remedē® System

PATIENT PATHWAY GUIDE

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THE remedē® SYSTEM PATIENT PATHWAY GUIDE

Overview and Justification

The **rem**edē® System was approved by the FDA in 2017 for the treatment of moderate to severe central sleep apnea (CSA) in adult patients. The device delivers phrenic nerve stimulation therapy to restore normal nighttime breathing. 151 patients with CSA, who had an Apnea Hypopnea Index (AHI) ≥ 20 events/hour and a Central Apnea Index (CAI) of at least 50% of all apneas, were enrolled in the **rem**edē Pivotal Trial. 91% of patients in the trial experienced an improvement in AHI at 12 months, while 79% had improvement in quality of life. Moreover, improvements in central apnea events, arousals, sleep quality and daytime sleepiness were maintained through 36 months in both the treatment and former control groups. The pivotal trial demonstrated a strong safety profile as well with 91% freedom from serious adverse events (SAE).[1,2]

Patient Pathway Description

In working with many different institutions with **rem**edē programs, we have established that the **rem**edē patient pathway can be divided into four distinct phases: Screening for sleep disordered breathing, patient selection, device implant, and therapy optimization and follow up. Each of these phases will be outlined in this document. The protocol examples herein are based on experience with programs of varying size and structure and are provided to guide successful development of a clinical pathway for patients who may benefit from treatment with the **rem**edē System.

The remedē Patient Pathway

PHASE 1 — SCREENING FOR SLEEP DISORDERED BREATHING

Background and Prevalence of SDB

Sleep disordered breathing (SDB) is estimated to affect up to 2 million Americans, with 80% of those patients having predominantly Obstructive Sleep Apnea (OSA), and about 20% having predominantly Central Sleep Apnea (CSA).[3] However, CSA is much more prevalent in cardiovascular patient populations.[4]

SDB is the most common comorbid condition in patients with heart failure (HF), as nearly three-quarters of all heart failure patients have some form of SDB. It is estimated that half of those suffer from predominantly Central Sleep Apnea.[4] Additionally, approximately 40% of patients with heart failure with reduced ejection fraction (HFrEF) have CSA.[5] CSA is associated with a two-fold increase of both HF hospitalizations and mortality among HF patients and can cause symptoms that resemble those commonly associated with HF.[6-8] Additionally, CSA has predicted new-onset HF in long-term prevalence studies.[9]

SDB is also prevalent in patients with Atrial Fibrillation (AF), with an estimated 74% of patients with AF having some form of SDB.[10] CSA is associated with a 2- or 3-fold increase in risk of developing AF.[11]

Pre-Screening Questionnaires

Patients with CSA often do not display common symptoms associated with SDB such as snoring and daytime sleepiness.[12] Common pre-screening questionnaires have not been validated in CSA and can fail to identify these patients, but can help identify risk factors for and symptoms of SDB.[12,13] The Epworth Sleepiness Scale (ESS), STOP-BANG and the Berlin Questionnaire have all be shown to have limited reliability in patients with cardiovascular (CV) disease.[13] Literature suggests that STOP-BANG scoring of ≥ 3 may be more reliable for detecting SDB in CV.[14] More general questions to assess HF patients for symptoms of excessive daytime fatigue, observed apneas, nocturnal dyspnea and impaired cognition may more accurately identify patients who need further screening for sleep apnea.[15] Respicardia has an example of a generic, though unvalidated, questionnaire in the Unbranded Patient Educational Brochure, which is included in the resources for this section.

