Transcranial Magnetic Stimulation as a Treatment of Depression and Other Psychiatric/Neurologic Disorders
Corporate Medical Policy

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Description

Transcranial magnetic stimulation (TMS) is a noninvasive method of delivering electrical stimulation to the brain. A magnetic field is delivered through the skull where it induces electric currents that affect neuronal function. Repetitive TMS (rTMS) is being evaluated as a treatment of depression and other psychiatric/neurologic disorders.

TMS involves placement of a small coil over the scalp; passing a rapidly alternating current through the coil wire, which produces a magnetic field that passes unimpeded through the scalp and bone, resulting in electrical stimulation of the cortex. The literature on rTMS for treatment-resistant depression (TRD) includes numerous double-blind, randomized sham-controlled short-term trials. Results of these trials show mean improvements of uncertain clinical significance across groups as a whole. The percentage of subjects who show a clinically significant response is reported at approximately 2 to 3 times that of sham controls, with approximately 15% to 25% of patients meeting the definition of clinical response. Based on the short-term benefit observed in randomized controlled trials (RCTs), clinical input, and the lack of alternative treatments aside from electroconvulsive therapy (ECT) in patients with TRD, rTMS may be considered medically necessary in patients with TRD who meet specific criteria.

For other psychiatric/neurologic conditions, the evidence is insufficient to determine whether rTMS leads to improved outcomes. The available clinical trials are small and report mixed results for a variety of conditions other than depression. There are no large, high-quality trials for any of these other conditions. Therefore, rTMS is considered investigational for other psychiatric/neurologic conditions.
Policy
Coding Information

Click the links below for attachments, coding tables & instructions.
Attachment I- CPT Code List & Instructions
Attachment II- ICD Code List

When a service may be considered medically necessary

Repetitive transcranial magnetic stimulation (rTMS) of the brain may be considered medically necessary as a treatment of major depressive disorder when all of the following conditions (1-3) have been met:

1. Confirmed diagnosis of severe major depressive disorder (single or recurrent) documented by standardized rating scales that reliably measure depressive symptoms; AND
2. Any one of the following (a, b, c, or d):
   a. Failure of 4 trials of psychopharmacologic agents including 2 different agent classes and 2 augmentation trials; OR
   b. Inability to tolerate a therapeutic dose of medications as evidenced by 4 trials of psychopharmacologic agents with distinct side effects; OR
   c. History of response to rTMS in a previous depressive episode (at least 3 months since the prior episode); OR
   d. Is a candidate for electroconvulsive therapy (ECT) and ECT would not be clinically superior to rTMS (eg, in cases with psychosis, acute suicidal risk, catatonia or life-threatening situation rTMS should NOT be utilized); AND
3. Failure of a trial of a psychotherapy known to be effective in the treatment of major depressive disorder of an adequate frequency and duration, without significant improvement in depressive symptoms, as documented by standardized rating scales that reliably measure depressive symptoms.

When a service is considered investigational

rTMS for major depressive disorder that does not meet the criteria listed above is considered investigational.

Continued treatment with rTMS of the brain as maintenance therapy is considered investigational.

Transcranial magnetic stimulation of the brain is considered investigational as a treatment of all other psychiatric/neurologic disorders, including but not limited to bipolar disorder, schizophrenia, obsessive- compulsive disorder, or migraine headaches.
Policy Guidelines

Repetitive transcranial magnetic stimulation should be performed using a U.S. Food and Drug Administration (FDA)–cleared device in appropriately selected patients, by physicians who are adequately trained and experienced in the specific techniques used. A treatment course should not exceed 5 days per week for 6 weeks (total of 30 sessions), followed by a 3-week taper of 3 TMS treatments in week 1, 2 TMS treatments in week 2, and 1 TMS treatment in week 3.

rTMS provided in the presence of one of the contraindications below may be considered not medically necessary:

a. Seizure disorder or any history of seizure with increased risk of future seizure; OR
b. Acute or chronic psychotic symptoms or disorders (such as schizophrenia, schizoaffective disorder) presenting within the current depressive episode; OR
c. Neurologic conditions that include epilepsy, cerebrovascular disease, dementia, increased intracranial pressure, a history of repetitive or severe head trauma, or with primary or secondary tumors in the central nervous system (CNS); OR
d. Presence of an implanted magnetic-sensitive medical device located 30 centimeters or less from the TMS magnetic coil or other implanted metal items, including but not limited to a cochlear implant, implanted cardioverter defibrillator (ICD), pacemaker, vagus nerve stimulator, or metal aneurysm clips or coils, staples, or stents.

