been considered and found ineffective or undesirable. This is noted to be a new recommendation based on very low quality evidence. The average post-procedure AHI was found in 7 case series and one randomized controlled trial to be 14.9, consistent with residual mild OSA. The authors noted that RFA studies have shown improvement in subjective sleepiness and, in one study, quality of life. Because cardiovascular complications of OSA are associated with even lower values of AHI, patients treated with RFA should receive follow-up assessments for residual AHI, even if symptoms have improved. The authors also note that long-term sequelae of RFA are not published.

The systematic review by Franklin et al. (2009) to evaluate the efficacy and adverse effects of surgery for snoring and OSA, discussed above, concluded that there was no significant effect on daytime sleepiness and quality of life after radiofrequency ablation.

There is insufficient evidence in the published medical literature to demonstrate the safety, efficacy, and long-term outcomes of RFVTR (e.g., Somnoplasty, Coblation) in the treatment of OSA.

Tongue-Base Suspension (e.g., The AIRVance System): The Repose Bone Screw System (Influence, Inc., San Francisco, CA) received FDA 510(k) approval on August 27, 1999. The device name was changed to AIRVance in 2011, and is marketed by MedTronic. The system is used to perform anterior tongue base suspension by fixation of the soft tissue of the tongue base to the mandible bone using a bone screw with pre-threaded sutures. It is indicated for the treatment of OSA and/or snoring. The AIRVance System has been proposed as a sole treatment of OSA and has also been use in conjunction with UPPP and radiofrequency ablation.

Bostanci et al. (2016) conducted a systematic review to evaluate existing research into the effectiveness and safety of two tongue base suspension (TBS) techniques (Repose® system and modified TBS) with or without uvulopalatopharyngoplasty (UPPP) in obstructive sleep apnea. Seven studies including 113 patients met the eligibility criteria for TBS as a stand-alone procedure. Four of seven studies including 62 patients used the Repose, and three studies including 51 patients used the modified TBS. The success rates were higher in the studies that used modified technique (74.5 %) than those that used the Repose (25.8%), (p<0.001). Ten studies including 300 patients met the eligibility criteria for TBS combined with UPPP. Seven of ten studies including 176 patients used the Repose and three studies including 124 patients used the modified TBS. The success rates in this group were similar between the modified TBS (73.4%) and Repose (67.6%), (p=0.341). When aggregate data of 413 patients were compared, the modified TBS was found to be associated with significantly higher success rates (73.7 vs. 56.7%, p<0.001). The evidence supports primarily grade C recommendations for the benefits of both techniques with or without UPPP. There is a trend toward improved outcome with the modified technique.

Kuhnel et al. (2005) conducted a prospective nonrandomized study (n=28) to demonstrate the efficacy of tongue base suspension with the Repose System in the treatment of OSA. PSG was performed before as well as three and 12 months after surgery. Lateral cephalometric radiography and videoendoscopy of the pharynx were performed preoperatively and postoperatively to identify morphological changes in the posterior airway space. A suspension suture anchored intraorally at the mandible was passed submucosally in the body of the tongue, with suture tightness adjusted individually. The posterior airway space was widened by at least 2 mm in 60% of cases. Daytime sleepiness improved subjectively in 67% of patients, and the RDI improved postoperatively in 55% of patients. The correlation between posterior airway space widening and the improvements in daytime sleepiness and respiratory disturbance index was not significant. The authors concluded that surgical intervention in obstructive sleep apnea syndrome with the Repose System does not result in permanent anatomical change in the posterior airway space.

Miller et al. (2002) conducted a retrospective analysis of the Repose System for the treatment of OSA to describe preliminary experience using the system in conjunction with UPPP in the multilevel surgical approach. The authors evaluated 19 consecutive patients undergoing UPPP and the Repose System tongue base suspension for the management of OSA during a one-year period (1998 through 1999). Fifteen patients had complete preoperative and postoperative PSG data. A 46% reduction in RDI was demonstrated at a mean of 3.8 months after surgery. The apnea index demonstrated a 39% reduction. The authors concluded that the Repose System in conjunction with UPPP has been shown to produce significant reductions in the RDI and apnea index, as well as a significant increase in oxygen saturation. Despite the improvement in these objective parameters, the overall surgical cure rate was only 20% (three of 15 patients) in this retrospective series. Further research is warranted to define the role of the Repose System in the management of obstructive sleep apnea patients.

There is insufficient evidence in the published medical literature to support the safety, efficacy, and long-term outcomes of the use of the Repose System in the treatment of OSA.

Tongue Implant (e.g., The ReVent System): The ReVent System (ReVent® Medical, Inc., Alamo, CA) has CE mark approval and is available on a limited basis in Europe. The device is not FDA-approved. The system is intended for use in stabilizing the tongue for the reduction of the incidence of tongue based airway obstruction in patients with OSA. The implants are inserted using a minimally invasive technique providing a light spring-like force to the tissue. After the implants heal into place with the looped ends acting as an anchoring mechanism, the bio-absorbable sections between the looped ends of the implants erode allowing the implants to contract over time. The spring-like force is designed to maintain an open airway (Pavelec, et al., 2016)

There is insufficient evidence in the published medical literature to support the safety, efficacy, and long-term outcomes of the use of the ReVent System in the treatment of OSA.

Tracheostomy: AASM practice parameters (Aurora et al., 2010), discussed above state that tracheostomy has been shown to be an effective single intervention to treat OSA. This operation should be considered only when other options do not exist, have failed, are refused, or when this operation is deemed necessary by clinical urgency. This recommendation is considered an Option; although tracheostomy is nearly always successful in

bypassing the upper airway obstruction and normalizing AHI, it is not recommended as primary therapy based on placing a high value on patient safety, autonomy, and quality of life.

Transpalatal Advancement Pharyngoplasty
Transpalatal Advancement Pharyngoplasty has been proposed as an alternative to traditional methods of reconstructing the upper pharyngeal airway. The procedure enlarges and stabilizes the upper pharyngeal airway by altering bone and soft tissue attachments of the posterior maxilla. The concept of transpalatal advancement pharyngoplasty is based on OSA pathophysiology in which the primary craniofacial predictor of OSA severity is maxillary constriction. The procedure increases the retropalatal airway size by combining a posterior maxillectomy with soft palate mobilization.