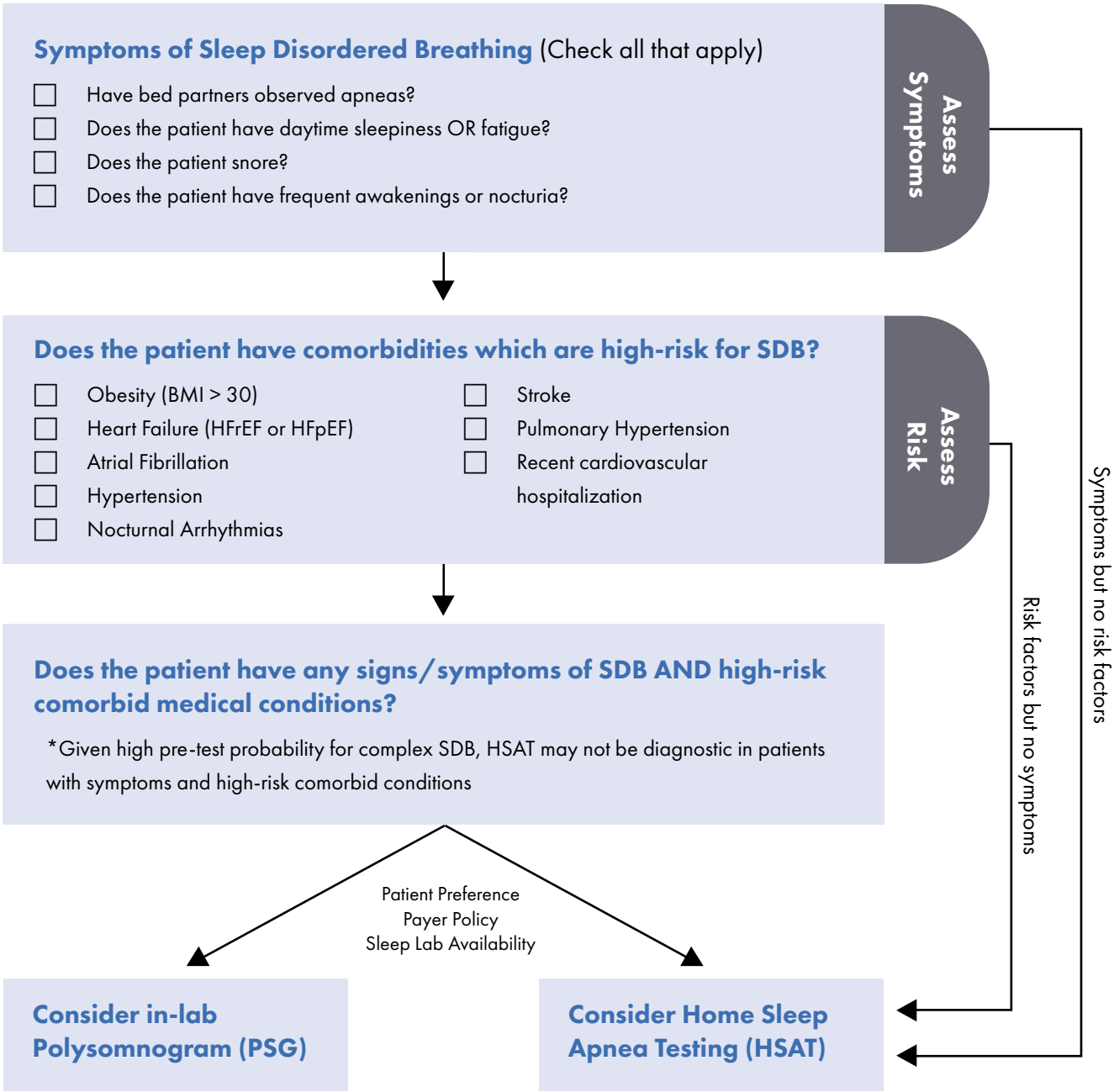
Opportunities for screening in cardiovascular settings include:

- Initial heart failure consultation visits
- Post discharge clinic visits following HF-related hospitalization
- Atrial Fibrillation patients prior to ablation procedures
- Cardiac device patients with documented Implantable Cardiac Defibrillator (ICD) shocks or arrythmias, particularly during nighttime hours

Sleep Apnea Testing

Sleep apnea testing can be performed with either home testing equipment (HSAT) or through in-lab polysomnography (PSG). Several available HSAT units can differentiate between obstructive and central apnea events, but home studies tend to underestimate the disease due to their inability to assess sleep time.[16] Patients with complex sleep apnea or other sleep-related issues may require PSG to accurately diagnose the burden of SDB. However, many factors including patient preference, sleep lab availability and insurance payer criteria may contribute to testing decisions. Refer to **Figure 1** – Outpatient Sleep Testing Decision Tree Example for one pathway option. An order template for sleep testing is included in the resources for this section.

Figure 1 – Sleep Testing Decision Tree Example



FEELING TIRED AND FATIGUED?

POOR SLEEP MAY BE CONTRIBUTING TO YOUR HEART DISEASE.

Do you have trouble concentrating?

Have you ever been told that you stop breathing while you sleep?

Have you been told that you snore when you sleep?

Have you ever been told you have Atrial Fibrillation?

Have you ever been told you have Heart Failure?

Have you been told in the past that you had Sleep Apnea?

WHY IS IT IMPORTANT TO BE EVALUATED FOR SLEEP APNEA?

Sleep apnea is a common condition for heart failure and atrial fibrillation (AFib) patients.

Sleep apnea is a serious condition associated with **hospitalizations, heart attacks, and even death**[1,2]

Half of people with heart failure or AFib have **sleep apnea**[3,4]

Sleep apnea symptoms – **fatigue, brain fog, and sleepiness** – are similar to those of heart failure and AFib

Sleep testing can be done in a single night, and often **in your own home**

Many treatment options are available, including those that **don't require a mask**

Talk to your healthcare provider today

to see if you should be tested for sleep apnea.

