



remedē[®] System Patient Manual

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The remedē[®] System Patient Manual

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1.0 INTRODUCTION

You and your doctor are considering the use of the **remedē**[®] System to treat your central sleep apnea (CSA). This guide is intended to inform you about CSA and the **remedē** System therapy.

2.0 GLOSSARY

APNEA – a temporary stopping of breathing during sleep.

AROUSAL – short period when sleep is disturbed by waking or moving to a lighter stage of sleep.

CSA – Central sleep apnea (CSA) is a condition in which breathing stops and starts often during sleep. CSA occurs when your brain is not sending signals to the muscle that needs to move when you breathe

DIAPHRAGM – a large muscle that extends across the bottom of the chest that is used for breathing. As the diaphragm contracts (squeezes), the volume of the chest increases and air is drawn into the lungs.

LEAD – a small, thin wire which carries the electrical impulse from the device to your phrenic nerve and can send data about your breathing back to your device.

HYPOPNEA – slow or shallow breathing during sleep with a decrease in blood oxygen levels.

OSA – Obstructive sleep apnea (OSA) is caused by a blockage of the upper airway causing pauses in breathing during sleep despite the effort to breathe.

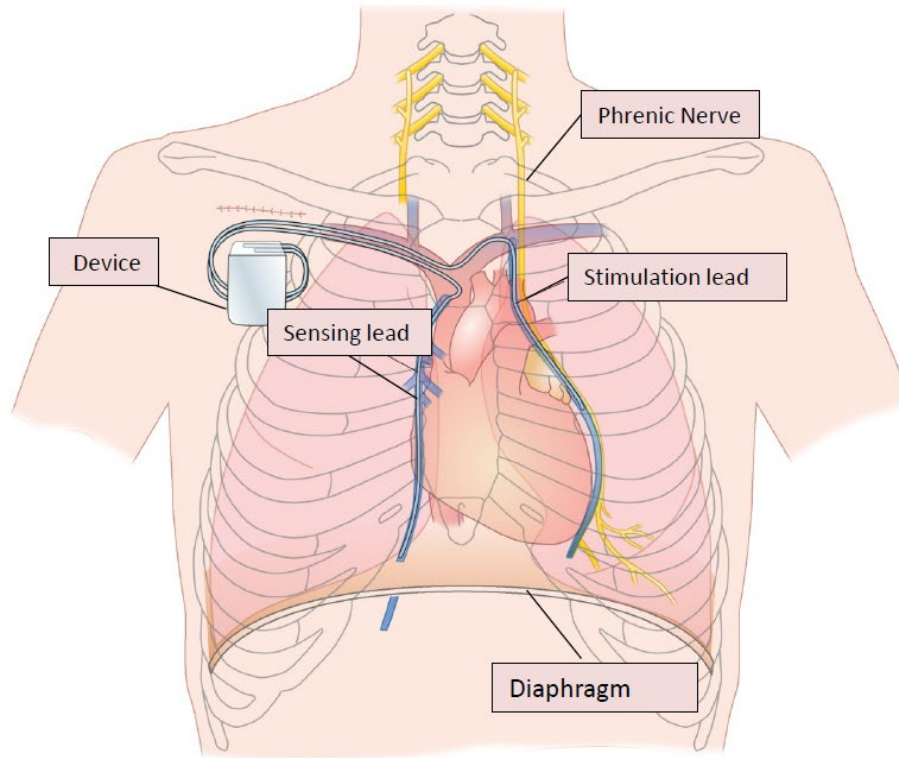
PHRENIC NERVE – a nerve that goes from the brain through the chest to the diaphragm. It carries data from the brain to signal when the diaphragm should contract.

3.0 WHAT IS THE REMEDĒ[®] SYSTEM

The **remedē**[®] System is a treatment option for adult patients with moderate to severe CSA. The device is an implantable system which uses stimulation of a nerve in the chest (phrenic nerve) to send signals to the large muscle between the chest and abdomen (the diaphragm). These signals stimulate breathing in the same way that the brain signals breathing.

