**(PRACTICE LETTERHEAD)**

**(Variable Field: Date)**

**(Variable Field: Insurance Company)**

**(Variable Field: Address)**

**(Variable Field: Patient Name)**

**(Variable Field: Policy Number)**

**(Variable Field: Group Number)**

**(Variable Field: Case Reference Number)**

**Re: Prior Authorization Request for NeuroStar TMS Therapy®**

**CPT Code(s):**

**90867: Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; initial,**

**including cortical mapping, motor threshold determination, delivery and management**

**90868: Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; subsequent**

**delivery and management, per session**

**90869: Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; subsequent**

**motor threshold re-determination with delivery and management**

**Diagnosis Code(s): (Insert applicable ICD-9 Code(s) for Major Depressive Disorder)**

To Whom It May Concern,

I am writing on behalf of my patient, (Patient Name), to request prior authorization approval for Transcranial Magnetic Stimulation (TMS) using the NeuroStar TMS Therapy System for the treatment of (his/her) Major Depressive Disorder. Having considered all treatment options for my patient, I consider NeuroStar TMS Therapy to be the most viable treatment option for my patient’s Major Depressive Disorder and it is therefore medically necessary. Additionally, I request that coverage and benefits be provided for NeuroStar Transcranial Magnetic Stimulation (TMS).

(Patient Name) is a (Age) year old (Male/Female) with a diagnosis of Major Depressive Disorder, (ICD-9 Code(s). (Patient Name) has been suffering from depression for (Insert X number of years or months/Timeframe) and has experienced symptoms affecting (his/her) well-being and quality of life. She/He experiences the following symptoms of depression: (Please insert all symptoms that affect his/her quality of life and activities of daily living).

(Patient Name) has tried previous treatments with medication (s) but has not found any alleviation of symptoms and has not shown any significant improvement; the treatments include the following: (Please insert the specific medication (s), dosage (s) and duration (s) here. List the medications and reasons for discontinuation, including any details regarding the side effects).

*(Please include the following information if applicable to the case regarding the patient’s prior ECT treatment.)* In addition to (Patient Name)’s resistance to medication treatment, (he/she) has undergone electroconvulsive therapy (ECT) for (Insert # of sessions and timeframe).

*OR*

*Please include the following information to the case if the patient has not had ECT treatment but has been considered for ECT.)* (Patient Name)’s has been considered for ECT as a potential treatment option for his/her condition; however, we have jointly made the determination that ECT would not be an appropriate treatment for the patient based on (Insert rationale).

*(Please include if hospitalization is applicable to the case.)* Also, the patient has been hospitalized for Major Depressive Disorder on these/this occasion(s) (Insert the timeframe and a detailed description).

*(Please include the following information if applicable to the case regarding the patient’s evidence based psychotherapy trials and outcomes*). Please find below a list of the patient’s psychotherapy trials and outcomes (list psychotherapy trials and outcomes) including the (insert # of sessions and timeframes) for depression.

For your reference, enclosed are clinical records documenting (Patient Name)’s history of symptoms and treatments that were tried and failed.

In October 2008, the NeuroStar TMS Therapy System was FDA cleared for general clinical use in the United States. NeuroStar TMS Therapy is indicated for the treatment of Major Depressive Disorder in adult patients who have failed to achieve satisfactory improvement from one prior antidepressant medication at or above the minimal effective dose and duration in the current episode. NeuroStar TMS Therapy involves the use of a treatment coil to deliver short magnetic energy pulses which produce small electrical currents in the underlying cerebral cortex. These small electric currents cause the neurons to depolarize to affect the release of neurotransmitters. NeuroStar TMS treatments typically take place for

4-6 weeks on an outpatient basis in the physician’s office or in an outpatient hospital setting.

Benefits of NeuroStar TMS Therapy in addition to its antidepressant effects include:

* It is a non-invasive and non-systemic antidepressant treatment
* It has been proven effective in patients who have not benefitted from initial antidepressant drug therapy
* It does not require any anesthesia or sedation,
* The patient remains awake and alert during the treatment
* It shows excellent tolerability and safety: the most common side effect associated with   
  treatment is scalp pain or discomfort which is generally mild to moderate in severity
* There is a rare risk of seizure with TMS Therapy with an incidence of 0.003% per treatment and less than 0.1% per acute treatment course.