[1] Costanzo MR, et al. *J Am Coll Cardiol* 2015; 65:72–84.
[2] Khayat R, et al. *J Card Fail* 2012; 18:534–540.
[3] Arzt M, et al. *J Am Coll Cardiol* 2016; 4:116–125.
[4] Bitter T, et al. *Dtsch Arztebl Int* 2009; 106:164–170.
MKT 1286, Rev C

SLEEP STUDY ORDER FORM

Patient Name: _____ Date of Birth: _____

Insurance Info: _____

Ordering Provider: _____ NPI: _____

I. STUDY REQUESTED

☐ Unattended Home Sleep Apnea Test (HSAT) G0398, G0399, 95800, 95801, 95806

☐ Attended In-Lab Diagnostic PSG 95810

II. REQUIRED CLINICAL INFORMATION (CHECK ALL THAT APPLY IN A-D)

A. What is the Suspected Diagnosis?

☐ Sleep Apnea, unspecified G47.30 ☐ Hypersomnia, unspecified G47.10

B. Signs and Symptoms (check all the apply)

Evidence of Excessive Daytime Sleepiness	*AND*	**Evidence Suggestive of Sleep Disordered Breathing**
☐ Disturbed or restless sleep		☐ Gasping or choking during sleep
☐ non-restorative sleep/non-refreshing sleep		☐ Witnessed apnea events
☐ Frequent unexplained arousals from sleep		☐ Cognitive deficits such as concentration/memory
☐ Fragmented sleep		☐ Morning headache
☐ Fatigue		☐ Experienced Apneas/Hypoxemia under anesthesia
☐ Waking feeling tired		☐ Snoring

Duration of signs and symptoms: ☐ Less than one month ☐ Greater than one month

C. Co-morbid Conditions (check all that apply)

☐ Pulmonary Hypertension

☐ Moderate to severe pulmonary disease

☐ Moderate to severe congestive heart failure (NYHA class III or IV) or LVEF lower or equal to 45%

☐ Neuromuscular/neurodegenerative disorder

☐ Chronic opioid medication use (include current med list/fq/dose)

☐ Refractory Atrial fibrillation or nocturnal dysrhythmias

☐ No known comorbid conditions

D. Epworth Sleepiness Scale Score: *OR* **STOP-Bang Score:**

Note: Include the most recent clinical notes, medication list, neck circumference and BMI.

MKT 1994

PHASE 2 – PATIENT SELECTION: TREATMENT DECISIONS IN CENTRAL SLEEP APNEA

Alternative Therapies

Despite several therapeutic options for OSA, CSA treatment is less-well defined in clinical data. To date, mask-based pressure therapies, oxygen, and a small number of medications have been evaluated in the treatment of CSA.[18] These treatment modalities for CSA have demonstrated limited effectiveness, poor adherence, and potential safety concerns in some populations.[17,19] Specifically, Adaptive Servo-Ventilation (ASV) is contraindicated in patients known to have heart failure with left ventricular ejection fraction of <45%.[18] CPAP and other therapies may be appropriate as first-line treatment in some patients with CSA.[20] Patients should be seen for follow up evaluation to assess effectiveness, compliance and tolerability based on individual clinical discretion. **Figure 2** illustrates one potential decision algorithm that may be used for determining candidacy for **rem**edē therapy.

