**SAMPLE APPEAL LETTER FOR THE remedē® SYSTEM - DEVICE REPLACEMENT**

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**Instructions for completing the sample appeal letter:**

1. Please customize the appeals template based on the medical appropriateness of the **rem**edē® System for your patient. Fields required for customization are **highlighted in yellow**.
2. It is important to provide the most complete information to assist with the appeals process.
3. After you have customized the appeals letter, please make sure to delete any specific instructions for completion that are highlighted throughout the letter so the health plan does not misinterpret this as a form letter.
4. If you have questions, please contact 1-952-540-4470 or email reimbursement@remede.zoll.com.

**LETTER OF PRESERVICE AUTHORIZATION APPEAL FOR THE remedē® SYSTEM PROCEDURE**

[Date]

To: [Insurance Company]

[Address]

[City, State, Zip]

Re: Request for Appeal of Denial for Preservice Prior Authorization for **transvenous phrenic nerve stimulation**

Patient: [Patient Name]

Group/policy number: [Number]

Diagnosis: **Central Sleep Apnea, G47.31**

Dear Sir or Madam:

I am writing on behalf of my patient, [PATIENT FULL NAME], to request reconsideration of coverage for the surgery and post-surgical care associated with the replacement device insertion of the **remedē® Phrenic Nerve Stimulation System**.

Prior authorization was denied by [Health plan name]for prior authorization and insurance coverage because [STATE REASON GIVEN IN DENIAL LETTER] as indicated in the enclosed letter dated [INSERT DENIAL LETTER DATE]. It is my position that the denial for this procedure is unwarranted and unsupported by the patient’s current medical status and is inconsistent with currently accepted medical practice. I have included information about my patient’s medical history and diagnosis of ***Central Sleep Apnea***, a statement summarizing my treatment rationale, and other documents that support the medical necessity of transvenous phrenic nerve stimulation in this clinical case.

**Demonstrated Medical Necessity**

[Patient full name]suffered from [□ Chronic fatigue/lack of energy □ Excessive daytime sleepiness □Memory/concentration problems □ Mood changes, such as depression or irritability □ Headaches □ Nighttime gasping]. [He/she] had attempted and failed conventional treatment including [□ supplemental oxygen therapy □ pharmacotherapy □ CPAP/mask desensitization □BiPAP] yet symptoms persisted that interfered with [his/her] safety, wellbeing and quality of life. [He/she] underwent insertion of the **remedē® Phrenic Neurostimulator** on[date] and has demonstrated meaningful clinically improvement.

[His/her] quality of life and well-being is greatly impacted by CSA and my medical judgment is that [patient name] will benefit greatly from ***continued phrenic nerve stimulation therapy*** which requires a device replacement at this time. Since being treated with phrenic nerve stimulation, [he/she] has shown marked improvement in their CSA and a significant improvement in their overall quality of life as documented by sleep apnea study measures including: [improvement of total AHI, Central Apneas/hour reduction, Mixed Apneas/hour reduction, Hypopneas/Hour reduction, Oxygen Desaturation Events/Hour reduction, improvement in REM sleep, improvement in CSA symptoms]. Without treatment [he/she] is also at risk for severe comorbid medical conditions including [Heart Failure, Atrial Fibrillation], increased risk of motor vehicle accident and reduced daytime productivity due to chronic fatigue.

In order to maintain this therapy benefit, the remedē IPG is required to be replaced due to [REASON (e.g. battery depletion)]. The [battery depletion] was indicated [by the elective replacement indicator (ERI) or end of life indicator (EOL)] shown on the device interrogation report dated [DATE OF REPORT]. According to the remedē System Clinician Use Manual, the remedē IPG replacement should occur as soon as possible given only an estimated 3 weeks of normal operation remain once the ERI is triggered. When the EOL indicator is shown, stimulation therapy has been disabled and the patient will not receive any therapy until the remedē IPG is replaced.

**Unmet Clinical Need**

Central sleep apnea (CSA) is caused by a delay in the brain’s response to changes in carbon dioxide (CO2) levels whereby the brain does not initiate breathing until the CO2 level has raised significantly above the normal level. This results in rapid deep breathing to expel the excess CO2 and continues until the CO2 level is far below normal levels. This leads to an extended “pause” of breathing, ranging in duration from roughly 10 to 40 seconds. Each episode results in surges of nor-epinephrine and hypoxia, increasing elapsed time below an oxygen saturation of 90%. CSA differs from Obstructive Sleep Apnea (OSA) in that OSA occurs as a result of the muscles in the upper airway relaxing or collapsing during sleep, narrowing the breathing passage, and impeding air flow.

Patients with CSA suffer from sleep disruptions and insufficient sleep as evidenced by frequent apneic and hypopneic events, oxygen desaturations, and increased arousals. CSA patients undergo hundreds of repeated cycles of oxygen desaturation, arousals and surges in sympathetic drive as demonstrated in the remedē® pivotal trial where patients averaged 45 events per hour.11 Sleep disruption results in life altering chronic fatigue, excessive daytime sleepiness, cognitive impairment, and depression, which substantially reduces quality of life.