The following should be present for the administration of rTMS:

a. An attendant trained in basic cardiac life support and the management of complications such as seizures, as well as the use of the equipment must be present at all times; AND
b. Adequate resuscitation equipment including, for example, suction and oxygen; AND
c. The facility must maintain awareness of response times of emergency services (either fire/ambulance or “code team”), which should be available within five minutes. These relationships are reviewed at least annually and include mock drills.

Background

TMS was first introduced in 1985 as a new method of noninvasive stimulation of the brain. The technique involves placement of a small coil over the scalp; passing a rapidly alternating current through the coil wire, which produces a magnetic field that passes unimpeded through the scalp and bone, resulting in electrical stimulation of the cortex. TMS was initially used to investigate nerve conduction; for example, TMS over the motor cortex will produce a contralateral muscular-evoked potential. The motor threshold, which is the minimum intensity of stimulation required to induce a motor response, is empirically determined for each person by localizing the site on the scalp for optimal stimulation of a hand muscle,
then gradually increasing the intensity of stimulation. The stimulation site for treatment of depression is usually 5 cm anterior to the motor stimulation site.

Interest in the use of TMS as a treatment for depression was augmented by the development of a device that could deliver rapid, repetitive stimulation. Imaging studies show a decrease in activity of the left dorsolateral prefrontal cortex (DLPFC) in depressed patients, and early studies suggested that high-frequency (eg, 5-10 Hz) TMS of the left DLPFC had antidepressant effects. Low-frequency (1-2 Hz) stimulation of the right DLPFC has also been investigated. The rationale for low-frequency TMS is inhibition of right frontal cortical activity to correct the interhemispheric imbalance. A combination approach (bilateral stimulation), or deep stimulation with an H1 coil, are also being explored. In contrast to electroconvulsive therapy, TMS does not require anesthesia and does not induce a convulsion.

rTMS is also being tested as a treatment for a variety of other disorders including alcohol use disorder, Alzheimer disease, neuropathic pain, obsessive-compulsive disorder, postpartum depression, Parkinson disease, stroke, posttraumatic stress disorder, panic disorder, epilepsy, dysphagia, Tourette syndrome, schizophrenia, migraine, spinal cord injury, fibromyalgia, and tinnitus. (See Policy No. 8.01.39 regarding rTMS for tinnitus.) In addition to the potential for altering interhemispheric imbalance, it has been hypothesized that high-frequency rTMS may facilitate neuroplasticity.

Regulatory Status

Devices for transcranial stimulation have received clearance by the FDA for diagnostic uses. One device, NeoPulse® (Neuronetics, Atlanta, GA), received approval in Canada, Israel, and the United States as a treatment for depression. Initially examined by the FDA under a traditional 510(k) application, the NeoPulse, now known as NeuroStar® TMS, received clearance for marketing as a “de novo” device in 2008. NeuroStar® TMS is indicated for the treatment of patients with depression for whom one 6-week course of antidepressant medication was ineffective. The Brainsway™ H-Coil Deep TMS device (Brainsway Ltd.) received FDA clearance in 2013. This device is indicated for the treatment of depression in patients who have failed to respond to antidepressant medications in their current episode of depression and is a broader indication than that of the NeuroStar® TMS, which specifies the failure of 1 course of antidepressant medication (FDA product code: OBP).

Note: An FDA advisory panel met in January 2007 to determine if the risk-to-benefit profile for the NeoPulse was comparable with the risk-to-benefit profile of predicate ECT devices. The panel was not asked for a recommendation regarding the regulatory determination of substantial equivalence for this 510(k) submission. Materials presented at the Neurological Devices Panel meeting are posted online (www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4273b1_00-index.htm).

In 2013, the Cerena™ TMS device (Eneura Therapeutics) received de novo marketing clearance for the acute treatment of pain associated with migraine
headache with aura. Warnings, precautions, and contraindications include the following:

- The device is only intended for use by patients experiencing the onset of pain associated with a migraine headache with aura.
- The device should not be used on headaches due to underlying pathology or trauma.
- The device should not be used for headaches caused by medication overuse.
- The device has not been demonstrated as safe or effective when treating cluster headache or chronic migraine headache.
- The device has not been shown to be effective when treating during the aura phase.
- The device has not been demonstrated as effective in relieving the associated symptoms of migraine (photophobia, phonophobia, and nausea).
- Safety and effectiveness have not been established in pregnant women, children under the age of 18, and adults over the age of 65.

The de novo 510(k) review process allows novel products with moderate or low-risk profiles and without predicates which would ordinarily require premarket approval as a class III device to be down-classified in an expedited manner and brought to market with a special control as a class II device.