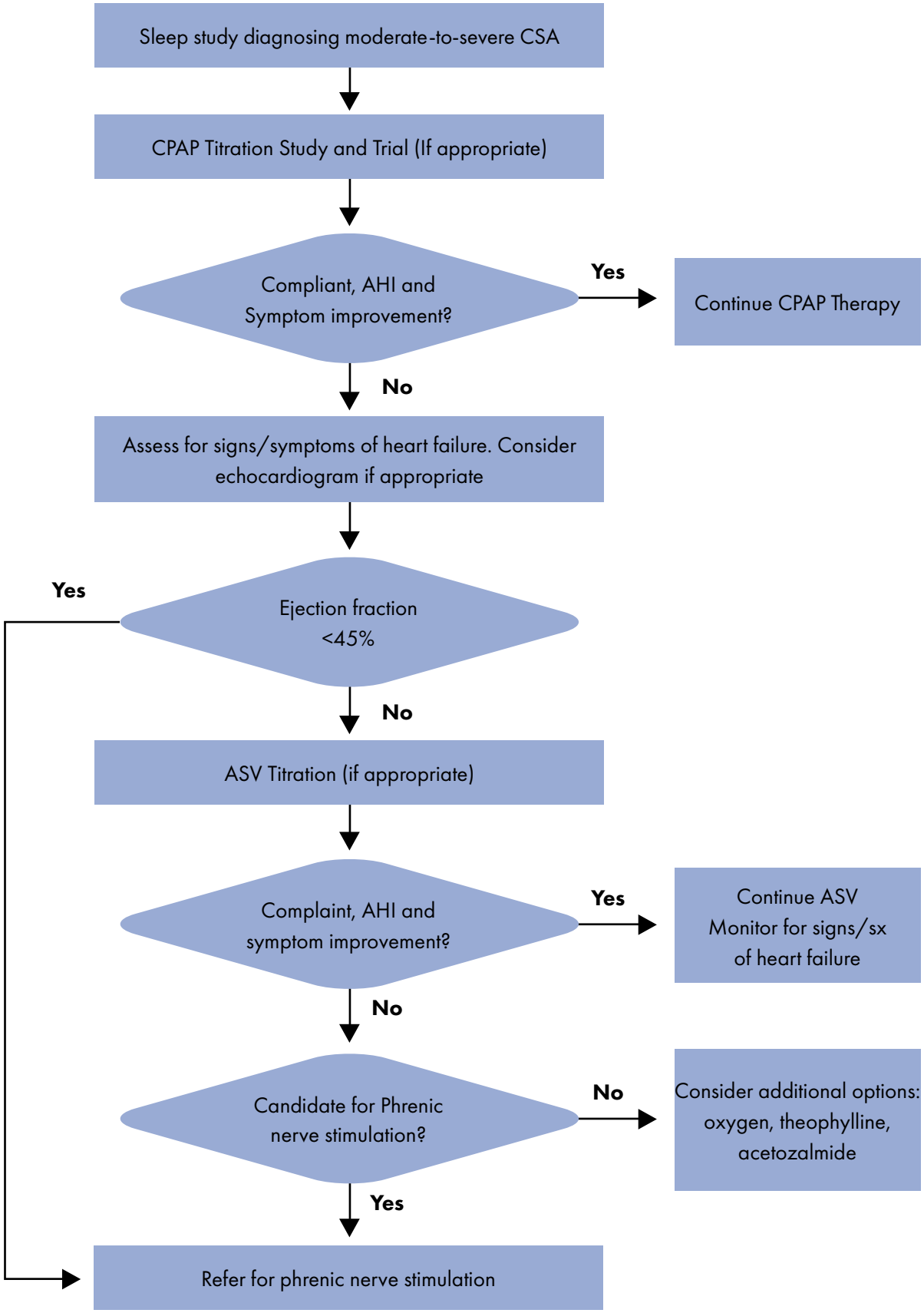
Identifying Existing CSA Patients

Patients previously established in sleep medicine clinics with CSA-predominant SDB can be identified though searching existing databases, including electronic medical records (EMR), sleep software databases, and compliance software programs used to monitor PAP use for multiple durable medical equipment (DME) companies. Such database searches are easy to perform and typically do not require facility Information Technology (IT) personnel to conduct.

Patient Education for the remedē System

Once patients are identified as potential candidates for the **rem**edē System for treatment of CSA, discussion about the device often occurs in both Sleep Medicine and Electrophysiology clinic settings. Patients and caregivers most often have questions and concerns about the implant procedure and how the therapy feels when active, along with general questions about CSA. The implant procedure is reviewed in section 3 below. Patients are often reassured that electrophysiologists perform similar procedures, such as pacemaker implants daily. An outline for patient discussion, as well as some of the most frequently asked questions are provided in the following pages. Patient brochures describing the therapy and procedure, as well as, the **rem**edē Frequently Asked Questions booklet are available for these discussions from your **rem**edē representative.

Figure 2 – remedē® Patient Selection Pathway Example



remedē Awareness Patient Letter Template

Dear, _____

Our records indicate that your last visit for sleep apnea follow up was DATE. Dr XX (or provider) would like to schedule a follow up visit to talk about how you are sleeping and whether your [insert current therapy] is working for you. Since your last follow up, we have new treatment options available that could potentially help treat your sleep apnea without the use of a mask at night.

At your earliest convenience, please call the [Sleep Medicine department at PHONE], Monday through Friday, 8:00 am to 4:00 pm to schedule an appointment. If you have any questions before your visit, please feel free to call us.

Dear, _____

When reviewing you CPAP data, we noticed that you may be having issues wearing your mask, or that it is not working ideally. [insert Dr/provider name] would like to schedule a follow up visit to talk about how you are sleeping and whether your [insert current therapy]) is working for you. New treatment options are now available that could potentially help treat your sleep apnea without the use of a mask at night.

At your earliest convenience, please call the [Sleep Medicine department at PHONE], Monday through Friday, 8:00 am to 4:00 pm to schedule an appointment. If you have any questions before your visit, please feel free to call us.

Review Central Sleep Apnea

- Obstructive vs Central Sleep Apnea
- **rem**edē website resource: remede.zoll.com/central-sleep-apnea/about-csa
- Review any past treatment experiences the patient has tried

How remedē works to treat CSA

- Overview video can be used here: remede.zoll.com/remede-system
- Show demo device

remedē Implant Procedure

- Implant typically outpatient procedure in cardiac cath lab
- Very similar to pacemaker implantation by cardiac electrophysiologists
- Video overview of implant and post-operative care available

Device Activation and Follow Up

- Therapy activated at a clinic visit 4-6 weeks following the implant procedure
- How the therapy activates (See FAQ)
- How the therapy feels (See FAQ)
- Hear from other **rem**edē patients: remede.zoll.com/patients/hear-from-others

Central Sleep Apnea

What is the difference between Central Sleep Apnea (CSA) and Obstructive Sleep Apnea (OSA)?

