Apnex Clinical Research Study

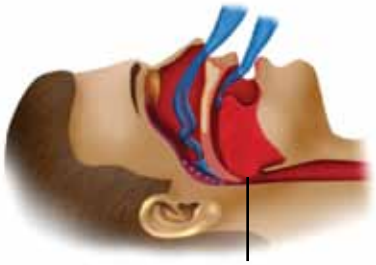
Investigational Implantable Device for Obstructive Sleep Apnea

Apnex Medical has developed an implantable device for people with obstructive sleep apnea. This investigational treatment is being evaluated in a clinical research study to determine if it is safe and effective in treating this condition. This brochure contains background information on the following topics: obstructive sleep apnea, the Apnex therapy option and the clinical study.

Obstructive Sleep Apnea Background

Obstructive sleep apnea is a common sleep disorder in which breathing is briefly and repeatedly interrupted during sleep. The "apnea" in sleep apnea refers to the airway being completely blocked. Some people have episodes of "hypopnea", which means the airway is partially, but substantially blocked. Both apneas and hypopneas cause loss of sleep and reduce the oxygen levels in the body. The severity of obstructive sleep apnea is measured by the apnea-hypopnea index (AHI), defined as the number of apnea and hypopnea events per hour of sleep.

Figure 1.



Obstructive sleep apnea occurs when the muscles fail to keep the airway open during sleep, as shown in Figure 1.

It is estimated 4% of the adult populations in the United States and Australia have moderate-to-severe obstructive sleep apnea, which occurs when a person's airway is completely or partially blocked at least 15 times per hour of sleep.[1,2]

Individuals that are suspected to have this condition are often referred to a sleep specialist doctor. This doctor will perform a sleep study to determine if a person has obstructive sleep apnea. Proper treatment can prevent or reverse the serious health risks and effects of the condition. Treatment options can include the following: lifestyle changes, positive airway pressure device (e.g. CPAP), oral appliances and surgery.

Untreated obstructive sleep apnea can have a severe effect on a person's health and lifestyle.[3] It can lead to excessive daytime sleepiness, resulting in an increased risk of motor vehicle and occupational accidents.[4,5] It is associated with an increased risk for the following conditions: coronary artery disease[6], stroke[7], high blood pressure[8], congestive heart failure[6] and Type 2 diabetes[9]. It is also associated with a significant increase in the risk of death.[10]

Condition	Increased Risk of Having Condition with Untreated OSA
Motor Vehicle Accidents	2 to 6.7
Occupational Accidents	2.2
Coronary Artery Disease	1.2 to 5.4
Stroke	1.6 to 3.1
High Blood Pressure	2.9
Congestive Heart Failure	2.4
Type 2 Diabetes	1.5
Death	3.8

The Apnex Therapy

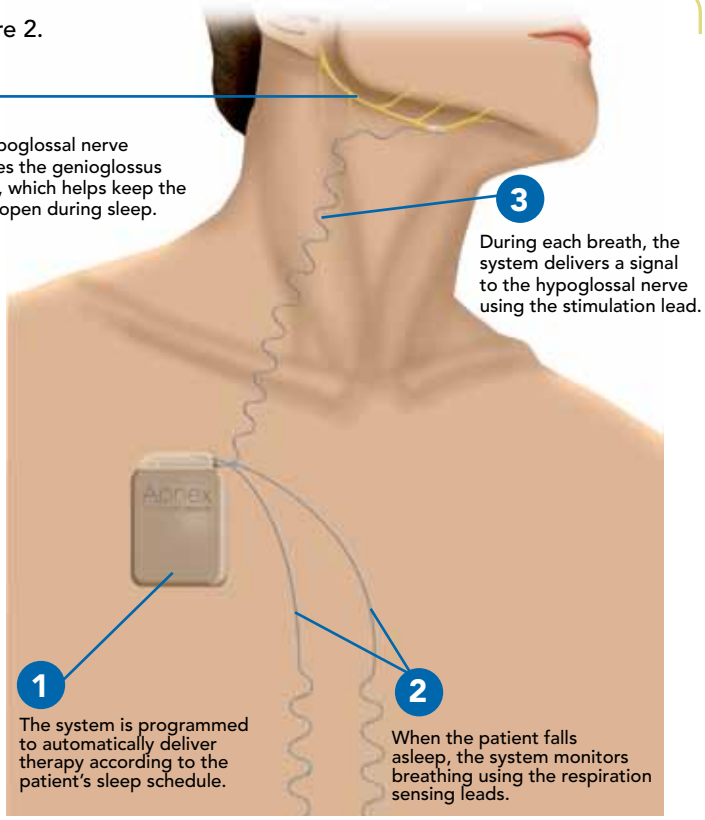
The Apnex Hypoglossal Nerve Stimulation (HGNS™) System is an implantable medical device that is being investigated in a clinical research study for the treatment of obstructive sleep apnea. It includes the following components:

- **Apnex Implantable Neurostimulator (INS device):** implanted below the collarbone
- **Apnex Respiration Sensing Leads (RSLs):** implanted under the skin and placed along the lower edge of the ribs and connected to the neurostimulator
- **Apnex Stimulation Lead (STL):** implanted under the skin and placed around the hypoglossal nerve in the neck region and connected to the neurostimulator
- **Apnex Therapy Controller:** can be used by patients to start or stop therapy to meet their sleep needs
- **Apnex Programmer System:** an external device used by doctors to non-invasively program the therapy settings

How It Works

The system is programmed to automatically deliver therapy according to a patient's sleep schedule. When the patient falls asleep, the system monitors breathing using the respiration sensing leads. During each breath, the system delivers a signal to the hypoglossal nerve using the stimulation lead. The hypoglossal nerve activates the genioglossus muscle, which helps keep the airway open during sleep. A description of how the system works is shown in Figure 2. The therapy stops according to the patient's programmed sleep schedule. Patients also have the option to use the therapy controller to stop and start therapy to meet their sleep needs.

Figure 2.



Surgical and Programming Procedures

The surgery associated with implanting the Apnex HGNS System is estimated to take about one to three hours. Patients may go home the same day as the surgery or they may stay overnight in the hospital. Patients can resume normal daily living activities soon after surgery. After a one month healing period, the system is programmed by a doctor during a sleep study to meet the unique needs of the patient.

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Clinical Study Goals

The goals of the study are to determine if the Apnex HGNS System will be safe and effective in people with moderate-to-severe obstructive sleep apnea. The Apnex HGNS System is anticipated to reduce the number of sleep apnea events and related symptoms, such as daytime sleepiness. If it is successful in treating obstructive sleep apnea, it has the potential to prevent or reverse the serious health effects and risks of this condition.

Participant Eligibility

A person will be considered for study participation if they meet the following key requirements:

- Moderate-to-severe obstructive sleep apnea
- Failed or does not tolerate CPAP therapy
- 21 to 70 years of age
- Body mass index (BMI) $\leq$ 37 kg/m^2

The clinical study doctor will provide information on additional requirements to determine if an individual qualifies for the study.

Clinical Study Plan

All patients will be implanted with the Apnex HGNS System. The device will be turned on one month after the implant procedure and a sleep study will be done to adjust therapy delivery. Additional follow-up visits will occur at 2, 3, 6, 12, 24 and 36 months.

Participant Requirements

All patients who enroll in the study are expected to adhere to the following guidelines:

- Patients must keep all follow-up appointments with the study doctor and sleep clinic at the scheduled times
- Patients should notify the study doctor of any changes in their condition, any new medications or medical treatments that may be considered for other health conditions

Potential Benefits of Participation

If this therapy is effective in treating obstructive sleep apnea, it could reduce its symptoms, such as daytime sleepiness and potentially prevent or reverse the serious health effects and risks of this condition.

The Apnex Therapy is anticipated to be easy to use and would allow a person to sleep naturally, without the use of CPAP or other equipment. It involves surgery that does not permanently remove or alter tissue, leaving open alternative treatment options.

It is possible that a participant's condition will not change with this treatment. Even if a participant does not experience an immediate benefit from this treatment, others may benefit from information obtained in the clinical study.

Potential Risks of Participation

The surgical risks associated with the Apnex HGNS System will be similar to the risks related to surgical procedures involving the neck, and implantation of a neurostimulator system. Study participants may be exposed to risks associated with the long-term use of the Apnex HGNS System. Other risks may exist that are not known at this time.

Patients that agree to participate in the study will sign an informed consent document after their doctor reviews with them all known risks associated with the treatment. Study participants will be monitored by their doctors on a regular basis to limit risks.

Taking the Next Step

Potential advances in technology require rigorous testing to determine their value. Involvement in this study will help determine if this treatment is safe and effective for millions of people who suffer from moderate-to-severe obstructive sleep apnea.

Individuals should be fully informed and be able to determine to the best of their ability whether enrolling in this clinical research study is right for them. Making that decision is not an easy task. Study doctors will respect any decision that is made.

Your consideration to be involved in this clinical research study reflects your effort to do as much as possible to treat your obstructive sleep apnea condition and reduce the serious health risks associated with it. The trade-off involved in your decision is evaluating an investigational treatment that has the potential to effectively treat your condition versus the unknown outcomes associated with this treatment.

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