**(PRACTICE LETTERHEAD)**

**(Variable Field: Date)**

**(Variable Field: External Review Company – Example: State’s Department of Insurance)**

**(Variable Field: Address)**

**(Variable Field: Patient Name)**

**(Variable Field: Policy Number)**

**(Variable Field: Group Number)**

**(Variable Field: *Please insert the information according to the type of appeal:***

***Preauthorization Appeal:* Case Reference Number**

***Claims Appeal:* Claims Reference Numbers and Dates of Service)**

**Re: External Review Level Reconsideration 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**

**(Variable Field: *Please* *only include the CPT code below when applicable to the patient’s case.*)**

**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)**

Dear Medical Reviewer,

I am filing an appeal on behalf of my patient, (Patient Name), who has been formally denied coverage for NeuroStar TMS Therapy, a safe and effective treatment that improves depressive symptoms for certain patients diagnosed with Major Depressive Disorder (MDD). In the denial dated, (Date), it was stated by (Insurance) that TMS Therapy is not eligible for coverage due to the following reason(s): *(Insert specific language from the denial letter,* e.g. *According to INSURERS Medical Policy #\_\_\_\_\_\_\_\_ TMS is considered experimental/investigational and therefore not covered; Further research regarding outcomes, long term safety and efficacy is needed to support the use of Transcranial Magnetic Stimulation; There are no extenuating circumstances such that the service is medically necessary.).* I request that as the qualified reviewing physician, you reconsider and overturn this insurer’s adverse coverage benefit determination based on the information supporting safety and efficacy and the patient’s individual case demonstrating medical necessity for the TMS Therapy.

In order to comply with mandatory URAC standards and to ensure a full and fair review, we request the reviewer assigned to this case possess the following qualifications: (1) Board certification in psychiatry; (2) Expertise in the clinical management of patients with mood disorders, including complicated and treatment resistant MDD; (3) Knowledge base in neuromodulation treatment modalities such as Vagus Nerve Stimulation (VNS) and Electro-Convulsive Therapy (ECT), including the efficacy, adverse event profile and potential medical complications of these different treatment options for MDD; (4) Completion of a TMS clinical training program for use of a FDA-cleared TMS delivery system.

*(This section has three (3) components of which one or all may be used based on the reason(s) for the denial: 1) BCBS-TEC OR A general experimental/investigational reason, 2) Durability, 3) Patient has not tried ECT. PLEASE REFER TO THE DENIAL LETTER AND APPLY THE NECESSARY INFORMATION.)*

**1) BCBS-TEC** *(OR)* **TMS Therapy is considered experimental/investigational:**

*(If the insurance company references the denial reason to BCBS-TEC assessment in the latest denial letter, please apply the following paragraph and the #1-5 criteria):*

It is my understanding that the (Insurance’s) Medical Policy is based on the Blue Cross Blue Shield Association Technology Evaluation Center (BCBS TEC) assessment which uses the following five criteria to determine if a treatment meets the recommended guidelines. I would like to review the clinical literature in the context of these five standard criteria to show that NeuroStar TMS Therapy does meet each of them.

*(OR)*

*(If the insurance company denies the request based on experimental/investigational reasons in the latest denial letter, please apply the following paragraph and the #1-5 criteria):*

According to the latest denial reason, NeuroStar TMS Therapy has been determined as experimental/investigational; therefore, it is not a covered benefit. (Insurance)’s decision does not reflect recent medical research, published treatment guidelines, and current psychiatric practice. I would like to review the clinical literature in the context of the following, points to demonstrate the safety and efficacy of NeuroStar TMS Therapy in response to the experimental/investigational denial.

1. **The technology must have final approval from the appropriate government regulatory bodies.**

In October 2008, the NeuroStar TMS Therapy system received market clearance from the US Food and Drug Administration to be used as an antidepressant treatment for patients with major depressive disorder via the De Novo 510(k) regulatory review pathway. The specific indication for use for the NeuroStar TMS Therapy system is “*for the treatment of adult patients with Major Depressive Disorder (MDD) who have failed to receive satisfactory improvement from one prior antidepressant medication at or above the minimal effective dose and duration in the current episode”.*

## The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.

**The acute safety and efficacy of TMS Therapy has been studied in two independent Level I trials:**

* 1. The safety and efficacy of a specific TMS treatment protocol for the acute treatment of major depression as delivered by a specific medical device, the NeuroStar TMS Therapy system [Neuronetics, Inc, Malvern, PA]),was established in the largest (N=301), multi-site (23 centers), 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.)
  2. A second, large (N=190) multisite (4) randomized sham-controlled trial has been reported and provides confirmation of the safety and efficacy of TMS in pharmacoresistant major depression (George, et al, 2010). This second study is particularly important since it was an NIH-sponsored study, and was therefore conducted independent of industry support.