Obstructive sleep apnea (OSA) and central sleep apnea (CSA) are both types of sleep apnea. In OSA, the breathing muscles (e.g. diaphragm) are activated appropriately but a narrowing of the passages in the upper airway (the tongue or throat) cause a blockage that prevents air from flowing freely. The obstruction can be due to bodily features or a relaxation of the muscles in the chest and neck during sleep. In CSA, the brain fails to send regular signals to the diaphragm. The lack of consistent signals leads to irregular nighttime breathing. Some people have both OSA and CSA and this is sometimes called complex sleep apnea. Determining how to address complex sleep apnea will take consideration and consultation with your physician regarding managing the complete picture of your sleep apnea.

The remedē® System

What is remedē?

remedē is a pacemaker-like device that stimulates your breathing muscles (via the phrenic nerve) to restore a normal breathing rate and rhythm during sleep. It is fully implantable and activates automatically each night.

How does remedē work?

remedē activates automatically each night to send signals to your diaphragm from the phrenic nerve to restore a normal breathing pattern. The signals cause your diaphragm to contract, drawing air into your lungs, just as in normal breathing. **rem**edē also monitors breathing signals while you sleep. Because the device is implanted and activates automatically, it does not require wearing a mask or other equipment at home.

What does remedē feel like?

In our experience, most people describe their first breaths with **rem**edē as taking a breath that you didn't plan on. Once activated, **rem**edē is designed to turn on once you are already asleep and operate without waking you up.

When will remedē activate at night?

The **rem**edē System is programmed to automatically begin therapy each night when **all three** of the following programmable conditions are met:

1) **Sleeping hours:** It is within your normal sleeping times; (for example, 11:00 PM to 6:00 AM)
2) **Sleeping posture:** You are in a sleeping posture (for example, a horizontal position)
3) **Activity:** Your activity level is representative of a sleeping or resting condition

Can I pause or turn remedē off?

If you roll over, sit up, or get out of bed, the therapy will pause and resume once the above three conditions are once again met.

The Implant Procedure

What are the risks associated with the remedē procedure or therapy?

As with any surgically implanted device, there are risks related to the implant procedure which may include, but are not limited to, pain, swelling and infection. Once the **rem**edē System is implanted and the therapy is activated, some people may experience discomfort from the therapy and/or from the presence of the device. The majority of these events are resolved on their own or by adjusting the therapy settings. The **rem**edē System may not work for everyone. There are additional risks associated with removing your system. If you and your doctor decide to remove the system, another surgery will be required.

What happens during the procedure?

The **rem**edē System is placed during a minimally invasive procedure by a cardiologist. The system is a battery powered device placed under the skin in the upper chest area with two small thin wires (leads), one to deliver the therapy (stimulation lead) and one to sense breathing (sensing lead).

How long does the battery last?

The latest models of the remedē System have batteries that typically last between 4-6 years. Some people may not need replacement for over 6 years. However, if higher levels of therapy are needed to normalize breathing, the battery may need to be replaced in 2 years or less.[21]

Will I have any limitations following the procedure?

Follow all advice from your doctor after the procedure. Most people can resume normal activity 7-10 days after he procedure. In most cases, your doctor will advise you to not raise your arm above the shoulder on the side the device is placed for 1-3 months.

What follow up visits are required?

You typically return about one month after implant to activate therapy. During this time, you recover and the device collects data on your sleeping and breathing patterns. At the visit, the clinician will activate and program **rem**edē to meet your needs. People typically return for additional clinic appointments to adjust programming and titrate the therapy. Once optimized, most clinicians will follow up 1-2 times per year.

Coverage and Cost

How much will I have to pay for remedē?

The hospital will work with your insurance plan to determine what, if any, of the cost is billed to you. Talk to your physician about insurance coverage, as many insurance companies work with clinicians to evaluate coverage for **rem**edē based on your individual case.

Is this therapy covered by insurance?

remedē is generally being reviewed for approval by insurance providers on a case-by-case basis. After determining that you are a candidate for **rem**edē, your doctor and their office staff will work with your insurance provider on securing coverage for the procedure.

What happens if the procedure is denied by my insurance company?

In most cases, you are able to appeal a denial by your insurance company and request further review of your case. Ask your physician about the **rem**edē Patient Access Program, which provides resources for supporting insurance prior authorization appeals.

remedē Awareness Referral Letter Template

remedē Awareness Referral Letter Template

[PHYSICIAN'S LETTERHEAD]

[DATE]
[DR. NAME]
[CENTER]
[ADDRESS]
[CITY, STATE ZIP]

Dear Dr. [NAME]:

As a [SLEEP PHYSICIAN OR INSERT OTHER PHYSICIAN SPECIALTY], you likely encounter patients who suffer from central sleep apnea (CSA). CSA is a serious breathing disorder leading to poor cardiovascular outcomes and negatively affecting quality of life. While some patients with CSA can be treated adequately, others may fail to respond to available treatment options and remain symptomatic. Mask intolerance, inability to effectively titrate, poor long-term compliance, and reduced ejection fraction all may be challenges you have encountered with central sleep apnea patients.