Volner et al. (2017) conducted a systematic review and meta-analysis to evaluate if apnea-hypopnea index (AHI) and lowest oxygen saturation (LSAT) improve after transpalatal advancement pharyngoplasty (TPAP) with OSA in adults. All studies that included patients who underwent TPAP alone were included in the analysis. Five studies met criteria (n=199). Although improvements were seen in both AHI and LSAT after TPAP, the authors recommend additional studies, especially prospective studies. Research comparing TPAP pharyngoplasty procedures without palatal advancement are needed to determine the optimal role for this procedure.

Evidence evaluating this technique is limited, consisting primarily of retrospective reviews. There is insufficient evidence in the published medical literature to determine the safety and efficacy of this procedure or to determine how it compares to available treatment options for OSA.

Uvulopalatopharyngoplasty (UPPP): UPPP increases the area of the retro-palatal airway by resection of the free edge of the uvula and soft palate in patients with collapse of the oropharyngeal and hypopharyngeal airways, or with some other anatomical impediment such as small retrolingual airways. UPPP may be combined with tonsillectomy and may also be performed sequentially with other surgical procedures. The success of UPPP is variable, with positive results most often seen in patients whose obstruction is limited to the retropalatal airway (Sher, et al., 1996; Sundaram, et al., 2005).

The recommendation for UPPP in the 2010 AASM practice parameters for surgical modification of the upper airway (Aurora, et al.), discussed above, states that UPPP does not reliably normalize the AHI in moderate to severe OSA; patients with severe OSA should therefore initially be offered PAP therapy, while those with moderate OSA should initially be offered either PAP therapy or an oral appliance. This recommendation differs from the previously published guideline that recommended UPPP for patients with narrowing or collapse of the retropalatal area.

Franklin et al. (2009) conducted a systematic review to evaluate the efficacy and adverse effects of surgery for snoring and OSA. The review included four randomized controlled trials of surgery vs. either sham surgery or conservative treatment in adults. The trials included outcome measures of daytime sleepiness, quality of life, AHI, and snoring. There was no significant effect on daytime sleepiness and quality of life after laser-assisted uvulopalatoplasty (LAUP). The AHI and snoring were reduced in one trial after LAUP but not in another. A total of 45 observational studies were also reviewed to evaluate adverse effects following surgical treatment. Persistent side-effects occurred after uvulopalatopharyngoplasty (UPPP) and uvulopalatoplasty (UPP), with difficulty swallowing, globus sensation, and voice changes commonly observed.

A Cochrane systematic review assessed the results of any surgery in the treatment of OSA in adults (Sundaram, et al., 2005). UPPP was one of several procedures evaluated. The authors concluded that available studies do not provide evidence to support the use of surgery in OSA because overall significant benefit has not been demonstrated. Long-term follow-up of patients who undergo surgical treatment is required to determine whether surgery is curative or whether the signs and symptoms of OSA tend to recur, requiring further treatment.

Sher (1996) conducted a systematic literature review with meta-analysis to provide an overview of the surgical treatment of OSA to provide the basis for the AASM practice parameters on this subject. Studies included in the meta-analysis provided preoperative and postoperative PSG data on at least nine patients treated with UPPP for OSA. Analysis of the UPPP studies revealed that this procedure is, at best, effective in treating less than 50% of patients with OSA. AASM practice parameters based on this review state that UPPP, with or without a

tonsillectomy, may be appropriate for patients with narrowing or collapse in the retropalatal region. The recommendations also state that effectiveness of UPPP is variable, and the procedure should only be performed when nonsurgical treatment options, such as PAP, have been considered.

Other Devices and Procedures

Atrial Overdrive Pacing: Atrial overdrive pacing by means of an implantable cardiac pacemaker has been proposed as a treatment for central sleep apnea patients and in certain OSA patients with some degree of heart failure. Atrial overdrive pacing consists of pacing at a rate higher than the mean nocturnal sinus rate. Investigators theorized that atrial overdrive pacing would improve vagal tone and increase upper airway muscle activity in patients with OSA.

Anastasopoulos et al. (2016) conducted a systematic review of 22 studies to evaluate the effect of different types of cardiac pacing on sleep-related breathing disorders in patients with or without heart failure. The included studies were classified according to the type of sleep disorder and the intervention undertaken. The authors reported that the evidence shows that cardiac resynchronization therapy, not atrial overdrive pacing, can reduce apneic events in central sleep apnea patients. Their effect on obstructive sleep apnea is controversial and pacing cannot be used alone as treatment of sleep-related breathing disorders. Further research is needed in order to elucidate the effect of these interventions in individual with sleep apnea.

Weng et al. (2009) conducted a meta-analysis of eight randomized controlled trials to determine the effects of atrial overdrive pacing on sleep apnea syndrome (n=129). Atrial overdrive pacing, as compared to non-pacing, reduced the apnea-hypopnea index (AHI) and increased the minimum arterial oxygen saturation (SaO2) significantly in the central sleep apnea-predominant trials. No statistically significant increase in minimum SaO2 was observed in the obstructive sleep apnea syndrome-predominant trials, however, and it was unclear whether AHI was reduced in these patients. The authors concluded that the role of atrial overdrive pacing in obstructive sleep apnea syndrome remains unclear.

Guidelines for device-based therapy published by the American College of Cardiology (ACC) and the American Heart Association (AHA) state that, a variety of heart rhythm disturbances my occur in OSA. Sinus bradycardia or pauses may occur during hypopneic episodes, and atrial tachyarrhythmias may also be observed, especially following an apnea episode. The guideline states that although a small retrospective trial demonstrated a decrease in central or OSA without reducing the total sleep time, subsequent randomized trials have not validated a role for atrial overdrive pacing in OSA (Epstein et al., 2008; 2012).

There is insufficient evidence to demonstrate the safety and efficacy of atrial overdrive pacing in the treatment of OSA.

Electrosleep Therapy: Electrosleep therapy consists of the application of short duration, low-amplitude pulses of direct current to the patient's brain via externally placed occipital electrodes. It has been used in the treatment of chronic insomnia, anxiety, and depression, but has also been used in disorders with possible psychosomatic components, such as asthma, spastic colitis, or tension headache, and for organic disorders, including essential hypertension. Scientific assessment of this technique has not been completed, and its efficacy in the treatment of OSA has not been established.