## **The positive results of these two controlled clinical trials provide adequate scientific data to permit conclusions regarding the effect of TMS on health outcomes.**

1. **The technology must improve the net health outcome. The technology’s beneficial effects on health outcomes should outweigh any harmful effects on health outcomes.**

Two Level 1 sham-controlled randomized studies provide consistent data documenting that TMS Therapy using a specific NeuroStar treatment protocol results in a significant improvement in acute depression, as assessed by improvement in standardized depression outcomes, i.e. HAMD24 and MADRS scores:

* 1. **The NeuroStar TMS Registration Trial (O’Reardon, 2007; Demitrack and Thase 2009)** **demonstrated clinically meaningful improvement on the primary outcome measure, baseline to endpoint change on the Montgomery-Asberg Depression Rating Scale at four weeks (MADRS, P=0.057, standardized effect size = 0.39). In a pre-specified analysis, those patients who had failed one antidepressant medication treatment of research-grade dose and duration (which comprised 54.5% of the overall study population) showed a strong, statistically significant, superior benefit for active TMS as compared to sham treatment as measured by MADRS change from baseline at four weeks (MADRS, P=0.0006, standardized effect size = 0.94.)**
  2. In the NIMH Sponsored Study (George 2010) the authors reported that there was a significant effect of active treatment on the proportion of remitters (15% active TMS vs. 4% sham control group, P=0.015), representing a 4.2 greater odds of reaching remission with active TMS compared to sham control.

A comprehensive review of the safety profile of TMS is provided by Janicak and colleagues (2008). TMS has a unique safety profile among depression treatments in that it is non-systemic and non-invasive. The primary side effect of the use of TMS that associated with treatment is discomfort or pain at the site of stimulation during active treatment. No seizures were reported in the clinical trials and since market introduction of the NeuroStar TMS system, the incidence of seizures has been rare, with < 0.003% of treatments resulting in the occurrence of seizure.

These results demonstrate that the health benefits of TMS Therapy outweigh the risks, therefore meeting the criterion that TMS improves net health outcome.

1. **The technology must be as beneficial as the established alternative treatments.**

Since head-to-head comparative trials were not conducted between TMS and antidepressant medication, this analysis requires an indirect comparison of TMS study outcomes to reference outcomes from studies using antidepressant medications. This is similar to the situation with different antidepressant medications which for registration trials are placebo-controlled and are not conducted as comparative trials. When comparing the results of TMS to antidepressant drug therapy, it is important to note that patients in the NeuroStar TMS registration trial had a treatment resistant form of depression, while in contrast, patients in the drug registration trials were typically receiving first line drug therapy, representing a bias against TMS.

NeuroStar TMS Therapy treatment effects for mean change from baseline meet or exceed the treatment effect size reported for 8 of 11 FDA-approved first-line pharmaceutical antidepressants (Demitrack, MA, Thase, ME, 2009), even though the NeuroStar TMS Therapy trial included a treatment resistant patient sample comparable in treatment resistance severity to those patients treated in research studies of ECT (Prudic, 2004). The pooled effect size (HAMD17) for antidepressant randomized controlled trials is 0.31 (95% CI: 0.26-0.36) while the effect size for NeuroStar TMS Therapy is 0.52 (95% CI: 0.21-0.83.) NeuroStar TMS Therapy treatment effect size for mean change from baseline also exceeds the treatment effects for atypical antipsychotic augmentation, the only pharmaceutical treatments that are FDA approved for the treatment of patients with treatment resistant major depression (Demitrack, MA, Thase, ME, 2009).

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. In 2011, the federally-funded Effective Health Care Program of the Agency for Healthcare Research and Quality (AHRQ), published a Comparative Effectiveness Review (Number 33), entitled, “Nonpharmacologic Interventions for Treatment-Resistant Depression in Adults”. Overall, the AHRQ Panel concluded that there is a substantial and well-replicated body of evidence from randomized, sham-controlled clinical trials that provide a “high strength of evidence” that TMS produces significantly greater decreases in depression severity, greater response rate and remission rate when compared to a sham treatment condition in the majority of peer-reviewed published clinical trials. Specifically, they noted that: ***“…rTMS averaged a decrease in depressive severity measured by the Hamilton Rating Scale for Depression (HAM-D) of more than 5 points relative to sham control, and this change meets the minimum threshold of the 3-point HAM-D difference that is considered clinically meaningful. Response rates were greater with rTMS than sham (also high strength of evidence); those receiving rTMS were more than three times as likely to achieve a depressive response as patients receiving sham procedure. Finally, rTMS was also more likely to produce remission than the control procedure (moderate strength of evidence); patients receiving rTMS were more than 6 times as likely to achieve remission as those receiving the sham.”*** The AHRQ Comparative Effectiveness report is particularly important because their findings represent a rigorously conducted, unbiased assessment of the available scientific evidence. They stand in a unique and authoritative position as a statement on the favorable scientific and clinical conclusions that can be drawn from the peer-reviewed, published literature on the use of TMS in depression. Finally, they are consistent with the prevailing conclusions in the broader scientific literature regarding the safety and efficacy of the use of TMS in pharmacoresistant major depression.