We now offer **rem**edē®, a therapy designed to treat central sleep apnea. remedē was FDA-approved for adult patients with moderate to severe CSA in 2017.[1] It is a fully implantable therapy that activates automatically each night. It uses electrical signals to stimulate the phrenic nerve and activate the diaphragm, maintaining a natural breathing pattern and rate while the patient is sleeping. It is approved for all etiologies of CSA, including CSA with concomitant heart failure.[1]

Phrenic nerve stimulation has shown through clinical trials to substantially improve sleep disordered breathing, sleep quality, and quality of life.[7]

- A mean reduction of 89% in the central apnea index from baseline to 12 months[2]
- Statistically significant improvements in apnea hypopnea index, arousals, oxygenation, and % REM sleep[2]
- 82% of patients reported an improvement in quality of life from baseline to 12 months[2]
- 95% of patients reported they would "elect to have the medical procedure again"[2]
- Peer-reviewed evidence, including 3-year efficacy and safety data recently published in SLEEP, can be found at remede.zoll.com/clinicians/publications

remedē is implanted by a cardiac electrophysiologist, in an outpatient procedure using similar techniques to a transvenous cardiac pacemaker implant. Therapy is activated approximately one month following implant. Patients typically require two or three additional appointments to fine-tune programmable therapy settings.

I would ask that as you evaluate patients in your daily practice, you consider referring patients who may be candidates for this therapy.

If you would like to learn more about the therapy or would like to discuss a specific case, please contact me directly at [INSERT PHONE OR EMAIL]. I look forward to working with you to offer an option for your patients.

Sincerely,

[DOCTOR NAME]
[TITLE]
[INSTITUTION]

PHASE 3 – **rem**edē® SYSTEM IMPLANT

Procedure Overview

The **rem**edē System implant procedure is typically performed by electrophysiologists (cardiologists specializing in cardiac device placement). The procedure is similar to contemporary techniques used to implant cardiac implantable electronic devices (CIEDs).[1,19] The implant procedure is performed in the cardiac electrophysiology laboratory under conscious sedation as the patient and physician must communicate during stimulation lead testing. Patient preparation and antibiotics are comparable to those used for (CIED) implants.[19] The **rem**edē System is placed in the pectoral region, typically on the right side. A single stimulation lead is placed in either the left pericardiophrenic vein or the right brachiocephalic vein. A sensing lead may be placed into the azygous vein to detect respiration. The **rem**edē Pivotal Trial demonstrated a 97% implant success rate, including those patients with concomitant cardiac devices.[1] Potential adverse events associated with the implant procedure are similar to those of cardiac device procedures and are detailed in the **rem**edē System Implant and Clinician Use Manual.[22]

Postoperative Considerations

Patient follow up after the implant is comparable to that of postoperative care for CIED procedures. A 7- to 14-day check of the surgical incision is recommended. To allow for lead stabilization and healing after the implant procedure, the **rem**edē System therapy should not be enabled for approximately 1 month following implant (**rem**edē® System Implant and Clinician Use Manual).[22] The **rem**edē device will be in monitoring mode during the period from implant to therapy initiation. This allows the device to collect information on the patient's sleeping patterns to include time, position, and hours of sleep.

Upon discharge, patients should be instructed as follows:

- It is normal to feel some discomfort from the surgical incision and to have some pain at the implant site for 2-6 weeks.
- It is best to limit the mobility of the right arm (or left arm if left-sided device placement) and avoid lifting the arm above shoulder level for several weeks after the implant procedure. This time period allows the leads and IPG to affix more securely in place and such movements could impair the healing process.
- Repetitive upper extremity activities and exercise can cause damaging stress and possible failure to permanent implanted leads. Active patients should be cautioned to avoid physical activities that could damage the implant site or the implanted system.
- Inform general practitioners and consulting physicians that the patient has an implanted stimulation system.
- Patients should carry the Device/Subject Identification Card at all times.

Resources

The following pages provide a procedure product reference guide and dictation template for the **rem**edē implant procedure.