The ***NeuroStar TMS Therapy System*** was the first TMS device to receive FDA clearance for therapeutic use in the United States for treatment of patients with major depression who failed to benefit from prior treatment with antidepressant medication. At this time, the NeuroStar TMS Therapy System (Neuronetics, Inc., Malvern, PA) is the only FDA-cleared TMS device that has multiple peer-reviewed publications in the scientific literature reporting data from well-designed, randomized, sham-controlled multisite clinical trials. This is the largest clinical evidence base for any TMS device. Please refer to the enclosed Bibliography regarding a comprehensive list of publications in support of safety and efficacy for NeuroStar TMS Therapy. The essential conclusions of these publications are summarized below. This provides the necessary scientific evidence to permit positive conclusions in technology reviews of TMS Therapy. This peer-reviewed, published scientific data meets the general principles of evidence-based medicine.

Specifically, there is adequate evidence to:

1) Permit scientific conclusions about the efficacy and safety of TMS;

2) Show that TMS improves the health outcomes of patients, and;

3) Demonstrate that TMS is as least as beneficial, if not superior to, pharmacologic

therapy in patients with depression that have not responded to prior antidepressant

medication.

The safety and efficacy of a specific TMS treatment protocol for the acute treatment of major depression (i.e., left dorsolateral, high frequency TMS), delivered by a specific medical device (i.e., the NeuroStar TMS Therapy System), was first established in the largest (N=301), multi-site (23 centers [20 in the US, and 3 non-US]), randomized sham-controlled trial ever conducted with TMS. This registration study was the principal basis for the FDA’s clearance of this specific device for clinical use in the United States in October of 2008 (Demitrack and Thase, 2009; Janicak, 2008; O’Reardon, 2007). The primary efficacy outcome in that study was change in the Montgomery-Asberg Depression Rating Scale (MADRS) total score from baseline measured at 4 weeks. Key secondary outcomes included changes in the 17- and

24-Item Hamilton Depression Rating Scale (HAMD17 and HAMD24) total scores at 4 and 6 weeks,

and also categorical outcomes defining response and remission on each of these rating scales.

A second, large (N=190) multisite (4 US academic sites) randomized sham-controlled trial has also been reported and provided confirmation of the efficacy of the NeuroStar TMS Therapy System in pharmacoresistant major depression (George, 2010). The primary outcome was the clinically significant, categorical outcome of remission, measured at 3 weeks. Key secondary outcomes included MADRS and HAMD24 score changes from baseline using the 24 item Hamilton Depression Rating Scale (HAMD24).

Both of these studies were rigorously sham controlled, used standardized endpoints for depression and utilized the NeuroStar TMS Therapy System with the same treatment protocol.

Since market introduction of the NeuroStar TMS Therapy System, Neuronetics conducted a prospective, naturalistic observational clinical trial at 42 clinical practice locations in the United States (Clinicaltrials.gov Identifier NCT001114477; Carpenter, et al., 2012). In this study, patients were enrolled who had a clinical diagnosis of major depressive disorder, and for whom the clinician had determined that TMS Therapy was the most appropriate clinical choice for the patient’s antidepressant treatment. Outcome assessments were obtained at baseline prior to initiation of treatment, at the point at which the clinician had determined that acute phase treatment had achieved maximum benefit, and at quarterly intervals for the next twelve months. Efficacy measures included clinician evaluation using the Clinical Global Impressions – Severity of Illness Scale (CGI-S), and patient-reported outcomes using the Inventory of Depressive Symptoms – Self Report version (IDS-SR), and the 9-Item Patient Health Questionnaire (PHQ-9).

The acute clinical outcomes of this study have been published in the peer-reviewed scientific literature (Carpenter, et al., 2012). The general demographic and clinical descriptive information of the 307 patients whose outcomes were observed in this study showed a recurrent course of illness in over 90% of patients. By CGI-S criteria, baseline depression severity was rated as moderately ill or worse (CGI-S ≥ 4) in 99% (303 of 307) of the population. Patients had received a mean (SD) of 2.5 (SD: 2.4) antidepressant medication treatment attempts at an adequate dose and duration, defined by rigorous research criteria. Over 54% of patients met research criteria for resistance to two or more antidepressant trials during the current episode. The average number of TMS sessions across the acute phase was 28.3 (SD:10.1, Range: 2 to 94), corresponding to an average duration of treatment of 42 days (SD:14.2, Range: 2 to 130).