Implanted Upper Airway Stimulation Devices

Inspire® Upper Airway Stimulation (UAS) (Inspire Medical Systems Inc., Maple Grove, MN) received FDA approval through the PMA process on April 30, 2014 (P130008). The implanted components of the Inspire therapy system consist of the Inspire II implantable pulse generator, the stimulation lead, and the respiratory sensing lead model. When therapy is on, the Inspire system detects the patient's respiratory effort and maintains airway patency with mild stimulation of the hypoglossal nerve. Therapy settings are stored in the pulse generator and configured by the physician using an external programmer. The patient uses the Inspire sleep remote to turn therapy on before sleep and to turn therapy off on awakening.

According to the FDA labeling, the Inspire system is indicated for treatment of a subset of patients with moderate to severe OSA (apnea-hypopnea index of ≥ 20 and ≤ 65). Inspire UAS may be used in adults 22 years of age and older who have been confirmed to fail or cannot tolerate PAP treatments (such as CPAP or BPAP) and who

do not have a complete concentric collapse at the soft palate level. PAP failure is defined as an inability to eliminate OSA (AHI of greater than 20 despite PAP usage), and PAP intolerance is defined as: (1) Inability to use PAP (greater than five nights per week of usage; usage defined as greater than four hours of use per night), or (2) unwillingness to use PAP (for example, a patient returns the PAP system after attempting to use it). In a 2017 PMA supplement (P130008/S021), the FDA granted approval to expand the AHI range from 20 to 65 events per hour to 15 to 65 events per hour. The device, as modified, will be indicated to treat a subset of patients with moderate to severe OSA (AHI of ≥ to 15 and ≤ 65).

Hypoglossal nerve stimulator devices that have not received FDA approval include the aura6000 (Imthera Medical Inc., San Diego CA) and HGNS® System (Apnex Medical, Inc, Minneapolis, MN). Apnex did not complete the clinical trial for approval by the FDA, however, and is no longer commercially available. In November 2014, ImThera Medical, Inc., received FDA approval to conduct an investigational device exemption trial for its THN3 clinical study. The THN3 study will evaluate the safety and effectiveness of the aura6000 system for moderate to severe OSA in individuals who are unable to comply or unwilling to try PAP therapy or other OSA treatments. Data from this clinical study will be used to support a Pre-Market Approval (PMA) application for the aura6000 system.

Hypoglossal nerve stimulation (HGNS) devices are implanted by a pulmonologist, thoracic surgeon, or other qualified physician. Hospitalization is generally not required for device implantation. Proposed therapies or surgeries related to hypoglossal nerve stimulation for treatment of OSA include adenotonsillectomy; CPAP; genioglossal advancement; hyoid suspension; mandibular-maxillary advancement; oral appliances; positive airway pressure (PAP); partial glossectomy; radiofrequency treatment; weight loss; positional therapy; tongue suspension; tracheostomy; uvulopalatopharyngoplasty (UPPP) (Hayes, 2016).

Strollo et al. (2014) conducted a multicenter single-group cohort study, the STAR trial (Stimulation Therapy for Apnea Reduction), to evaluate the safety and effectiveness of a surgically implanted upper airway stimulation device (Inspire UAS) for the treatment of patients with moderate to severe OSA who had difficulty either accepting or adhering to CPAP therapy (n=126). The mean age was 54.5 years and mean BMI was 28.4. The primary outcome measures were apnea-hypopnea index (AHI) and oxygen desaturation index (ODI) (the number of times per hour of sleep that the blood oxygen level drops by ≥ 4 percentage points from baseline). Secondary outcomes were Epworth Sleepiness Scale (ESS), Functional Outcomes of Sleep Questionnaire (FOSQ), and percentage of sleep time with the oxygen saturation less than 90%. The median AHI score at 12 months decreased 68% from 29.3 events/hour to 7.4 events/hour (p<0.001). Scores on the FOSQ and ESS indicated significant improvement at 12 months; the increase in the FOSQ score exceeded the 2.0 point increase typically considered to be a clinically meaningful improvement, and the ESS score at 12 months was consistent with normalization of the measure (i.e., score <10.0). At 12 months, the criteria for the co-primary outcomes of AHI reduction and reduction in ODI were met by 66% and 75% of participants, respectively. Consecutive patients with a response were included in a randomized, controlled therapy withdrawal trial. In this randomized phase the mean AHI did not differ significantly from the 12-month score in the initial phase among the 23 patients in the therapy-maintenance group (8.9 and 7.2 events/hour, respectively). The AHI was significantly higher in the 12 participants in the therapy withdrawal group (25.8 vs. 7.6 events/hour, p<0.001). (The device was turned off in the therapy withdrawal group).The rate of serious adverse events was less than 2%. The lack of a control group limits the validity of the results of this study. Follow-up studies of the same patient population at 18, 24 and 36 months, indicate that the treatment effects are maintained over time. Limitations are the same as the original study (Strollo, et al., 2015; Soose, et al., 2016; ≥, et al., 2016).

Gillespie et al. (2017) reported the four year outcomes of the STAR trial as described above (Stroll et al., 2014). A total of 91 of the 126 participants completed the four year follow-up. This study focused on the self-reported patient secondary outcomes collected every six months through a total of 48 months. Secondary outcome measures include subjective sleepiness and sleep-related quality of life with the validated Epworth Sleepiness Scale (ESS) and the Functional Outcomes of Sleep Questionnaire (FOSQ) and snoring level. Daytime sleepiness as measured by ESS was significantly reduced (p=0.01), and sleep-related quality of life as measured by FOSQ significantly improved (p= 0.01) when compared with baseline. Soft to no snoring was reported by 85% of bed partners. At 48 months three participants had undergone elective explantation of the Inspire UAS system, three died and 25 participants were lost to follow-up. Two patients required reoperation

between 36 and 48 months for lead-related failure. The reported main study limitation was the increased number of patients lost to follow-up at 48 months compared with 36 months (25 versus 4).