remedē® System

Product Reference Guide

	ITEM	MANUFACTURER	PART/ORDER NUMBER	DESCRIPTION	RECOMMENDED INVENTORY ON HAND
Manufacturer Specific	PG	Respicardia (ZOLL)	1001, 1100, 1600	**rem**edē PG	2
	Lead	Respicardia (ZOLL)	4065, 4165, 4665	respi**stim** LQS, 65cm	2
	Lead	Respicardia (ZOLL)	3102, 3652	respi**stim** R Lead – 24mm dia., normal length	2
	Lead	Respicardia (ZOLL)	3103, 3653	respi**stim** R Lead – 20mm dia., extended length	Reps Carry
	Catheter	Respicardia (ZOLL)	7120-S	respi**guide** 120°	2
	Catheter	Merit Medical	57538CS-WOR	Impress 5F CS Catheter, 75cm	2
	Catheter	Merit Medical	57538CSV-WOR	Impress 5F CS VERT Catheter, 75cm	2
	Catheter	Merit Medical	1628-043	Impress 5F AZYGOS Right, 75cm	2
	Accessory	Pressure Products	SS-SA-09	9F Sealing Adapter	2
	Accessory	Respicardia (ZOLL)	1007	Test Adapter	Reps Carry
	Accessory	Medtronic	6232ADJ	Adjustable Slitter	2
Physician Preference	Guidewire	Physician preference		0.014" Floppy	3
	Guidewire	Physician preference		0.014" Stiff	2
	Guidewire	Physician preference		0.018"	2
	Guidewire	Physician preference		0.035" angled floppy	2
	Guidewire	Physician preference		0.035" access J-wire	2
	Catheter	Physician preference		9Fr Multipurpose Right Sided Coronary Sinus Guide Catheter	2
	Lead	Physician preference		IS-1 Bipolar CS (LV) Lead, 4Fr dia. preferred	1
	Accessory	Physician preference		Y-connector and hemostasis valve	2
	Accessory	Physician preference		IS-1 standard Port plug	4
	Accessory	Physician preference		8Fr x 13cm hemostatic introducer sheath, splitable	2
	Accessory	Physician preference		Disposable pacing cables	2
	Accessory	Physician preference		Programming Wand Sterile Sleeve	2
	Accessory	Physician preference		Guidewire Torque Device	2

Indication for use: The **rem**edē System is an implantable phrenic nerve stimulator indicated for the treatment of moderate to severe Central Sleep Apnea (CSA) in adult patients. **Contraindications:** The **rem**edē System is contraindicated for use in patients with an active infection or patients known to require magnetic resonance imaging (MRI). See the Instructions for Use for complete information regarding the procedure, indications for use, contraindications, warnings, precautions, and potential adverse events.
Rx Only.
The **rem**edē® System, **rem**edē® EL System, and **rem**edē® EL-X System have received FDA approval. The **rem**edē® System model 1001 has received CE Mark approval.

ZOLL MEDICAL CORPORATION

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For subsidiary addresses and fax numbers, as well as other global locations, please go to www.zoll.com/contacts.

Printed in the U.S.A.
MKT0021, Rev F

ZOLL®

DICTATION FORM

remedē® System

Date: Date

remedē Representative: _____

Patient Sticker:

Implanting Physician
Name:
Phone:
Hospital:

Following Physician	
Name:	Phone:
Hospital:	

remedē Information		
Model #:	Serial #:	Implant Date:

Lead Information				
	Company	Implant Date	Model #	Serial #
Left Stim	Respicardia (ZOLL)			
Right Stim	Respicardia (ZOLL)			
Sensing Lead				

Measured Data				
Cath(-)/Anode(+)	PW/Frequency	Thresholds: mA	Impedance: Ohms	ERS (Y/N)

Best Pair/Concomitant Testing						
Best Pair			Concomitant Device Testing			
Cath(-) Anode(+)	Output: mA/PW/Freq	Impedance (ohms)	Company	PPM/ICD/CRT	Output	Result

Explanted/Capped/Attempted Not Implanted				
Company	Model #	Serial #	Explant Date	Status

Device and Lead/s Stickers		
remedē	Sensing Lead	Stimulation Lead

Rx Only. The **rem**edē® System, **rem**edē® EL System, and **rem**edē® EL-X System have received FDA approval. The **rem**edē® System model 1001 has received CE Mark approval.

MedEd1866, Rev B

PHASE 4 – OPTIMIZATION AND FOLLOW UP OF THE **rem**edē PATIENT

Therapy Initiation Visit

- Four to six weeks following the implant procedure, the patient will be seen in clinic for therapy initiation. During this 1-hour visit, the **rem**edē device information will be analyzed and parameters customized to fit the patient's tolerability and sleeping patterns. The **rem**edē device will begin working that evening at the programmed sleeping start time, once it detects that the patient is in the sleeping posture and not moving. See the Patient Follow Up and Therapy Optimization Guide for detailed visit instructions.