This treatment starts and stops on its own and does not require you to wear anything on your face. No equipment is needed at home. The **remedē** System includes a battery powered device placed under the skin in the upper chest area, a thin wire (lead) to deliver the therapy (stimulation lead), and a second, optional lead to sense breathing (sensing lead). These leads are placed in blood vessels in the chest.

The picture below shows the device placed under the skin in the upper chest, the lead placed in a blood vessel near a phrenic nerve, the lead used to sense breathing and the muscle that moves when you breathe (diaphragm).



After implantation during an office visit, your doctor will make changes to the device using a computer, similar to a tablet computer. The computer is connected to a small device called a wand similar in size to a remote control for a television. The wand is placed over your device and allows the doctor to program it and evaluate the therapy. Your doctor may use information from a sleep study completed at home or in the sleep laboratory to assist in programming the device.

After programming the device, your system will automatically turn on when you lie down and rest during your normal sleep time. While therapy is on, rolling over, sitting or standing up will suspend the therapy temporarily.

4.0 INDICATION FOR USE

The **remedē**® System is indicated to treat moderate to severe central sleep apnea (CSA) in adult patients.

5.0 WHY DOCTORS USE THE REMEDĒ® SYSTEM FOR CENTRAL SLEEP APNEA

Doctors use this device because it has been shown to benefit patients with central sleep apnea.

6.0 WHO CANNOT HAVE THE REMEDĒ® SYSTEM

The **remedē**® System should not be placed if you have an active infection.

The **remedē** System cannot be used with magnetic resonance imaging (MRI). MRI imaging is a non-invasive test that doctors may use to diagnose various conditions such as strokes, cancer, and joint problems. If you are known to need this testing, the **remedē** System is not an option for you.

7.0 WARNING: THINGS YOU MUST DO TO AVOID SERIOUS HARM

- Carefully read all warnings, precautions, and instructions before use
- Activity after the procedure. Do not raise your arm above the shoulder on the side the device is placed for 1-3 months. Follow all other advice from your doctor after the device is placed. Failing to follow this advice can cause the leads to get pulled out of place and you might need a second procedure.
- Observing the implant site after the procedure. If you see redness or swelling at the site of the device, call your doctor without delay. Failing to call your doctor could result in a severe infection and the device may need to be removed.
- Carry your ID card. You should carry the **remedē**® System ID card with you at all times. Because the device is placed in the chest similar to heart devices, it could be mistaken for a heart device by doctors. This could delay medical care in an emergency.
- Diathermy (the production of heat in the body using electric current which may be used to treat muscle spasms, injuries and bursitis). Do not allow a healthcare provider to use any kind of diathermy on your body. Energy from diathermy can be sent through your device or leads causing tissue damage, which may result in severe injury or death. Diathermy also can damage your device or leads.

- Magnetic resonance imaging (MRI/NMR). **Do not undergo MRI** if you have the **remedē** System. MRI could cause serious injury such as tissue damage or permanent damage to the device.
- Other stimulation devices. Prior to the procedure, be certain your doctor knows if you have another stimulation device. Following the **remedē** System implantation, contact your doctor if you have other stimulation devices implanted or if you suspect an interaction between the devices such as an ICD shock or changes in your heart rhythm. The **remedē** System may be used if you have another stimulation device such as a heart pacemaker or defibrillator; special testing will be needed to ensure the devices are not interacting. Devices that interact with each other could result in these devices working incorrectly. For example, electrical pulses from the **remedē** System may interact with how your cardiac device sees electrical signals from your heart and could result in inappropriate response. Some inappropriate responses may include an unnecessary ICD shock or lack of electrical impulses to make the heart beat. If surgical revisions are made to either the **remedē** System or the other concomitant implanted device in the future, or if you are implanted with a new stimulation device, special testing will be needed to ensure there are no interactions.
- Pacemakers. The **remedē** System should be used with caution if your heart does not beat without a pacemaker.
- Environmental concerns. Electronic equipment such as that designed to prevent theft and airport metal detectors may affect the **remedē** System. Alert security personnel about the System and request a manual search if possible. If walking through a surveillance system, do not remain near this system longer than needed.
- Radiofrequency. Common radiofrequency sources (such as found in identification badges and anti-theft tags) have the potential of affecting normal **remedē** System operation. A distance of at least 40 centimeters should be kept between the implanted device and any radiofrequency source.
- Electrical and magnetic concerns. Electrical and magnetic equipment have the possibility of interacting with the **remedē** System. Stay away from high powered electromagnetic fields such as arc welding units, induction furnaces, induction stoves, resistance welders, radio or microwave transmitters and linear power amplifiers. Avoid equipment using magnetic fields such as stereo speakers, bingo wands, magnetic badges and magnetic therapy products.
- Injury. Avoid activities likely to cause a blow to the skin over the device. This could damage the device or skin over the device.