Woodson et al (2018) reported the five year outcomes of the STAR trial as described above (Stroll et al., 2014). This study evaluated the safety and effects of upper airway stimulation (UAS) therapy on the propensity for daytime sleepiness, as measured by the Epworth Sleepiness Scale (ESS); daytime functioning, as measured by the Functional Outcomes of Sleep Questionnaire (FOSQ); intrusive snoring, as reported by participant and bed partner; and (4) sleep-disordered breathing, as found in an overnight polysomnography (PSG). Of the 126 participants who underwent implantation, 97 (78%) completed the 5-year follow-up visit. Of the 97 patients meeting the 5-year follow-up protocol, 71 volunteered for an overnight in-laboratory polysomnographic evaluation. A total of 21 were lost to follow-up within the prespecified time frame; five died of unrelated causes; and three had the device explanted. Patients who did and did not complete the protocol differed in baseline AHI, oxygen desaturation index, and Functional Outcomes of Sleep Questionnaire scores but not in any other demographics or treatment response measures. Improvement in sleepiness (Epworth Sleepiness Scale) and quality of life was observed, with normalization of scores increasing from 33% to 78% and 15% to 67%, respectively. AHI response rate (AHI <20 events per hour and >50% reduction) was 75% (n=71). When a last observation carried forward analysis was applied, the responder rate was 63% at five years. Serious device-related events all related to lead/device adjustments were reported in 6% of patients. The authors report that the biggest limitations of this study are related to the lack of a control group and the assessment of treatment effects other than withdrawal of stimulation at 12 months. The study group was predominantly male, obese, CPAP intolerant, and of European descent, conclusions about generalizability to women and other ethnic groups may require additional study.

Boon et al. (2018) conducted a retrospective and prospective registry study (n=301) to collect retrospective and prospective objective and subjective outcome measures across multiple institutions (n=10) in the United States and Germany. Patients were included who had moderate to severe OSA, were intolerant to CPAP, and were undergoing upper airway stimulation (UAS) implantation. Baseline demographic and sleep study data were collected. Objective and subjective treatment outcomes, adverse events, and patient and physician satisfaction were reviewed. The study cohort consisted of a middle-aged and primarily male (82%), Caucasian (97%), and overweight population. The authors reported that mean AHI decreased from 35.6 to 10.2 events per hour (p<0.0001), and Epworth Sleepiness Scale scores decreased from 11.9 to 7.5 (p<0.0001) from baseline to the post-titration visit. The post-titration visit occurs after the therapy has been optimally titrated, approximately two to six months after implant. In general, it is the first office visit after titration. The mean and median follow-up duration was 134 and 123 days after implant, respectively. Patients utilized therapy for 6.5 hours per night. There were low rates of procedure- and device-related complications. At the post-titration visit, 63 adverse events were reported for 54 (18% of 301) patients. Clinical global impression scores demonstrated that the majority of physicians (94%) saw improvement in their patients. symptoms with therapy. The majority of patients (90%) were more satisfied with UAS than CPAP. This study is limited by the homogenous patient population.

Heiser et al. (2017a) conducted a multicenter single-arm prospective study (n=60) to obtain additional safety and efficacy data on the use of selective upper airway stimulation (i.e. Inspire UAS) during daily clinical routine. Key study selection criteria were based on those established from the STAR trial. Every patient who received an implant of selective upper airway stimulation was included in this trial (apnea-hypopnea index ≥15/h and ≤65/h and body mass index \35 kg/m^2). Before and six months after surgery, a two-night home sleep test was performed. Data regarding the safety and efficacy were collected. Every patient reported improvement in sleep and daytime symptoms. The average usage time of the system was 42.9 ± 11.9 h/wk. The median apnea-hypopnea index was significantly reduced at six months from 28.6/h to 8.3/h. No patient required surgical revision of the implanted system. The lack of a control group and limited follow-up limits the validity of the results of this study.

Heiser et al (2017b) conducted a single-center prospective study (n=30) to analyze the application and outcome of UAS with the Inspire device in patients with moderate to severe OSA. The mean age was 59.6 years with thirty patients being male. Data at twelve months was reported. The mean pre-implantation AHI of 32.9/h could be reduced to 7.1/h after 12 months (p<0.001). The mean pre-implantation oxygen saturation and desaturation index (ODI) of 30.7/h could be reduced to 9.9/h (p=0.004). The mean pre-implantation ESS of 12.6 could be reduced to 5.9 (p=0.006). Serious adverse events did not occur. Therapy adherence was a

usage of 6.6 h/night after 12 months. The lack of a control group, small sample size and limited follow-up limits the validity of the results of this study.

Steffen et al (2017) conducted a multicenter prospective single-arm study (n=60) reporting on objective and patient-reported outcome after 12 months of implantation of an upper airway stimulation (UAS) device. The study included patients with moderate-to-severe obstructive sleep apnea (OSA) who could not adhere to continuous positive airway pressure. Key study exclusion criteria included body mass index>35 kg/m^2, apnea–hypopnea index (AHI) <15 or>65, or complete concentric collapse at the soft palate during sedated endoscopy. Data collection at six- and 12-month visit include home sleep test and patient-reported outcome measures. The median AHI reduced from 28.6 to 9.5 from baseline to 12 months. Patient-reported outcome measured in Epworth Sleepiness Scale and Functional Outcomes of Sleep Questionnaire both improved significantly from baseline to 12 months. The average usage time was 39.1±14.9 hours per week among all participants based on recordings by the implanted device. One patient requested a removal of the device for cosmetic and other personal reasons and was completed without sequelae. The lack of a control group, small sample size and limited follow-up limits the validity of the results of this study.

In a retrospective study, Mahmoud et al (2017) reported if prior airway surgery for obstructive sleep apnea (OSA) had increased benefit following implantation with a hypoglossal nerve stimulator. Following implantation with hypoglossal nerve stimulator device, the outcomes of patients who underwent prior airway surgery for OSA were compared with those who did not. Primary outcome measures included apnea-hypopnea index (AHI) and nadir oxyhemoglobin saturation (NOS) as measured by polysomnography. Secondary outcome measures included Epworth Sleepiness Scale. Forty-seven patients underwent implantation with hypoglossal nerve stimulator. Of these, 30 patients had undergone prior airway surgery for OSA, whereas 16 did not. Mean preoperative AHI and NOS were 39.3 and 78% for all patients, 39.4 and 79% for patients with prior airway surgery, and 39.1 and 77% for patients without prior surgery. Mean postoperative AHI and NOS were 3.9 and 91% for all patients, 4.2 and 91% for patients with prior surgery, and 3.4 and 93% for patients without prior surgery (p=0.756 and 0.053, respectively). There were no major adverse events noted in this study.

