PACIFIC PHOENIX GROUP

NeuroStar TMS Therapy® Patient Guide for Treating Depression

This **NeuroStar TMS Therapy® Patient Guide for Treating Depression** provides important safety and use information for you to consider about treating depression using the NeuroStar TMS Therapy System. It does not take the place of consultation and advice from your physician. For a complete discussion of indications for use, contraindications, precautions, warnings, and potential side effects, talk to your doctor. Specifically, talk with your doctor about:

- How this device is used
- Who can be treated with this device
- Who should not be treated with this device
- Warnings
- Side effects

Your doctor's phone number: ☐☐☐ ☐☐☐ ☐☐☐☐

Introduction to NeuroStar TMS Therapy

Your doctor has prescribed NeuroStar TMS Therapy® to reduce the symptoms of your depression. TMS stands for "Transcranial Magnetic Stimulation". In NeuroStar TMS Therapy, TMS is delivered by the NeuroStar TMS System as powerful magnetic field pulses. NeuroStar TMS Therapy has been shown to be safe and effective in the treatment of adult patients with depression who have failed to receive satisfactory improvement from prior antidepressant medication in the current episode.

NeuroStar TMS Therapy is performed in your doctor's office under his or her care. The treatment is non-invasive and non-systemic which means that it does not involve surgery and does not circulate in the blood stream throughout the body. Treatment with NeuroStar TMS Therapy does not involve anesthesia or sedation, and patients are awake and alert during the treatment session. A typical treatment course consists of 5 treatments per week over a 4-6 week period for a total of 20-30 separate treatment sessions. Each treatment session lasts 37.5 minutes. You should discuss the number of treatments and treatment schedule with your doctor.

NeuroStar TMS Therapy is not an appropriate treatment for all patients with depression. You should review this patient guide and discuss the information with your doctor in order to determine if NeuroStar TMS Therapy is an appropriate treatment option for you.

How Does NeuroStar TMS Therapy Work?

During treatment with the NeuroStar TMS System, the NeuroStar treatment coil is positioned gently on the left front side of the head over a region of the brain called the Left Prefrontal Cortex. By sending short bursts of electricity through the treatment coil, the NeuroStar TMS System generates magnetic fields that turn on and off very rapidly. These magnetic fields are the same type and strength as those used in magnetic resonance imaging (MRI) machines.

The rapidly pulsing magnetic fields that are generated by the NeuroStar go directly through the hair, scalp and skull and create small electric currents in the area of the brain directly under the treatment coil. The electric currents created in the brain make nerve cells in that region become active and affect other nerve cells deep in the brain that are involved in mood.

When Can NeuroStar TMS Therapy Be Used?

Indication for Use

NeuroStar TMS Therapy is indicated for the treatment of Major Depressive Disorder in adult patients who have failed to receive satisfactory improvement from prior antidepressant medication in the current episode.

When Should NeuroStar TMS Therapy Not Be Used?

NeuroStar TMS Therapy delivers a magnetic field that could cause any metal objects that are near the device to move or to get hot.

- NeuroStar TMS Therapy should not be used in patients who have magnetic-sensitive metals implanted in their head or within 12 inches of the NeuroStar treatment coil.
- NeuroStar TMS Therapy should not be used in patients who have an implanted device that may not properly function in the presence of the NeuroStar TMS System, even if the device is located outside this (12 inch) distance.

Your doctor will ask you to list any metal devices or objects in your head or body in order to determine if those devices could be affected by the NeuroStar TMS System. Use of NeuroStar TMS Therapy in the presence of these objects could result in serious injury or death.

Standard amalgam dental fillings are not affected by the magnetic field and are acceptable in patients being considered for treatment with NeuroStar TMS Therapy.

Effectiveness of NeuroStar TMS Therapy

The effectiveness of NeuroStar TMS Therapy for the treatment of depressed patients who failed to receive satisfactory improvement from prior antidepressant medication in the current episode was demonstrated in two clinical trials in 498 patients with depression through 6 weeks of treatment.

These trials each had one group treated with a clinical trial version of the NeuroStar TMS System (real TMS), while another group received a placebo treatment. Patients in these trials had already received one or more antidepressant medication treatments in their current episode of depression.

In one trial that was a company-independent study funded by the National Institute of Mental Health, the main outcome was remission which means having no remaining symptoms of depression. Patients who were treated with the TMS device were 4 times more likely to achieve remission compared to patients receiving inactive treatment as assessed using a scale for measuring depression, the clinician-rated 24-Item Hamilton Depression Rating Scale (odds ratio: 4.05 (95% confidence interval (CI), 1.28-12.83).). In

the second trial, the main outcome was symptom improvement using the clinician-rated depression rating scale known as the Montgomery-Asberg Depression Rating Scale. In this trial, patients with one prior antidepressant medication treatment achieved the main outcome which showed a three-fold improvement in symptoms with real TMS as compared to the placebo treatment (-7.1 points real TMS vs -2.1 points placebo treatment).