A total of 265 patients (86.3% of the enrolled population) completed acute treatment. The clinician-assessed response rate (CGI-S) was 58.0% and remission rate was 37.1%. Patient-reported response rate ranged from 56.4% to 41.5% and remission rate ranged from 28.7% to 26.5%, (PHQ-9 and IDS-SR, respectively). The outcomes under conditions of general clinical use are indistinguishable from those reported in open-label clinical trials of NeuroStar TMS Therapy in research study populations. These data validate the efficacy of NeuroStar TMS Therapy reported in published randomized controlled clinical trials, and further support it as an effective and well tolerated treatment for those who have failed to benefit from antidepressant medication.

The longer term durability after acute treatment with NeuroStar TMS Therapy has been documented in two separate clinical studies. In the first report, Janicak and colleagues (2010) described the clinical outcome in six months of follow up in a cohort of 99 patients who had benefited from acute treatment in the Neuronetics-sponsored registration study, and who then had successfully transitioned to maintenance antidepressant medication monotherapy during a 3 week transition. Long-term durability of effect was then examined over the subsequent six months. During this period of follow up, the chosen maintenance antidepressant medication could not be switched or combined with other antidepressant medications, however TMS could be re-administered if patients met protocol-specified criteria for symptom re-emergence. In this analysis, only 10 of 99 patients (10%; Kaplan-Meier survival estimate = 12.9%) relapsed during the 6 months of follow-up. Thirty-eight patients (38.4%) met criteria for symptom worsening during the long term follow up interval, and 32/38 (84.2%) re-achieved symptomatic benefit when adjunctive TMS was administered.

These data from a controlled research setting were recently confirmed in a separate patient population from the naturalistic observational study described above (Carpenter, et al., 2012.). Patients (N=257) were tapered from their acute treatment TMS regimen, and consented to long-term follow up of their clinical and treatment outcomes over the next twelve months. Clinical assessments (CGI-Severity of Illness, PHQ-9 and IDS-SR) were obtained at 3, 6, 9, and 12 months. A total of N=205 patients provided data across the entire study period.

Compared with baseline scores obtained prior to acute treatment, there was a statistically significant reduction in mean CGI-S, PHQ-9 and IDS-SR total scores at the end of acute which was sustained throughout the one year follow-up. The proportion of patients who achieved remission at the conclusion of acute treatment remained similar to that observed following the conclusion of the long term 12-month follow up phase: CGI-S (total score 1 or 2), 41.2% (end of acute) and 45.1% (end of long term); PHQ-9 (total score < 5), 31.1% (end of acute) and 37.0% (end of long term); IDS-SR (total score <15), 29.7% (end of acute) and 29.3% (end of long term).

As a further demonstration of the durability of the acute benefit of NeuroStar TMS Therapy, among those patients (N=78) who had achieved complete remission at the end of the acute treatment phase (QIDS-SR <6), the proportion of patients who subsequently experienced illness relapse was only 29.5% (defined as a QIDS-SR total score ≥ 11 at any observation time point during the long term follow-up, N=23 patients, indicating that nearly three-quarters of patients who achieved remission at the end of acute treatment did not experience relapse of their illness over 21 months of long term follow-up.

Following completion of tapering of acute treatment with NeuroStar TMS Therapy, only 93 of the 257 patients in long term follow-up (36.2% of all patients) subsequently received reintroduction of TMS based on clinician decision for clinical worsening. In this group, the mean [SD] number of additional TMS treatment days was 16.2 [21.1] over the 12-month long term follow up.

These two studies provide consistent evidence supporting the view that NeuroStar TMS Therapy demonstrates a statistically and clinically meaningful durability of acute response over one year of follow-up. Following successful acute treatment with NeuroStar TMS Therapy, the incidence of illness relapse in a treatment resistant patient population is low. In both of these studies, maintenance of acute benefit was observed under a regimen of continuation antidepressant medication and access to TMS reintroduction for symptom recurrence.

Additionally, recent meta-analyses and comprehensive technology reviews also provide support that TMS is an evidence-based treatment option for patients who have failed to benefit from initial acute phase treatment of major depression.

One of the most recently published meta-analyses, and among the largest to date (Slotema, et al, 2010) examined data from 34 studies involving 1,383 patients. These authors reported an effect size of 0.55 (95% confidence interval 0.38 to 0.72) for the use of TMS in the treatment of depression, and concluded that, “…TMS deserves a place in the standard toolbox of psychiatric treatment methods, as it is effective for depression and has a mild side effect profile...”.