In a retrospective case series study, Shah et al (2018) compared outcomes in patients with moderate to severe OSA who underwent hypoglossal nerve stimulation (HNS) surgery (Inspire Medical Systems) and those who underwent traditional airway reconstructive surgery, specifically uvulopalatopharyngoplasty (UPPP). Patients who underwent HNS implantation (n=20), all with moderate to severe OSA, inability to adhere to positive pressure therapy, and compliant with previously published inclusion criteria, were compared to a historical cohort that were intolerant of CPAP with similar inclusion criteria who all underwent UPPP (n=20) with some also undergoing additional procedures such as septoplasty/turbinate reduction. For the HNS group device activation and initiation of therapy was completed at one month after surgery with follow up polysomnography testing done 2–3 months after implantation. For the UPP group, the timing of follow-up polysomnography ranged from 2 to13 months after surgery with most patients (17/20) completing the postoperative sleep study between 3 and 6 months. Data including body mass index (BMI), pre- and post-implant apnea-hypopnea index (AHI) were assessed. For patients who underwent HNS, mean preoperative BMI was 28.0. Mean AHI decreased significantly from 38.9-4.5. All patients achieved an AHI < 20 post implant with 65% (13/20) with an AHI ≤ 5. For patients who underwent traditional airway surgery, mean preoperative BMI was 27.5; mean AHI decreased from 40.3-28.8. The lack of a control group, small sample size and limited follow-up limits the validity of the results of this study.

Huntley et al (2018) conducted a retrospective study comparing demographic and polysomnographic data and proportion of patients achieving surgical success using upper airway stimulation (UAS) or expansion sphincter pharyngoplasty (ESP). The ESP cohort consisted of 33 patients. The mean preoperative AHI, O2 nadir, Epworth Sleepiness Scale (ESS), and BMI were 36.47, 82.63, 10.69, and 29.6, which improved to 13.47, 84.84, 7.00, and 29.92 postoperatively. There was a 63.64% success rate. The UAS cohort consisted of 75 patients. The mean preoperative AHI, O2 nadir, ESS, and BMI were 36.76, 80.24, 11.18, and 29.50, which improved to 7.25, 88.71, 5.36, and 29.36 postoperatively. The success rate was 86.67%. There was a significant difference in gender, age, preoperative AHI, postoperative AHI, postoperative O2 nadir, surgical success, and patients reaching an AHI less than 10 and 5. The authors reported that future studies with prospectively randomized patients would be needed to explore these preliminary conclusions.

Huntley et al (2017) conducted a two-center case series study of patients undergoing UAS at Thomas Jefferson University Hospital (TJUH) and University of Pittsburgh Medical Center (UPMC). The investigators recorded demographic data, Epworth Sleepiness Scale (ESS), and preoperative and postoperative polysomnographic information. They compared outcome data between institutions and subsequently combined the cohorts and compared baseline to posttreatment results. A total of 63 UAS device implantations were performed at TJUH and 57 at UPMC. Those patients who completed a postoperative titration PSG and outpatient follow-up were included in this study. This consisted of 48 patients at TJUH and 49 at UPMC The mean time from UAS implantation to postoperative PSG was 90.39 days at TJUH and 85.23 days at UPMC. The TJUH cohort consisted of 30 males and 18 females with a mean age of 60.88 years and body mass index of 29.29. The mean preoperative apnea-hypopnea index (AHI), O_2 nadir, and ESS were 35.88, 80.96, and 11.09, respectively. The mean postoperative AHI, O_2 nadir, and ESS were 6.34, 88.04, and 5.77, respectively. The UPMC cohort consisted of 30 males and 19 females with a mean age of 62.84 years and body mass index of 27.74. The mean preoperative AHI, O2 nadir, and ESS were 35.29, 79.58, and 10.94, respectively. The mean postoperative AHI, O2 nadir, and ESS were 6.28, 84.35, and 6.60, respectively. We found no difference in patients reaching a postoperative AHI less than 15, 10, and 5 when comparing the cohorts. After combining cohorts, we found a significant improvement in postoperative AHI, O2 nadir, and ESS compared to preoperative values. The lack of a control group, small sample size and limited follow-up limits the validity of the results of this study.

In a retrospective case series study (n=20), Kent et al (2016), reported outcome measures and objective adherence data for patients treated with hypoglossal nerve stimulation (HNS) therapy for moderate to severe obstructive sleep apnea (OSA). All patients had moderate to severe OSA, were unable to adhere to positive pressure therapy, and met previously published inclusion criteria for the commercially available implantable HNS system. Data included demographics, body mass index (BMI), apnea-hypopnea index (AHI), Epworth Sleepiness Score (ESS), nightly hours of device usage, and procedure- and therapy-related complications. Mean BMI was unchanged postoperatively (26.5 -26.8 kg/m²). Mean AHI (33.3 6 -5.1) and mean ESS (10.3- 6.0) decreased significantly. Seventy percent (14/20) of patients achieved a treatment AHI <5, 85% (17/20) an AHI <10, and 95% (19/20) an AHI <15. Average stimulation amplitude was 1.89 V after titration. Adherence monitoring via device interrogation showed high rates of voluntary device use (mean 7.0 h/night). The lack of a control group, small sample size and limited follow-up limits the validity of the results of this study.

Certal et al. (2015) conducted a systematic review of the evidence regarding the efficacy and safety of hypoglossal nerve stimulation as an alternative therapy in the treatment of OSA. A total of six prospective studies with 200 patients were included in this review. Studies were included that evaluated the efficacy of hypoglossal nerve stimulation to treat OSA in adults with outcomes for apnea-hypopnea index (AHI), oxygen desaturation index (ODI), and effect on daytime sleepiness (Epworth Sleepiness Scale [ESS]). Tests for heterogeneity and subgroup analysis were performed. At 12 months, the pooled fixed effects analysis demonstrated statistically significant reductions in AHI, ODI, and ESS mean difference of -17.51 (95% CI: -20.69 to -14.34); -13.73 (95% CI: -16.87 to -10.58), and -4.42 (95% CI: -5.39 to -3.44), respectively. Similar significant reductions were observed at 3 and 6 months. Overall, the AHI was reduced between 50% and 57%, and the ODI was reduced between 48% and 52%. Despite using different hypoglossal nerve stimulators in each subgroup analysis, no significant heterogeneity was found in any of the comparisons, suggesting equivalent efficacy regardless of the system in use. The authors reported that further studies comparing hypoglossal nerve stimulation with conventional therapies are needed to definitively evaluate outcomes.