The conclusions of the AHRQ report have been independently examined by the New England Comparative Effectiveness Public Advisory Council (CEPAC). CEPAC is an independent, 19-member organization composed of clinicians, patient and public health advocates, representatives of state public health programs and regional private payers from New England states. Their mission is to produce actionable information to aid regional policymakers in the medical policy decision-making process.

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 payor expenditures of providing TMS as a covered benefit.

Specifically, the CEPAC Panel arrived at the following conclusions:

* In a Panel vote on the fundamental question: ***“For patients who have TRD[Treatment Resistant Depression], is the evidence adequate to demonstrate that rTMS provides a net health benefit equivalent or superior to usual care (i.e., general supportive psychotherapy with or without continued use of antidepressant medication)?”***, 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.
* In a Panel vote on the separate question: ***“For patients who have TRD, is the evidence adequate to demonstrate that rTMS provides a net health benefit equivalent or superior to ECT? “***, the CEPAC Panel again voted **majority in support** of 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 payors of covering TMS ranges from $0.21 - $0.59, or a relatively modest 0.07 - 0.2% increase in plan costs.***

Verification of these research outcomes has been provided by a recently published study which evaluated the clinical outcomes of NeuroStar TMS Therapy in routine clinical practice (Carpenter, et al, 2012.) In this study, acute outcomes for NeuroStar TMS Therapy under conditions of general clinical use, were comparable to those shown in open-label clinical trials and for patients across a range of treatment resistance and illness morbidity.

TMS Therapy has a favorable safety profile, particularly as compared to antidepressant drug therapy which is associated with numerous systemic side effects. As described above, there is adequate evidence that TMS is at least as effective as antidepressant drug therapy in treating depression in patients who have failed to benefit from prior antidepressant medication. Therefore, considering the data in total, TMS Therapy presents a strong benefit to risk ratio, especially when compared to antidepressant medications.

1. **The improvement obtained with TMS Therapy is attainable outside of investigational settings.**

NeuroStar TMS Therapy is now in widespread clinical use across the country 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 psychiatric hospitals and private physician’s offices.

Also, TMS Therapy has received positive medical policy coverage - Medicare coverage policies in states such as Delaware, District of Columbia, Maryland, New Jersey, Pennsylvania, Massachusetts, New Hampshire, Maine,

Vermont, Rhode Island, Tennessee, Alabama and Georgia, and large insurance entities with medical and behavioral coverage policies such as HealthNet/MHN and Anthem [to include these states Nebraska, Rhode Island, Pennsylvania, Georgia, Connecticut, New York, Ohio, Wisconsin, Indiana, Colorado, California, Missouri, New Hampshire and Virginia] and positive medical necessity guidelines with behavioral health payer entities such as Magellan.

*(Please choose the denial reference if the Payer refers to the BCBS Technology Evaluation Criteria OR if the general denial reference is “experimental/investigational”).*

In summary, the NeuroStar TMS Therapy system meets the five BCBS Technology Evaluation Criteria.

*(OR)*

In summary, the NeuroStar TMS Therapy system is not experimental investigational, as demonstrated by the supportive evidence.

**2) DURABILITY**

Your letter of denial letter states that there is a lack of long term durability data to support the efficacy and safety of Transcranial Magnetic Stimulation (TMS) Therapy.

Long-term outcomes following acute treatment with the NeuroStar TMS Therapy system have been described

(Janicak, et al, 2010.) This report describes the clinical outcome in six months of follow up in a cohort of 99 patients

who had benefited from acute treatment with to up to six weeks of NeuroStar TMS Therapy, 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 agents, however, TMS could be re-administered if patients met protocol-specified criteria for symptom re-emergence. Relapse was the primary outcome. In this analysis, 10 of 99 patients (10%; Kaplan-Meier survival estimate = 12.9%) met protocol-specified relapse criteria during the 6 months of follow-up. Thirty-eight (38.4%) met criteria for symptom worsening

and 32/38 (84.2%) re-achieved symptomatic benefit with adjunctive TMS.

This study describes the durability of effect after acute benefit with Transcranial Magnetic Stimulation Therapy.