- Pregnancy. The safety and effectiveness of the **remedē** System has not been tested during pregnancy.
- Injury of the phrenic nerve. The **remedē** System may not work in patients with a prior injury to the phrenic nerve.
- Medical procedures. Certain medical procedures and equipment can interact with the **remedē** System causing changes to the **remedē** System or interference with the medical equipment. You should tell your physician about your **remedē** System prior to the use of any of the following: electrocautery, radiofrequency ablation, radiation, CT scan (computed tomography), therapeutic ultrasound, external defibrillation, patient monitoring equipment or transcutaneous electrical stimulation (TENS).
- Scuba diving or hyperbaric chambers. Do not dive below 10 meters (33 feet) of water or enter hyperbaric chambers above 2.0 atmospheres absolute (ATA). Pressures below 10 meters (33 feet) of water (or above 2.0 ATA) can damage your stimulator or leads. Before diving or using a hyperbaric chamber, discuss the effects of high pressure with your doctor.
- Cellular phones. The **remedē** System contains a filter to prevent most phones from interacting with the device function. To further decrease the risk of this interaction you should observe these cautions:
 - Do not place phones in the chest area (e.g. in shirt pockets) on the same side as the device.
 - Maintain at least 10 inches between the device and the phone, even if the phone is not on.
 - Hold the phone to the ear farthest from the device.

It is possible that phones placed close to the **remedē** System while it is active could result in stronger stimulation than programmed. The phone also could prevent the system from saving data about your breathing.

8.0 WHAT HAPPENS WHEN THE REMEDĒ® SYSTEM WEARS OUT

Your battery will be monitored by your doctor at regular visits to know when the battery runs low. If the battery runs low between visits, you may notice that you no longer can identify stimulation when you awaken at night. Contact your doctor about the possibility of your battery running low if you are not aware of stimulation under normal conditions for several nights or become increasingly tired.

The battery of the device is inside the device placed under the skin. When the battery runs low, a small cut will be made in the skin and the entire device will be removed and replaced. The leads unplug from the device and are plugged into the new device. This procedure takes less time than the first implant procedure.

9.0 RISK OF USING THIS DEVICE

The safety profile below is based on the clinical trial involving 151 patients discussed in section 17.0. There were no unanticipated events involving the **remedē®** System. The types of adverse events reported in the clinical trial are expected with an implanted device.