The 2016 AAO-HNS Position Statement: Hypoglossal Nerve Stimulation for Treatment of Obstructive Sleep Apnea (OSA) considers upper airway stimulation via the hypoglossal nerve for the treatment of adult OSA syndrome to be an effective second-line treatment of moderate to severe OSA in patients who are intolerant or unable to achieve benefit with PAP. This is not an evidence-based practice guideline rather the position statement is based on an informal process of expert or committee consensus (AAO-HNS website).

The 2009 AASM Clinical Guideline for the Evaluation, Management and Long-Term Care of Obstructive Sleep Apnea in Adults does not mention the use of a hypoglossal nerve stimulator device as treatment option for the treatment of OSA (Epstein, et al., 2009).

The 2013 American College of Chest Physicians Clinical Guideline on Management of Obstructive Sleep Apnea in Adults does not mention the use of a hypoglossal nerve stimulator device as treatment option for the treatment of OSA (Qaseem, et al., 2013).

In a 2016 Hayes Directory Report on Hypoglossal Nerve Stimulation for Treatment of Obstructive Sleep Apnea the authors concluded that the overall quality of the evidence evaluating hypoglossal nerve stimulation is very low. A small evidence base was identified pertaining to the efficacy and safety of HGNS for the treatment of OSA. Six studies were included for review (n=8-126), with 9 associated follow-up or subgroup reports, for a total of 15 publications). Studies identified for review included six pretest/posttest studies (Schwartz, et al., 2001; Eastwood, et al., 2011; Van de Heyning, et al., 2012; Mwenge, et al., 2013; Strollo, et al., 2014; Heiser, et al., 2015). Associated reports involved subsequent publications with follow-up data; additional outcomes (e.g., patient-reported quality-of-life measures); overlapping samples; and/or subgroup analyses (Oliven, et al., 2003; Schwartz, et al., 2012; Vanderveken, et al., 2013; Kezirian, et al., 2014; Woodson, et al., 2014; Safiruddin, et al., 2015; Strollo, et al., 2015; Soose, et al., 2016; Woodson, et al., 2016). Follow-up ranged from 1– 36 months. The authors reported that "for use of hypoglossal nerve stimulation (HGNS) for the treatment of moderate-to-severe obstructive sleep apnea (OSA) in adult patients for whom continuous positive airway pressure has failed to provide relief there is a paucity of good-quality comparative studies with sufficient sample sizes assessing HGNS for OSA. The limited number of available studies presented consistent improvements in apnea-hypopnea index, oxygen desaturation index, and airflow mechanics for OSA patients. Inconsistent evidence generally indicated that quality-of-life measures did improve, but that sleep efficiency and/or sleep architecture parameters did not improve". The procedure may carry risks for complications and post-implantation surgical procedures. Additionally, better-quality studies are required to define the patient population that is most likely to respond to HGNS. In the February 2018 annual review of the Hayes Directory Report, the authors reported that no newly published evidence was reported in the literature that would change the existing report (Hayes, 2016; 2017; 2018).

There is insufficient evidence in the published medical literature to demonstrate the safety, efficacy, and long-term outcomes of implanted upper airway hypoglossal nerve stimulation in the treatment of OSA. Further studies comparing hypoglossal nerve stimulation with conventional therapies are needed to definitively evaluate outcomes. There are multiple ongoing and unpublished hypoglossal nerve stimulation clinical trials that can be found at the ClinicalTrials.gov website.

Injection Snoreplasty: Injection Snoreplasty is a nonsurgical treatment for snoring that involves the injection of a hardening agent into the upper palate. Sodium tetradecyl sulfate is the most common hardening agent used. Following the injection, scar tissue is reported to pull the uvula forward to eliminate palatal flutter associated with snoring. There is no evidence in the published medical literature to demonstrate the safety and efficacy of injection Snoreplasty in the treatment of OSA.

Night Shift™ Sleep Positioner: The Night Shift Sleep Positioner (Advanced Brain Monitoring, Carlsbad, CA) is proposed for patients with positional obstructive sleep apnea and snorers. The device is worn on the back of the neck and will vibrate when the user starts to back sleep warning the user to change positions. There is insufficient evidence to demonstrate the safety and efficacy of this device in the treatment of OSA.

Provent™ Device: The Provent Professional Sleep Apnea Therapy device (Ventus Medical, Inc., Belmont, CA) received U.S. Food and Drug Administration (FDA) Approval through the 510(k) process on February 6, 2008 for use in the treatment of OSA. The Provent device consists of a single-use nasal insert composed of soft foam surrounding a valve body constructed of a urethane polymer. The valve body contains a silicone valve mechanism that acts to increase the expiratory pressure by creating expiratory resistance, resulting in airway positive back pressure during expiration. A device is inserted into each nostril and held in place by adhesive tape.

Riaz et al. (2015) conducted a systematic review and meta-analysis to evaluate the effectiveness of nasal expiratory positive airway pressure (nasal EPAP) devices or Provent as treatment for OSA. Eighteen studies (n=920) were included. Nasal EPAP (Provent) reduced AHI by 53.2%, oxygen desaturation index by 41.5% and improved lowest oxygen saturation by 3 oxygen saturation points. Overall there were no clear characteristics (i.e., demographic factors, medical history, and/or physical exam finding) that predicted favorable response to

these devices. Limited evidence suggests that high nasal resistance could be associated with treatment failure. The authors concluded that additional studies are needed to identify demographic and polysomnographic characteristics that would predict therapeutic success with nasal EPAP (Provent).

In a pilot evaluation of the Provent nasal expiratory resistance device, Colrain et al. (2008) recruited 24 patients with an AHI > 5 and six patients with primary snoring. Exclusion criteria included basal metabolic index (BMI) > 35. Patients were evaluated with PSG on two consecutive nights; PSG alone was performed on one night, and PSG was combined with the Provent device on the alternate night. The AHI and oxygen desaturation both decreased significantly with use of the device (p<0.001 and p < 0.1, respectively). The percentage of time spent above 90% oxygen saturation also increased significantly with device use (p < 0.05). There were no significant changes in measures of sleep architecture. Because of the study design, small number of participants and data from a single night of treatment, conclusions cannot be drawn from this pilot study.