The conclusions of the AHRQ report have been independently examined by the New England Comparative Effectiveness Public Advisory Council (CEPAC). CEPAC is federally funded by the Agency for Healthcare Research and Quality (AHRQ) as part of its RAPID (Regional Adaptation for Payer Policy Decisions) initiative and is directed by the Institute for Clinical and Economic Review (ICER), a leading academic comparative effectiveness research group based at the Massachusetts General Hospital’s Institute for Technology Assessment. The CEPAC Panel rigorously reviewed the quality of the evidence provided in the original AHRQ report, and they extended the conclusions of that report by providing a detailed analysis of the anticipated direct impact on payer expenditures of providing TMS as a covered benefit.

The CEPAC Panel voted majority in support of the conclusion that the scientific evidence on TMS demonstrates that TMS is clearly equivalent or superior to usual care. The conclusion that the scientific evidence on TMS demonstrates that TMS provides a net health benefit that is equivalent or superior to the use of ECT. Finally, in a detailed economic analysis, the CEPAC Panel noted that using reasonable epidemiologically-based assumptions regarding the projected utilization of TMS in practice, *on a per member per month (PMPM) basis, the cost impact to payers of covering TMS ranges from $0.21 - $0.59, or a relatively modest 0.07 - 0.2% increase in plan costs.*

NeuroStar TMS Therapy is now in widespread clinical use across the United States at nearly 500 centers, including institutions such as, Kaiser Permanente Hospital, Vanderbilt University, Ohio State University Harding Hospital, University of Texas Southwestern Medical Center, Stanford University, Mayo Clinic – Rochester MN, University of Michigan Depression Center of Excellence, Walter Reed Army Hospital, UCLA, the Harvard Medical System, Boston Medical Center, Johns Hopkins University, Cornell University, Boston University, Brown University – Butler Hospital, UMDNJ- University of Medicine and Dentistry of New Jersey, Lindner Center of Hope, Medical University of South Carolina, Southern Illinois University, University of South Florida, University of Florida, Dent Neurologic Institute, Sheppard Pratt Center for Anxiety and Depression, and at freestanding hospitals and private physician’s offices.

TMS Therapy has received positive medical policy coverage nationwide. Medicare coverage policies (Local Coverage Determinations-LCD) have been issued in states such as Delaware, District of Columbia, Maryland, New Jersey, Pennsylvania, Alabama, Georgia, Florida, Puerto Rico, the Virgin Islands, Arkansas, Colorado, Louisiana, Mississippi, New Mexico, Oklahoma, Texas, North Carolina, South Carolina, Virginia, and West Virginia. Furthermore, large insurance entities have provided medical and behavioral coverage policies such as Anthem BCBS (including these states: BCBSGeorgia, Connecticut, Empire BCBS New York, Ohio, Wisconsin, Indiana, Colorado, Anthem BCCalifornia, Missouri, New Hampshire, Nevada, Maine and Virginia), BCBS Federal Employee Program, Blue Shield of California, Independence BC, BCBS Massachusetts, BCBS Michigan, Blue Care Network of Michigan, BCBS Nebraska, Premera BC, BCBS Rhode Island, BCBS South Carolina, HealthNet/MHN, MVP Healthcare, Priority Health, Tufts Health Plan, VT Medicaid, and RI Medicaid only through Neighborhood Health Plan of RI. Additionally, behavioral health carve-out plans such as Magellan,

Value Options, and OPTUM have proven treatment guidelines when determining medical necessity for TMS Therapy.

Due to (Patient Name)’s history and previous treatment trials to treat Major Depressive Disorder,

I have determined that this patient is a clinically appropriate candidate for NeuroStar TMS Therapy.

I am requesting that you consider the supportive documentation and the full benefits that TMS Therapy provides patients suffering from this debilitating condition to render a positive decision for coverage of this treatment option. If I can provide any additional information to facilitate your review, please do not hesitate to contact me.

Thank you for your time and consideration regarding this matter.

Sincerely,

**(Physician’s Name)**

**(Name of Practice)**

**(Address)**

**(Phone Number)**

**(Fax Number)**

*Enclosures:* Patient’s Clinical Notes

AMA CPT I Coding Approval Letter

Bibliography of Publications

Executive Summary

FDA Clearance Letter

*References:*

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