9.1 Safety Profile (Through 12 Months)

Risk	Subjects with Harm	Harm
RISKS DUE TO THE PROCEDURE		
Pain in the chest where the device was placed	7 out of 151 subjects (5%)	Non-serious – pain occurred at the implant site
Abnormal liver function (blood test)	1 out of 151 subjects (<1%)	Serious – abnormal liver function after the procedure required more time in the hospital
Chest pain not related to the heart	1 out of 151 subjects (<1%)	Serious – caused the hospital stay to be longer
Back pain	1 out of 151 subjects (<1%)	Non-serious – back pain
Tear in the wall of a blood vessel	1 out of 151 subjects (<1%)	Non-serious – required monitoring by the doctor
Low oxygen level	1 out of 151 subjects (<1%)	Non-serious - oxygen levels were low requiring the use of oxygen
Skin rash due to contrast dye	1 out of 151 subjects (<1%)	Non-serious – mild rash with itching
Diarrhea	1 out of 151 subjects (<1%)	Non-serious – mild loose stools after the procedure

Risk	Subjects with Harm	Harm
RISKS DUE TO THE DEVICE		
Bruising or swelling near the remedē® System	1 out of 151 subjects (<1%)	Serious – swelling under the skin required a longer hospital stay
	9 out of 151 subjects (6%)	Non-serious – swelling and bruising of the skin
Swelling or redness near the remedē® System	4 out of 151 subjects (3%)	Non-serious – redness and swelling of the skin
Out of range or elevated lead measurements	5 out of 151 subjects (3%)	Non-serious – measurements collected by the device were out of expected range, but therapy continued to be delivered
Device pushing on skin (erosion)	2 out of 151 subjects (1%)	Serious – required the remedē System to be moved during a procedure
Blood clot in arm	2 out of 151 subjects (1%)	Non-serious – pain and swelling in arm required blood thinner medication
Skin irritation around a stitch	2 out of 151 subjects (1%)	Non-serious – irritation around one of the stitches
Error in programming device	2 out of 151 subjects (1%)	Non-serious – settings were programmed incorrectly in the office
Implant site infection	2 out of 151 subjects (1%)	Serious - required the entire remedē System to be removed (device and leads)
	1 out of 151 subjects (<1%)	Non-serious - pain and swelling required antibiotics
Stimulation lead pulled out of the blood vessel	2 out of 151 subjects (1%)	Serious - required a procedure to place the lead back into the vessel
	1 out 151 subjects (<1%)	Non-serious – the remedē System was unable to deliver therapy
System lead malfunction	1 out 151 subjects (<1%)	Serious –requiring a second procedure
Stimulation lead moved within the vessel preventing stimulation	1 out of 151 subjects (<1%)	Serious – required a procedure to put the lead back in position
	1 out of 151 subjects (<1%)	Non-serious – the doctor programmed the device to deliver therapy in the office
Inadequate lead position	1 out of 151 subjects (<1%)	Non-serious – the lead was unable to deliver therapy

Risk	Subjects with Harm	Harm
RISKS DUE TO THE THERAPY		
Discomfort in the lower chest area because of the therapy	48 out of 151 (25%)	Non-serious – discomfort in the lower chest area which usually resolved with programming of the remedē ® System
Discomfort somewhere other than the lower chest area because of the therapy	1 out of 151 (<1%)	Serious – pain in the shoulder or chest due to therapy which required a procedure
	15 out of 151 subjects (9%)	Non-serious – discomfort that required an extra visit to the doctor to program the device
Inability to get to sleep	2 out of 151 subjects (1%)	Non-serious – decreased ability to get to sleep at night
Inappropriate defibrillator shock	1 out of 151 (<1%)	Serious – Interaction with intracardiac cardioverter defibrillator resulted in the heart device delivering a shock when it was not needed. The remedē System was reprogrammed to prevent future interactions.
	1 out of 151 (<1%)	Non-serious – Interaction with intracardiac cardioverter defibrillator resulted in an alarm from the cardiac device. No changes were needed to either device.

The following risks have been seen with implantation of other transvenous stimulation devices (such as cardiac devices) in published literature but were not seen during clinical trials with the **remedē** System: decreased kidney function (2%), collapsed lung (2%), trouble breathing (<1%), skin burns from radiation (<1%), stroke (<1%), bleeding which needed a blood transfusion (<1%), tear in the heart or blood vessels requiring surgery (<1%), low blood pressure (<1%), anxiety (<1%), irregular heartbeat (<1%), and death (<1%).