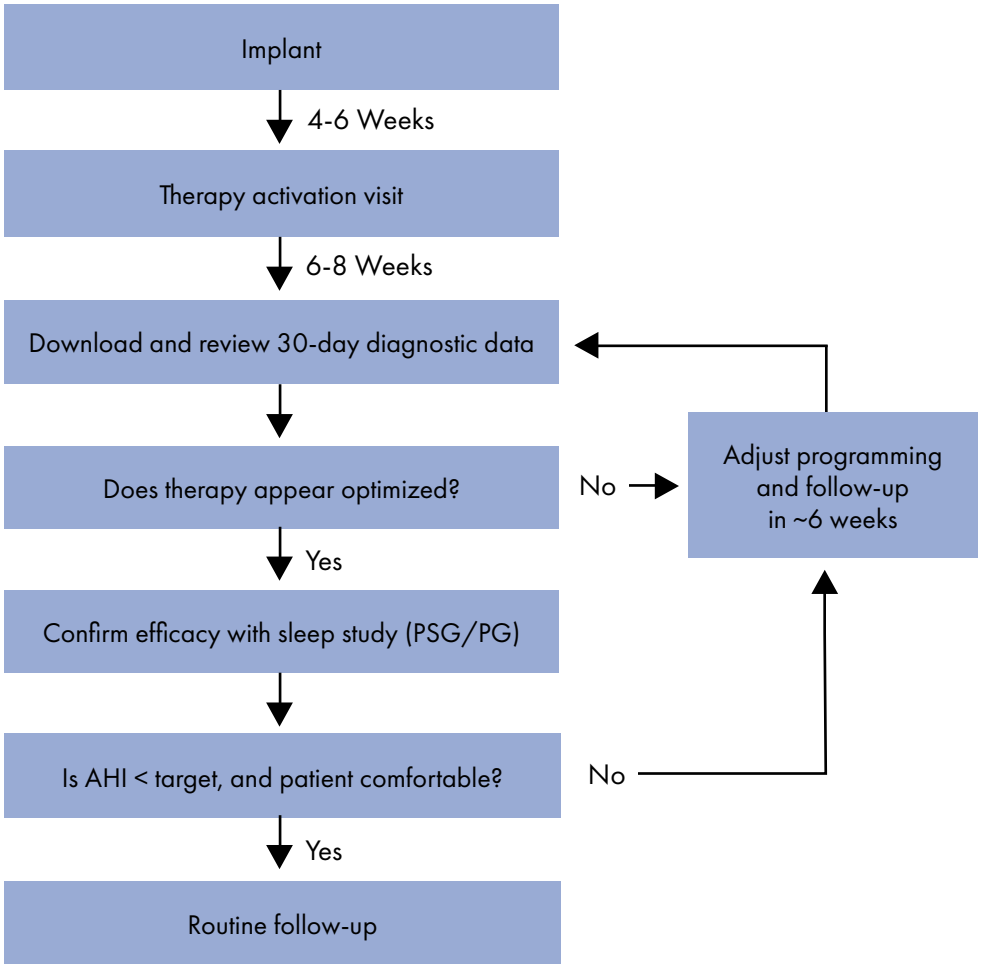
Therapy Optimization Visits

- Therapy optimization visits of approximately 30-45 minutes will be scheduled every 6 to 12 weeks to allow for device assessment and programming changes to obtain optimal therapy for each individual patient. Patients typically require 2-to-3 follow up visits to achieve optimal therapy settings. See the Patient Follow Up and Therapy Optimization Guide for detailed visit instructions.

Long Term Follow Up

- Once therapy is optimized, clinic visits of 15-20 minutes should occur every 3 to 6 months to review the patient's subjective information, device data, and battery status.

Figure 3 – remedē® Device Optimization and Follow Up Pathway



Goal of Therapy

The goal for treatment with the **rem**edē® System is to normalize breathing. This may, however, be limited by patient tolerance or airway obstruction.

Target AHI

The target AHI should be determined by the physician based on patient tolerance and therapy efficacy at the second visit.

Optimization

Optimization is defined as attaining the AHI goal or reaching the maximum tolerated stimulation.

References

[1] Costanzo, MR, et. al. Transvenous Neurostimulation for Central Sleep Apnoea: A Randomised Controlled Trial. *Lancet* 2016; 388: 974–82.
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[21] FDA PMA P160039, Supplement 006, Physician Manual.
[22] **rem**edē® System Implant and Clinician Use Manual.

Important Safety Information
The **rem**edē® System is indicated for moderate to severe Central Sleep Apnea (CSA) in adult patients. A doctor will need to evaluate the patient's condition to determine if the **rem**edē System is appropriate. Patients will not be able to have an MRI or diathermy (special heat therapies) if the **rem**edē System is implanted. The **rem**edē System may be used with another stimulation device such as a heart pacemaker or defibrillator; special testing will be needed to ensure the devices are not interacting. As with any surgically implanted device, there are risks related to the surgical procedure itself which may include, but are not limited to, pain, swelling, and infection. Once the therapy is turned on, some patients may experience discomfort from stimulation and/or from the presence of the device. The majority of these events are resolved either on their own or by adjusting the therapy settings. The **rem**edē System may not work for everyone. There are additional risks associated with removing the system. If it is decided to remove the system, another surgery will be required. Be sure to understand all of the risks and benefits associated with the implantation of the **rem**edē System. For further information please visit remede.zoll.com, call 952-540-4470 or email info@remede.zoll.com. **Indication for use:** The **rem**edē System is an implantable phrenic nerve stimulator indicated for the treatment of moderate to severe Central Sleep Apnea (CSA) in adult patients. **Contraindications:** The **rem**edē System is contraindicated for use in patients with an active infection or patients known to require magnetic resonance imaging (MRI). See the Instructions for Use for complete information regarding the procedure, indications for use, contraindications, warnings, precautions, and potential adverse events.
Rx Only.
The **rem**edē® System, **rem**edē® EL System, and **rem**edē® EL-X System have received FDA approval. The **rem**edē® System model 1001 has received CE Mark approval.

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