The CSA cycle leads to repeated cycles of oxygen desaturation and increased sympathetic drive. Within the heart failure population, where CSA is most prevalent, CSA has been shown to double the risk of cardiovascular mortality and significantly increase the rate of heart failure hospitalizations.[[1]](#footnote-1),[[2]](#footnote-2) ONLY KEEP IF PATIENT HAS HEART FAILURE

**Comparison of Current Treatment Options for Central Sleep Apnea**

Three forms of positive airway pressure or PAP have been used to treat CSA despite the poor quality of evidence:

* ***Continuous positive airway pressure*** (CPAP), is considered a standard first line therapy for OSA. In contrast, its role in CSA is less certain, due to the different underlying pathophysiology and the lack of robust data from randomized studies. Even so, many physicians have considered PAP an initial treatment of CSA, in part due to an obstructive component in some cases of CSA, the relative low cost and simplicity of PAP, and the lack of other treatment options. However, it is

important to note that the FDA approved indication for PAP does not include CSA and the underlying pathophysiology is fundamentally different between OSA and CSA.[[3]](#footnote-3)

* ***Bilevel Positive Airway Pressure*** (Bi-PAP) offers positive airway pressure in a spontaneous timed mode. Bi-PAP does not have an approved indication for CSA and there have been no randomized, controlled trials of Bi-PAP in the treatment of CSA.5
* ***Adaptive-Servo Ventilation*** (ASV), Another form of PAP therapy, Adaptive-Servo Ventilation (ASV), is recommended by the American Academy of Sleep Medicine (AASM) to normalize the apnea-hypopnea index (AHI) for the treatment of CSA related to CHF in adults with an ejection fraction > 45% or mild CHF.[[4]](#footnote-4) However, ASV has been shown to increase mortality in patients with reduced ejection fraction and FDA has issued a black box warning against usage of ASV with these patients.[[5]](#footnote-5)

***Oxygen Therapy*** has a history of use to treat CSA. Although oxygen therapy is often considered for CSA patients, it suffers from a similar lack of evidence as pharmacological therapy. There have been no large, positive randomized controlled trials supporting its use for treating CSA.

***Pharmacological Therapy*** with respiratory stimulants can also be tried with CSA patients. However, no respiratory stimulant medication is labeled for CSA and the data available to support their use for CSA is limited to very short studies with very small study groups. Acetazolamide, which is more commonly used to treat altitude sickness, has been studied in one study with a treatment cohort of 12 patients for 6 days. The CSA data for theophylline is comprised of one randomized study following 15 patients with CSA and heart failure over 5 days of therapy and a second study that was non-randomized and evaluated only 13 patients for a duration of just 5–7 days.[[6]](#footnote-6) Respiratory stimulant therapies are significantly associated with side effects.[[7]](#footnote-7) The potential adverse effects include cardiac arrhythmias and central nervous system excitability that require close monitoring making them a poor choice for CSA, particularly in patients with concurrent cardiac disease.

The ***remedē System*** consists of an implantable neurostimulator of the phrenic nerve that is designed to stabilize the breathing pattern and restore sleep throughout the night for patients with CSA. The system activates automatically at night removing compliance issues and the need for patient interaction. By stimulating the nerve that controls the diaphragm, it utilizes a physiologic mechanism similar to natural breathing.

**Phrenic Nerve Stimulation with the** **remedē® System**

The **remedē® System** is the ***only*** device approved by the FDA (PMA P160039, October 2017) as a transvenous **implantable phrenic nerve stimulator indicated to treat moderate to severe central sleep apnea (CSA) in adult patients**.

The system includes an implantable pulse generator (IPG) and a transvenous lead for unilateral stimulation of the phrenic nerve as well as a sensing lead, as needed. The remedēIPG is programmed via telemetry using the remedēsystem programmer.

Key outcomes of the **remedē® Phrenic Nerve Stimulation System** include:

* In an RCT, the remedē system showed clinically meaningful results in AHI (apnea- hypopnea index) reduction, improved oxygen saturation, and a range of important sleep metrics for CSA patients.[[8]](#footnote-8)
* The treatment effects are clearly durable over time, with clinical data demonstrating sustained treatment effect to 12, 24, 36 and 60 months.[[9]](#footnote-9),[[10]](#footnote-10),[[11]](#footnote-11)
* Patient compliance is assured by automatic nightly therapy activation.
* Post hoc clinical data suggests the remedē system produces comparable treatment effects in CSA patients with and without HF.[[12]](#footnote-12)
* Post hoc clinical data demonstrated TPNS improves CSA in patients who either previously used PAP and stopped (for reasons such as poor tolerability or ineffective therapy) or were PAP-naïve (no prior PAP therapy attempted).[[13]](#footnote-13)
* There is a strong safety profile.11

**Clinical & Economic Value Evidence**

The following evidence will assist you in your evaluation of the technology and indications for the remedē system:

In the pivotal randomized, controlled, multicenter trial, 151 patients were implanted with the remedē transvenous phrenic nerve stimulation system and demonstrated a significant reduction in the severity of central sleep apnea including improvements in sleep metrics, quality of life, and procedure toleration. The mean central apnea index (CAI) was reduced by 81% in the treatment group versus 11% in the control group at the 6 month visit, and 87% of the treated patients experienced a reduction in the apnea hypopnea index compared to 48% in control. Improvement in quality of life was reported by 79% and 12% of treated and control subjects at 6 months, respectively. Ninety-one percent of subjects did not experience a serious adverse event related to the implant procedure, device or delivered therapy through 12 months post implant. Of the nine percent experiencing an event, none of the events led to death and all resolved without sequelae.8 The implant success rate was high (97%) and serious implant procedure related complications, including lead dislodgements, were low and comparable to those of other implantable transvenous systems.8

The follow up to the pivotal trial included both a 12-month follow up on the treatment population and 6-month results from a second treatment cohort of patients from the original control group. This study demonstrated that the severity of sleep apnea, sleep metrics and quality of life measure were sustained from 6 to 12 months. Following 12 months of therapy, the treatment group experienced a 93% reduction in the mean of the central apnea index, and, 91% of patients experienced a reduction in their overall apnea/hypopnea index from baseline to 12 months. Additionally, 82% of patients experienced an improvement in their quality of life and 95% of implanted patients would elect to have the procedure again. In addition, this study showed that the results were replicated in the second cohort of patients treated, with similar improvements in sleep metrics, quality of life and a strong safety profile.9

The long-term efficacy and safety of phrenic nerve stimulation was assessed on patients from the pivotal trial for 60 months. Sleep metrics show consistent and sustained improvement throughout the follow-up period. Serious adverse events adjudicated as related to the implant procedure, device or delivered therapy occurred in 10% of patients (15/151) through the 24-month visit with no additional related SAEs reported between 24-60 months.10,11 This data supports the beneficial effects of long-term phrenic nerve stimulation in patients with CSA are sustained through 5 years.

Phrenic nerve stimulation to treat central sleep apnea has been studied in over 275 patients with significant improvements in key clinical measures, improved patient satisfaction, and a strong safety profile. Seven peer-reviewed clinical studies, including a randomized controlled pivotal trial with 151 patients have been published. A summary of the clinical evidence is included for your review.

Your prompt and thorough review and approval of this appeal is appreciated to support access to this vital and beneficial treatment for your member. Please contact me if you need additional information or to discuss.

Sincerely,

Physician Name

**Enclosures:**

Appeal Form (if provided by plan)

Chart notes including sleep study test results

FDA Letter

Clinical Fact Sheet/Evidence Table

1. Khayat R et al. Central sleep apnea is a predictor of cardiac readmission in hospitalized patients with systolic heart failure. J Card Fail 2012;18:534–40. [↑](#footnote-ref-1)
2. Khayat, R et al. Sleep disordered breathing and post-discharge mortality in patients with acute heart failure, European Heart Journal 2015;36 1463–1469. [↑](#footnote-ref-2)
3. Federal Register. “Classification of the Positive Airway Pressure Delivery System.” 83 FR 52964: 52964-52966. [↑](#footnote-ref-3)
4. Aurora et al. Updated Adaptive Servo-Ventilation Recommendations for the 2012 AASM Guideline. *Journal of Clinical Sleep Medicine* 2016; Vol. 12, No. 5: 757-761 [↑](#footnote-ref-4)
5. Cowie et al. Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure. *The New England Journal of Medicine* 2015. [↑](#footnote-ref-5)
6. Aurora et al., SLEEP, 2012;35:17-40. [↑](#footnote-ref-6)
7. Costanzo, et al. JACC 2015; 65: 72-84. [↑](#footnote-ref-7)
8. Costanzo MR, Ponikowski P, Javaheri S, et al. Transvenous neurostimulation for central sleep apnea: a randomised controlled trial. *Lancet*. 2016;388(10048):974–982. [↑](#footnote-ref-8)
9. Costanzo MR, Ponikowski P, Javaheri S, et al. remedē System Pivotal Trial Study Group. Sustained 12 Month Benefit of Phrenic Nerve Stimulation for Central Sleep Apnea. *Am J Cardiol.* 2018; 121:1400-1408 [↑](#footnote-ref-9)
10. Fox H, Oldenberg O, Costanzo MR, et al. Long-term efficacy and safety of phrenic nerve stimulation. Sleep. doi.org/10.1093/sleep/zsz158. [↑](#footnote-ref-10)
11. Costanzo MR et al. Transvenous phrenic nerve stimulation for treatment of central sleep apnea. Five-year safety and efficacy outcomes. Nat Sci Sleep 2021: 13 515-526. [↑](#footnote-ref-11)
12. Costanzo MR, Ponikowski P, Coats A, et al. Phrenic nerve stimulation to treat patients with central sleep apnea and heart failure. *Eur J Heart Fail* 2018;20:1746-1754. [↑](#footnote-ref-12)
13. Schwartz AR, Goldberg LR, McKane S, Morgenthaler TI. Transvenous Phrenic Nerve Stimulation improves central sleep apnea, sleep quality and quality of life regardless of prior positive airway pressure-treatment. Sleep and Breathing. 2021 Mar 20. [↑](#footnote-ref-13)