Some adverse events may require additional procedures. In the study discussed above nine of 151 subjects (6%) required a second procedure to alter or remove the device and/or leads. Three subjects had a lead which moved requiring a second procedure to put the lead back into place. Two subjects with the device pushing on the skin required that a second procedure be completed to move the device. Two subjects developed an infection at the site the device was implanted and required a second procedure to remove the device and leads. One subject had a lead which failed and instead of having the lead replaced, the subject opted to have the device and leads

removed. One subject had pain outside the lower chest area and a procedure was done to move the lead; however, the lead could not be placed successfully and the device and leads were removed.

10.0 BENEFITS OBSERVED USING THE REMEDĒ® SYSTEM

Over the first six months of therapy, the majority of patients can expect their quality of sleep to improve with an average of 24 fewer sleep apnea events each hour of sleep, 15 fewer arousals from sleep per hour and better quality of life. Fifty-one percent of patients had a reduction of at least half the total number of events per hour compared to only 11% of patients without treatment. Improved quality of life was reported with fewer symptoms of sleepiness and better overall health with 60% of treated patients stating their health was moderate to markedly improved at 6 months. Other benefits of this system include improved oxygen levels in the blood while sleeping and increased time in rapid eye movement (REM) sleep (deep sleep) which leads to improved quality of sleep.

11.0 WHAT HAPPENS BEFORE THE REMEDĒ® SYSTEM IMPLANT

In order for your doctor to evaluate if the **remedĒ®** System is a good option for you, you will need to have a sleep study to make sure that the treatment with the **remedĒ** System is the right treatment for you.

To prepare you for the implant procedure, you will have a physical exam to make sure that you are in the best health possible and are on the right medicine for all of your health conditions. You also may have blood tests to check your kidney function and blood counts. On the day of the procedure, you will be asked to not eat or drink anything before the procedure.

12.0 WHAT HAPPENS IN THE IMPLANT PROCEDURE

The **remedĒ®** System implant procedure takes an average of two to three hours and is performed under light sedation. Patients usually stay awake but are drowsy during the procedure. Your length of hospital stay is usually one day, but will depend on your health, how well you tolerate the procedure and how fast you recover.

During the area of the chest where the device will be placed is cleaned with a special soap and sterile towels will be placed over the area.

The leads are placed into blood vessels in your chest area. One of the leads is placed into a blood vessel near the nerve that moves the large breathing muscle (diaphragm). In some cases, another (optional) lead is placed into a blood vessel near the ribs to measure breathing. The leads are then

attached to the device. The device is placed below the skin on either the right or left side of the chest. Stitches are usually used to close the cut.

The doctor will use a type of x-ray with contrast dye to see the leads in the body. The x-ray will also be used to confirm that the leads are in the correct position.

13.0 WHAT HAPPENS AFTER THE PROCEDURE

After the procedure, it is important that you follow the advice given to you by your doctor about caring for the site where the device is placed, attending all appointments, and adhering to approved activities. You should take all your medicine as prescribed by your doctor.

After the procedure, you can return to most of your normal routine within a week. After the device site heals, your device should be painless. Some patients may be able to detect a slight bump under the skin which cannot be seen when a shirt is worn. You will be asked not to lift your arm above shoulder height (typically 1-3 months after the implant procedure).

About one month after your procedure, therapy will be started. Over the first three months of therapy, you will work with your doctor to ensure that the therapy is set up for your individual needs. Once the therapy is adjusted for you, you will need check-up visits every 3-6 months. In the first few months after the therapy begins, you may be aware of the movements of your diaphragm at night. This shows that the therapy is active. Most patients adjust to the therapy within the first 3 months.

If therapy is uncomfortable, see your doctor who can adjust your settings for better comfort. You may roll while in bed to stop therapy for a short time to allow you to fall back asleep. Sitting or standing also will stop therapy for a short time. If there is a reason to switch your therapy off for a longer period of time, your doctor can do so. Please let your doctor know if you plan to have any medical procedures. The device and the leads may be removed if necessary.