Berry et al. (2011) conducted a randomized controlled trial to evaluate treatment with expiratory positive airway pressure (EPAP). Patients with OSA with an AHI of ≥ 10 were assigned to treatment with the Provent device (n=127) or a similar-appearing sham device (n=123) for three months. During the first week of treatment, after at least three nights of device use, PSG was performed on two non-consecutive nights once with and once without the device. After three months of treatment, patients were re-evaluated, and two additional PSGs were performed on non-consecutive nights (device on, device off). At week one, the median AHI (device on vs. off) was significantly lower with EPP (5.0 vs. 13.8 events/hour, p<0.0001) but not with sham treatment (11.6 vs. 11.1 events/hour). Over three months of treatment, Epworth Sleepiness Scores decreased from 9.9 ± 4.7 to 7.2 ± 4.2, p<0.0001), and the median percentage of reported nights used for the entire night was 88.2%.The authors acknowledged limitations of the study, including the large number of exclusion criteria that prevent generalizing the results of this study to less selected populations, and the fact that adherence determination was based on patient reporting rather than objective data.

Although EPAP with the use of the Provent device is a promising treatment option, additional well-designed studies are needed to determine how this device compares to currently available options in the treatment of OSA in terms of safety, efficacy, and long-term outcomes.

The American Board of Internal Medicine's (ABIM) Foundation Choosing Wisely® Initiative: The following recommendation from the American Academy of Sleep Medicine states:
- Don't perform positive airway pressure re-titration studies in asymptomatic, adherent sleep apnea patients with stable weight.

Use Outside the U.S.
A European Respiratory Society (ERS) task force report evaluated non-CPAP therapies, including mandibular advancement devices (MADs), for the treatment of OSA (Randerath et al., 2011). The report states that MADs reduce sleep apneas and subjective daytime sleepiness and improve quality of life compared to control treatments. CPAP is more effective at reducing the number of sleep apneas, but the positive effects on symptoms and health are similar, and patients generally prefer MAD over CPAP. The device should be custom-made, evaluated, and should advance the mandible at least 50% of maximal protrusion. The authors noted that a titration procedure is essential, since the improvement in symptoms is not a precise indicator of treatment success, and long-term follow-up should be performed. Tongue retaining devices (TRD), however, were not recommended for patients with OSA. They may be used, however, in selected patients with mild to moderate OSA when other treatments have failed or are not possible. Patients may have a trial with the device if treatment effect is monitored and strict follow-up is performed.

Guidance issued by the National Institute for Health and Clinical Excellence (NICE, United Kingdom) in 2007 states that the current evidence on soft palate implants for OSA raises no major safety concerns, but there is inadequate evidence that the procedure is efficacious in the treatment of this potentially serious condition for which other treatments exist. The guidance states that soft palate implants should therefore not be used to treat this condition.

National Institute for Health and Clinical Excellence (NICE, United Kingdom) issued updated interventional procedure guidance on radiofrequency ablation of the soft palate in 2014, stating that current evidence suggests

that, there are no major safety concerns associated with the procedure as a treatment for snoring. The evidence on the short-term efficacy of the procedure is adequate, although uncertainties remain about its efficacy in the longer term. The NICE guidance states that this procedure should not be used without special arrangements for audit, consent and research.

Appendix A
Usual maximum amount of PAP accessories (CGS Administrators, 2017)

Supply Description	Quantity
Tubing with integrated heating element for use with positive airway pressure device (A4604)	1 per 3 months
Combination oral/nasal mask, used with continuous positive airway pressure, each (A7027)	1 per 3 months
Oral cushion for combination oral/nasal mask, replacement only (A7028)	2 per 1 month
Nasal pillows for combination oral/nasal mask (A7029)	2 per 1 month
Full face mask used with positive airway pressure device (A7030)	1 per 3 months
Full face mask interface, replacement for full face mask (A7031)	1 per 1 month
Cushion for use on nasal mask interface (A7032)	2 per 1 month
Pillow for use on nasal cannula type interface (A7033)	2 per 1 month
Nasal interface (mask or cannula type, used with positive aiway pressure (A7034)	1 per 3 months
Headgear used with positive airway pressure device (A7035)	1 per 6 months
Chinstrap used with positive airway pressure device (A7036)	1 per 6 months
Tubing used with positive airway pressure device (A7037)	1 per 3 months
Filter, disposable, used with positive airway pressure device (A7038)	2 per 1 month
Filter, nondisposable, used with positive airway pressure device (A7039)	1 per 6 months
Water chamber for humidifier, used with positive airway pressure device, replacement, each (A7046)	1 per 6 months

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
   2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Non-Surgical Treatment

Considered medically necessary when criteria in the applicable policy statements listed above are met for the treatment of obstructive sleep apnea. Considered not medically necessary for the treatment of snoring in the absence of obstructive sleep apnea.

CPT®* Codes	Description
94660	Continuous positive airway pressure ventilation (CPAP), initiation and management

HCPCS Codes	Description
A4604	Tubing with integrated heating element for use with positive airway pressure device
A7027	Combination oral/nasal mask, used with continuous positive airway pressure device, each
A7028	Oral cushion for combination oral/nasal mask, replacement only, each
A7029	Nasal pillows for combination oral/nasal mask, replacement only, pair
A7030	Full face mask used with positive airway pressure device, each
A7031	Face mask interface, replacement for full face mask, each
A7032	Cushion for use on nasal mask interface, replacement only, each
A7033	Pillow for use on nasal cannula type interface, replacement only, pair
A7034[†]	Nasal interface (mask or cannula type) used with positive airway pressure device, with or without head strap
A7035	Headgear used with positive airway pressure device
A7036	Chinstrap used with positive airway pressure device
A7037	Tubing used with positive airway pressure device
A7038	Filter, disposable, used with positive airway pressure device
A7039	Filter, non-disposable, used with positive airway pressure device
A7044	Oral interface used with positive airway pressure device, each
A7045	Exhalation port with or without swivel used with accessories for positive airway devices, replacement only
A7046	Water chamber for humidifier, used with positive airway pressure device, replacement, each
E0470	Respiratory assist device, bi-level pressure capability, without back-up rate feature, used with noninvasive interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device)
E0471	Respiratory assist device, bi-level pressure capability, with back-up rate feature, used with noninvasive interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device)
E0472	Respiratory assist device, bi-level pressure capability, with backup rate feature, used with invasive interface, e.g., tracheostomy tube (intermittent assist device with continuous positive airway pressure device)
E0561	Humidifier, non-heated, used with positive airway pressure device
E0562	Humidifier, heated, used with positive airway pressure device
E0601	Continuous airway pressure (CPAP) device