**3) PATIENT SHOULD HAVE/HAS NOT TRIED ECT**

The letter of denial letter states that my patient (has not tried/should try) a course of electroconvulsive therapy (ECT).

Please refer to the ECT information in the sections below which describe the medical necessity reasons according to this patient’s case.

Although ECT may be used as a treatment for pharmacoresistant depression, its efficacy and durability of effect may be limited. A study involving 342 patients at seven hospitals in the New York metropolitan area conducted to determine the effectiveness and remission rates with ECT in a community setting concluded that the remission rate was 30.3%-46.7%

(Prudic J. et al 2004.) Among remitters being maintained with continuation ECT, the percent remaining in remission at

24 weeks was 37.1%. This compares with NeuroStar TMS Therapy open-label trial remission rates of 30% (Demitrack, MA, Thase, ME, 2009 ) and durability of effect study data wherein 73.2% of patients who met criteria for remission on

study entry remained in remission at the six month study completion (Janicak, et al, 2010.) Also, TMS has a more benign safety profile than ECT and does not include the complications associated with anesthesia, the cardiac risks, or the risk of cognitive disturbance.

I am also requesting that you consider the medical necessity demonstrated by (Patient’s Name)’s history of Major Depressive Disorder and the previous treatments tried and failed to support the use of Transcranial Magnetic Stimulation Therapy in my patient.

The AMA defines "medical necessity" as services or items reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. Medical guidelines employed for medical decision-making must be flexible and allow for deviations from the guideline in order to incorporate the patient's unique medical factors. Specifically, medical necessity decisions require careful review of patient specific variables such as age, sex, race or ethnicity, co-morbidities, socioeconomic considerations, treatment history, family medical history, treatment compliance record, potential side effects, allergies and patient's concerns and goals regarding treatment options.

The CPT Editorial Research and Development committee of the AMA has granted TMS Therapy Category I CPT codes. The AMA has determined that TMS Therapy is consistent with current medical practice, is widely practiced throughout the country and has the support of the relevant medical societies.

Effective January 1, 2011, the following CPT I codes are to be used for reporting TMS Therapy medical services according to the two main phases of the treatment. These two codes are CPT 90868 (TMS treatment; initial, including delivery and management) and 90868 (TMS treatment; subsequent delivery and management, per session). Another code, 90869 (TMS treatment; subsequent motor threshold re-determination with delivery and management), has been issued for use only in accordance with the clinical need of re-assessing the motor threshold (MT).

Because of the multitude of patient-specific variables that need to be considered, the patient’s treating physician is in the best position to assess the medical necessity of a specific treatment and to determine the optimal course of therapy. NeuroStar TMS Therapy is the appropriate treatment, and medically necessary for my patient, because (Insert Reason).

In my clinical judgment, TMS Therapy is the safest and most effective treatment option for my patient at this time.

(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).

She/He endorses the following symptoms of depression: (Please insert all symptoms that affect his/her quality of life and activities of daily living).

The patient has tried the following treatments, but has not found any alleviation of symptoms, and has not shown any significant improvement as a result of these treatment modalities.

The patient has been administered a pharmacological regimen that has included (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).

*(Regarding ECT Treatment, please include which option applies to the patient’s case):*

In addition to (Patient Name)’s resistance to medication treatment, (he/she) has undergone electroconvulsive therapy (ECT). *(Please insert # of sessions, timeframe and results including side effects and tolerability.).*

*(OR)* 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 hospitalization if 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).

(Patient Name) is currently in (psychotherapy and/or cognitive therapy) for the treatment of (his/her) depression.

*(The following is only applicable if this request is a Claims Appeal. Please add the following only for patients who have received TMS Therapy):*

Furthermore, I ask that you consider the fact that this patient has not benefitted from multiple exposures to psychopharmacologic agents such as \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. The patient responded well to NeuroStar TMS Therapy with a marked reduction in symptoms and tolerated the treatments well with (no/minimal) side effects. (He/She) experienced additional benefits such as (Include all benefits and results from the treatment i.e., a highly improved level of daily functioning/etc.).

I appreciate your review of the peer reviewed references, as well as the medical records I have included, as additional support for TMS Therapy for my patient. I am also available to discuss this case and the treatment directly. You may contact me at (Physician’s Phone Number), if needed. Please notify me in writing of your coverage decision as soon as possible.

Sincerely,

**(Physicians’ Name)**

**(Name of Practice)**

**(Address)**

**(Phone Number)**

**(Fax Number)**

*Enclosures:* Corresponding Denial Letters

Patient’s Clinical Notes

AMA CPT I Coding Approval Letter

Bibliography of Publications

Executive Summary

FDA Clearance Letter

*References:*

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