14.0 WHEN TO CALL YOUR DOCTOR

You should call your doctor right away if there is redness, swelling, warmth, or drainage from the site of the **remedē®** System. This may be caused by an infection which could be serious. Contact your doctor if your arm becomes swollen, if pain persists after the healing of your incision, or if you develop a fever that does not go away in two or three days.

You should call your doctor if you experience any discomfort from stimulation not located in the lower chest area or if stimulation causes difficulty sleeping over several nights or during a time that you do not expect to be sleeping. In addition, it is important to contact your doctor if you have other stimulation devices implanted or if you suspect an interaction between the devices.

15.0 WHERE YOU CAN FIND OUT MORE

Your primary resource for all questions and requests is your doctor.

As an additional resource, you may contact ZOLL Respicardia, Inc

Address: 12400 Whitewater Drive, Suite 150, Minnetonka, MN 55343

Phone: 952-540-4470

Website: remede.zoll.com

16.0 TRAVEL

There are no travel restrictions. If you are traveling to a different time zone, inform your doctor prior to your trip to have the device programmed to the local time if needed.

17.0 CLINICAL STUDIES

The **remedē**® System was studied in several clinical trials. The risks and benefits described above were found during a clinical trial which enrolled 151 subjects in the US and Europe. All subjects enrolled in the study were implanted with the **remedē** System and then half of the subjects had therapy turned on. The other half waited until after 6 months to have therapy started. The study was designed to see if patients on therapy were more likely to have a reduction in the number of CSA events compared to patients without therapy. Safety was determined by looking at all harm that occurred due to the procedure, **remedē** System or therapy.

Fifty-one percent of patients had a reduction of at least half the total number of events per hour compared to only 11% of patients without treatment. Safety (as reported above) showed a low risk of harm due to the procedure, **remedē** System or therapy. In addition to the comparison between the patient groups, the **remedē** System showed a decrease in episodes of low oxygen, a decrease in sleep arousals and an improvement in deep sleep. Patients also reported feeling better with 79% percent of treated subjects reported improved overall health after six months of therapy and 94% of subjects replied that they would have the procedure and therapy again.

18.0 MORE ABOUT CENTRAL SLEEP APNEA

18.1 Definition of CSA

The term ‘sleep apnea’ is used to describe a disorder in which you stop breathing during sleep for 10 seconds or more and then restart breathing. Lack of breathing (apnea) or shallow breathing (hypopnea) disrupts the oxygen supply to your brain and other parts of your body. There are two types of sleep apnea:

- Central sleep apnea (CSA) occurs when your brain is not sending the correct signals to the muscle that needs to move when you breathe.
- Obstructive sleep apnea (OSA) occurs when you try to breathe but the upper airway is partially or completely blocked.

Moderate sleep apnea is defined as at least 15 periods of either shallow breathing or pauses in breathing per hour while sleeping. Severe sleep apnea is defined as at least 30 periods of shallow breathing or pauses in breathing per hour.

Both CSA and OSA lead to poor sleep quality and may result in serious health consequences, including an increased risk for heart problems.

Because CSA and OSA have different causes, some treatment options for CSA and OSA are different. The **remedē®** System, which your doctor recommended, is designed specifically to treat CSA.

18.2 Causes of CSA

CSA can occur as the result of a variety of diseases or CSA can occur for no apparent reason. It also can be caused at high altitude or with the use of certain medicine. CSA has been found in patients with heart failure, heart rhythm problems, stroke, and kidney disease.

18.3 Diagnosing CSA

CSA is diagnosed using either a sleep test at home (polygraphy) or by testing in a sleep laboratory (polysomnography). The degree of CSA is determined by counting the number of apneas (episodes when you do not breathe) and hypopneas (episodes where you have shallow breathing) during each hour of sleep. Most healthy people have five or less episodes each hour of sleep. Treatment is typically recommended if a patient has more than 15 apnea or hypopnea episodes per hour.