A third trial that did not include a placebo treatment for comparison, evaluated outcomes of patients receiving treatment using the NeuroStar TMS Therapy System as part of routine clinical use in real world settings. Patients experienced significant improvement in symptoms where one-half of patients responded to treatment (50% reduction in symptoms) while one-third had no symptoms of depression by the end of treatment as shown using the clinician-rated Clinical Global Improvement – Severity of Illness scale that measured overall health improvement.

What Happens After NeuroStar TMS Therapy Treatment?

In the third trial described above, following completion of this therapy, all patients received ongoing treatment with an antidepressant medication. Some patients also received another course of treatment with NeuroStar TMS Therapy if their symptoms came back. Most patients continued to do well using standard maintenance antidepressant medication and routine follow up with their physician. Overall, 36.2% of patients required retreatment with TMS over 12 months to relieve their depression symptoms. If a patient needed retreatment, they received an average of about 16 treatments over the course of the 12 months of follow-up. For patients who had no symptoms after TMS treatment, (i.e., remission), 29.5% experienced a recurrence of their illness (i.e., illness relapse) at some time during a 12 month period of follow up.

Relapse into depression may occur without follow-up treatment. You should discuss long-term treatment planning with your doctor. Further details on the study can be obtained from your doctor.

Limitations of NeuroStar TMS Therapy

NeuroStar TMS Therapy is indicated for patients who have failed to receive satisfactory improvement from prior antidepressant medication in their current episode of depression. NeuroStar TMS Therapy has not been evaluated in patients who have had no prior treatment with antidepressant medication. It is important that your doctor evaluate your antidepressant medication history to determine if NeuroStar TMS Therapy is right for you.

Most patients who benefit from NeuroStar TMS Therapy begin to experience results by the fourth week of treatment, and will usually receive benefit by six weeks. Some patients may experience results in less time. A goal of antidepressant treatment is to have all the symptoms of depression go away (remission). Your doctor will discuss with you when to end treatment with this goal in mind. In clinical trials, NeuroStar TMS Therapy was administered for six weeks so it is unknown whether longer treatment would be effective for your depression.

NeuroStar TMS Therapy has not been evaluated in patients with psychoses or psychiatric emergencies where a rapid improvement is needed such as patients at risk of suicide.

As with any antidepressant, there is a risk of worsening of your depression during treatment with NeuroStar TMS Therapy. Contact your doctor immediately if symptoms persist or worsen. The device was shown to be safe and effective in patients who had been able to stop taking their antidepressant medications. If you feel that your depression worsens when you stop your antidepressant medications, contact your doctor immediately. This therapy has not been demonstrated to be safe and effective for patients who have a suicide plan.

NeuroStar TMS Therapy Safety Information

The safety of NeuroStar TMS Therapy was determined in two clinical trials (where one-half of patients received real TMS and one-half received placebo treatment) of 498 patients with moderate to severe Major Depressive Disorder who ranged in age from 18 to 70 years, and who had failed to achieve satisfactory improvement from prior antidepressant treatment.

- Less than 5% of all patients dropped out of the clinical trials because of side effects from the treatment.
- There was no weight gain, sexual problems, stomach problems, sleepiness, and dry mouth which are side effects that commonly occur with antidepressants taken by mouth.
- There were no deaths or seizures in patients who took part in the clinical trials.
- There was no change in memory function during the clinical trials.
- There was no change in hearing function during the clinical trials (earplugs were used)

This section provides information about side effects observed with the use of the NeuroStar TMS Therapy System in clinical trials. Warnings and precautions to be considered prior to receiving NeuroStar TMS Therapy are also provided and should be discussed with your doctor to determine what, if any, precautions should be taken during your treatment with NeuroStar TMS Therapy.

Worsening Depression or Suicidality

Depression is a serious medical illness. Not all patients treated with an antidepressant will get better with treatment. Because of this, some patients may experience worsening of their depression before they begin to see improvement of their symptoms. NeuroStar TMS Therapy may require up to 4-6 weeks of treatment before symptom improvement occurs and has not been studied in patients who need rapid improvement in their depression symptoms.

You should inform your doctor if your symptoms do not improve, or if they get worse. If you have thoughts of death or suicide you should immediately discuss this with your doctor. Your doctor will determine whether NeuroStar TMS Therapy should be discontinued and, if so, what other treatment options are available. You should be carefully monitored for worsening symptoms, signs or symptoms of suicidal behavior and/or unusual behavior. Families and caregivers should also be aware of the need to observe the patient and notify the treatment provider if symptoms worsen.