[†]Note: Considered Experimental/Investigational/Unproven when used to report interface consisting of boil and bite mouthpiece connected to nasal inserts (e.g., CPAP PRO®)

Considered Experimental/Investigational/Unproven when used to report the Winx® Sleep Therapy System:

HCPCS Codes	Description
A7002	Tubing, used with suction pump, each
A7047	Oral interface used with respiratory suction pump, each
E0600	Respiratory suction pump, home model, portable or stationary, electric

Oral Appliance Therapy

Considered medically necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
E0485	Oral device/appliance used to reduce upper airway collapsibility, adjustable or non-adjustable, prefabricated, includes fitting and adjustment
E0486	Oral device/appliance used to reduce upper airway collapsibility, adjustable or non-adjustable, custom fabricated, includes fitting and adjustment

ICD-10-CM Codes	Description
G47.33	Obstructive sleep apnea (adult) (pediatric)

Considered not medically necessary:

ICD-10-CM Codes	Description
	All other codes

Considered Experimental/Investigational/Unproven when used to report the MATRx oral appliance titration study:

CPT®* Codes	Description
95810	Polysomnography; age 6 years or older, sleep staging with 4 or more additional parameters of sleep, attended by a technologist
95811	Polysomnography; age 6 years or older, sleep staging with 4 or more additional parameters of sleep, with initiation of continuous positive airway pressure therapy or bilevel ventilation, attended by a technologist
95999	Unlisted neurological or neuromuscular diagnostic procedure

Surgical Treatment

Considered medically necessary when criteria in the applicable policy statements listed above are met for the treatment of obstructive sleep apnea. Considered not medically necessary for the treatment of snoring in the absence of obstructive sleep apnea.

CPT®* Codes	Description
21193	Reconstruction of mandibular rami, horizontal, vertical, C, or L osteotomy; without bone graft
21194	Reconstruction of mandibular rami, horizontal, vertical, C, or L osteotomy; with bone graft (includes obtaining graft)
21195	Reconstruction of mandibular rami and/or body, sagittal split; without internal rigid fixation

21196	Reconstruction of mandibular rami and/or body, sagittal split; with internal rigid fixation
21198	Osteotomy mandible segmental
21199	Osteotomy, mandible, segmental; with genioglossus advancement
21206	Osteotomy, maxilla, segmental (eg, Wassmund or Schuchard)
21685	Hyoid myotomy and suspension
31600	Tracheostomy, planned (separate procedure);
31601	Tracheostomy, planned (separate procedure); younger than 2 years
42145	Palatopharyngoplasty (eg, uvulopalatopharyngoplasty, uvulopharyngoplasty)
42820	Tonsillectomy and adenoidectomy; younger than age 12
42821	Tonsillectomy and adenoidectomy; age 12 or over
42825	Tonsillectomy, primary or secondary; younger than age 12
42826	Tonsillectomy, primary or secondary; age 12 or over
42830	Adenoidectomy, primary; younger than age 12
42831	Adenoidectomy, primary; age 12 or over
42835	Adenoidectomy, secondary; younger than age 12
42836	Adenoidectomy, secondary; age 12 or over

Considered Experimental/Investigational/Unproven when used to report uvulectomy as a stand-alone procedure for the treatment of OSA:

CPT®* Codes	Description
42140	Uvulectomy, excision of the uvula

Additional Procedures/Services

Considered Experimental/Investigational/Unproven for the treatment of obstructive sleep apnea:

CPT®* Codes	Description
30801	Ablation, soft tissue of inferior turbinates, unilateral or bilateral, any method (eg, electrocautery, radiofrequency ablation, or tissue volume reduction); superficial
30802	Ablation, soft tissue of inferior turbinates, unilateral or bilateral, any method (eg, electrocautery, radiofrequency ablation, or tissue volume reduction); intramural (ie, submucosal)
33206	Insertion of new or replacement of permanent pacemaker with transvenous electrode(s); atrial
41512	Tongue base suspension, permanent suture technique
41530	Submucosal ablation of the tongue base, radiofrequency, 1 or more sites, per session
42160	Destruction of lesion, palate or uvula (thermal, cryo or chemical)
42950	Pharyngoplasty (plastic or reconstructive operation on pharynx)
64568	Incision for implantation cranial nerve (eg, vagus nerve) neurostimulator electrode array and pulse generator
0466T	Insertion of chest wall respiratory sensor electrode or electrode array, including connection to pulse generator (List separately in addition to code for primary procedure)

HCPCS Codes	Description
C9727	Insertion of implants into the soft palate; minimum of three implants
S2080	Laser-assisted uvulopalatoplasty (LAUP)

Considered Experimental/Investigational/Unproven when used to report cautery-assisted palatal stiffening operation (CAPSO), injection Snoreplasty, or transpalatal advancement pharyngoplasty:

CPT®* Codes	Description
42299	Unlisted procedure, palate, uvula

Considered Experimental/Investigational/Unproven when used to report electrical devices (e.g., Night Shift™ Sleep Positioner) or Provent™ Professional Sleep Apnea Therapy Device:

HCPCS Codes	Description
E1399	Durable medical equipment, miscellaneous

Considered Experimental/Investigational/Unproven when used to report electrosleep therapy:

CPT®* Codes	Description
95999	Unlisted neurological or neuromuscular diagnostic procedure

Considered Experimental/Investigational/Unproven when used to report tongue implant (e.g., ReVent System):

CPT®* Codes	Description
41599	Unlisted procedure, tongue, floor of mouth

*Current Procedural Terminology (CPT®) ©2017 American Medical Association: Chicago, IL.

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