As part of the diagnosis, doctors measure how many of the apnea and hypopnea episodes are due to CSA and the number of times you wake up during the night. Oxygen levels in your blood (oxygen saturation) vary while you are asleep and are measured during sleep studies. From this data, your doctor can decide the best course of treatment.

19.0 DEVICE/PATIENT IDENTIFICATION CARD

A patient ID card will be given to you by your doctor to identify that you have a **remedē®** System. Please carry this card on your person at all times.

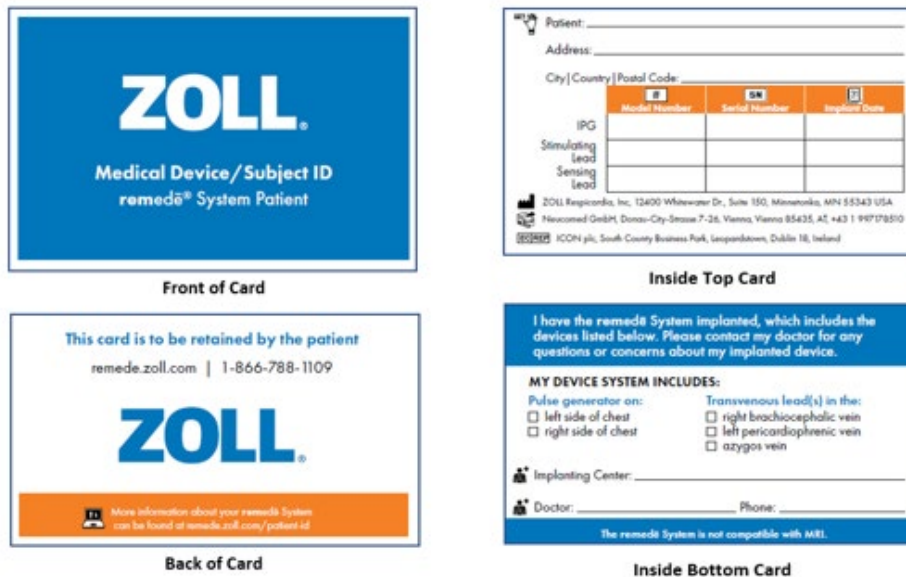










Figure 1: Patient ID Card Example

19.1 Symbols Used on the Patient ID Card

Refer to the Patient ID card for applicable symbols.

Symbol	Description
	Patient Name
	Patient Information Website
	Health Care Center or Doctor
	Date
	Model Number
	Serial Number

Symbol	Description
	Distributor
	Authorized representative in the European Community/ European Union

20.0 SUMMARY

The **remedē**® System is indicated for adult patients that have moderate to severe central sleep apnea. The system stimulates the phrenic nerve to stabilize breathing at night. The therapy starts and stops on its own at night and does not require any equipment at home. Studies have shown that patients have fewer apnea episodes, improved sleep and improved quality of life with the **remedē** System. Nine percent of the patients in the **remedē** System Pivotal Trial experienced a serious adverse event related to the implant procedure, the **remedē** System or the delivered therapy. Implant procedure or device risks include bleeding, blood vessel damage, low blood pressure, and puncture of the lung or heart. In addition, there may be pain, bruising, swelling, redness or infection at the implant site. Therapy related risks primarily include discomfort or pain in the lower chest which, in the majority of patients, were addressed by device reprogramming. Please discuss with your physician your individual potential for benefits and risks. If you receive the **remedē** System, follow your doctor’s advice to ensure effective therapy and protect you and your system from damage.

ZOLL Respicardia, Inc.

12400 Whitewater Drive, Suite 150

Minnetonka, MN 55343 USA

Phone: (952) 540-4470

Fax: (952) 540-4485

E-mail: info@Respicardia.com

remede.zoll.com

Legally Authorized European Representative:

ICON plc

South County Business Park

Leopardstown, Dublin 18

Ireland