Other Risks

Seizures (sometimes called convulsions or fits) have been reported with the use of TMS devices. No seizures were observed with use of the NeuroStar TMS System in clinical trials that included over 15,000 treatment sessions. Since the introduction of the NeuroStar TMS System into clinical practice, seizures have been rarely reported. The estimated risk of seizure under ordinary clinical use is approximately 1 in 30,000 treatments (0.003% of treatments) or 1 in 1000 patients (0.1% of patients). You should discuss with your doctor if you have had a seizure, or if you have a medical condition that you have been told may put you at increased risk of having a seizure. Your doctor will decide if it is appropriate for you to receive NeuroStar TMS Therapy.

The safety and effectiveness of NeuroStar TMS Therapy has not been established in the following patient populations or clinical conditions through a controlled clinical trial.

- Patients who cannot tolerate withdrawal of antidepressant medications.
- Patients who have a suicide plan or have recently attempted suicide
- Patients with seasonal affective disorder
- Patients younger than 22 years of age or older than 70 years of age

- Patients with history of substance abuse, obsessive compulsive disorder or post-traumatic stress disorder. Patients with a psychotic disorder, including schizoaffective disorder, bipolar disease, or major depression with psychotic features.
- Patients with neurological conditions that include a history of seizure, cerebrovascular disease, dementia, increased intracranial pressure, movement disorders, having a history of repetitive or severe head trauma, or with primary or secondary tumors in the CNS.
- Patients with metal in or around the head, including metal plates, aneurysm coils, cochlear implants, occular implants, deep brain stimualtion devices and stents.
- Patients with implants controlled by physiological signals, including pacemakers, implantable cardioverter defibrillators, and vagus nerve stimulators.
- Patients with major depressive disorder who have failed to receive clinical benefit from ECT or VNS.
- Patients who are pregnant or nursing

The NeuroStar TMS System produces a loud click with each magnetic pulse, patients treated with the NeuroStar TMS System must always wear earplugs or similar hearing protection devices with a rating of 30dB or higher of noise reduction during treatment. In clinical trials, NeuroStar TMS Therapy had no effect on hearing when earplugs were used.

The long term effectiveness of NeuroStar TMS Therapy for treating depression has not been evaluated in clinical studies where one-half of patients received real TMS and one-half received placebo. In other clinical studies, NeuroStar TMS Therapy was safely tolerated in patients for periods up to 24 continuous weeks, and no negative effects of treatment were seen during a 6 month follow-up period. However, effectiveness has not been established for treatment beyond a six week course.

Longer term effects of exposure to the NeuroStar TMS System magnetic field are not known. However, exposure to other devices (such as MRI scanners) with the same type and strength of magnetic fields produced by the NeuroStar TMS System coil are not associated with significant short-term or long-term safety concerns.

Adverse Events

Temporary pain or discomfort at the area of the head where the treatment coil was placed was reported in about a third of patients who were treated with the NeuroStar TMS System, while this occurred in less than 5% of patients treated with sham (placebo), suggesting that this is due to the NeuroStar treatment. Inform your doctor if you experience discomfort during treatment. Your doctor can decrease the NeuroStar TMS dose or temporarily move the NeuroStar TMS coil slightly to ease or eliminate the discomfort. Treatment site discomfort went away rapidly with time, usually getting better within the first week of treatment.

Headaches were reported by about half of the patients who took part in the clinical trial regardless of whether they were treated with real TMS or with the sham (placebo) treatment. In general, the headaches got better over time, and could be relieved by using common over-the-counter pain medications such as acetaminophen.

The following table presents a summary of adverse events that occurred in one clinical trial in ≥5% of the patients treated with NeuroStar TMS Therapy and at least twice as often as was seen in patients treated with placebo treatment. Similar results were seen in the second clinical trial. Safety information is provided from all patients who had been treated in the clinical study.

Table 1. Adverse Events Reported with NeuroStar TMS Therapy: (Study 101, Incidence with Active TMS > 5% and at Least Twice the Rate with Sham Treatment)

Event Type	Active TMS (N=165 Patients) N%	Sham TMS (N=158 Patients) N%
Eye pain	10 (6.1)	3 (1.9)
Toothache	12 (7.3)	1 (0.6)
Application site discomfort	18 (10.9)	2 (1.3)
Application site pain	59 (35.8)	6 (3.8)
Facial pain	11 (6.7)	5 (3.2)
Muscle twitching	34 (20.6)	5 (3.2)
Pain of skin	14 (8.5)	1 (0.6)

For more information on TMS, visit the Neuronetics Web site: https://pacpx.com/