Rationale

This policy is updated periodically with searches of the MEDLINE database, with the most recent literature update performed through October 30, 2014. At the time this policy was created, the U.S. Food and Drug Administration (FDA) had not cleared transcranial magnetic stimulation (TMS) as a therapeutic device for any neuropsychiatric disorder, including depression. On November 9, 2015, the NeuroStar® TMS received FDA marketing clearance as a de novo device for therapy of patients with treatment-resistant depression (TRD) who have failed one 6-week course of antidepressant medication.

Following is a summary of the key literature to date, focusing on systematic reviews and randomized controlled trials (RCTs). The evidence review is divided by indication and by key differences in treatment protocols, specifically high-frequency left dorsolateral prefrontal cortex (DLPFC) stimulation, low-frequency (1-2 Hz) stimulation of the right DLPFC, combined high-frequency and low-frequency stimulation, and deep brain stimulation.

Depression

Over the last decade, there has been a trend to increase the intensity, trains of pulses, total pulses per session, and number of sessions. Unless otherwise indicated in the trials described next, stimulation was set at 100% to 120% of motor threshold, clinical response was defined as an improvement of 50% or more on the Hamilton Rating Scale for Depression (HAM-D), and remission was considered to be a score of 7 or less on the HAM-D. Refer to the 2009 meta-analysis by Schutter for a summary of
study characteristics and stimulation parameters used in trials conducted prior to 2008.

**Blue Cross and Blue Shield Technology Evaluation Center**

TEC published assessments of repetitive TMS (rTMS) for depression in 2009, 2011, and 2013. These TEC Assessments demonstrate that the available evidence is inconclusive regarding the effect of TMS on health outcomes. Limitations of the evidence include:

- Equivocal efficacy in the 3 largest sham-controlled trials of TMS,
- Uncertain clinical significance of the short-term anti-depressant effects found in meta-analyses, which are also at high risk of bias due to the inclusion of numerous small trials and potential for publication bias,
- Limited evidence beyond the acute period of treatment, and
- Lack of comparison with standard therapy (a second course of antidepressant therapy) in the population for whom TMS is indicated (patients who have failed one 6-week course of antidepressant medication).

**Efficacy of nonpharmacologic interventions against other nonpharmacologic interventions (KQ1a)**

**Direct evidence**

- The available head-to-head literature concerning the efficacy of the nonpharmacologic interventions for tier 1 TRD was limited to 2 fair trials (both in major depressive disorder-only populations). One compared electroconvulsive therapy (ECT) and rTMS, and the other compared ECT and ECT plus rTMS. They showed, with low strength of evidence, no differences between treatment options for depressive severity, response rates, and remission rates. No trial involved a direct comparison of psychotherapy with another nonpharmacologic intervention.

**Indirect evidence**

- Trials were identified that compared a nonpharmacologic intervention, generally rTMS, vagus nerve stimulation (VNS), or psychotherapy, with a control or sham procedure in tier 1 populations (ie, patients who had 2 or more prior treatment failures with medications). The number of these trials with the same or similar control group was very small and could not be pooled quantitatively. They assessed the potential benefits of nonpharmacologic interventions versus controls by calculating mean changes in depressive severity, relative risks of response, and relative risks of remission.

- rTMS was beneficial relative to controls receiving a sham procedure for all 3 outcomes (severity of depressive symptoms, response rate, remission rate). rTMS produced a greater decrease in depressive severity (high strength of evidence). Specifically, rTMS averaged a decrease in depressive severity measured by the HAM-D (>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 3 times as likely to achieve a depressive response as patients receiving a 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.
Efficacy of nonpharmacologic interventions compared with antidepressant pharmacotherapies (KQ 1b).

**Direct evidence**
- No direct evidence was identified for rTMS.

Maintenance of remission or prevention of relapse (KQ 2).

**Direct evidence**
- In terms of maintaining remission (or preventing relapse), there were no direct comparisons involving ECT, rTMS, VNS, or cognitive behavioral therapy (CBT).

**Indirect evidence**
- Three fair trials compared rTMS with a sham procedure and found no significant differences.

However, too few patients were followed during the relapse prevention phases in 2 of the 3 studies, and patients in the third study received a co-intervention, providing insufficient evidence for a conclusion.

**AHRQ Authors’ Conclusions**
The evidence review suggests that comparative clinical research on nonpharmacologic interventions in a TRD population is early in its infancy, and many clinical questions about efficacy remain unanswered. Interpretation of the data is substantially hindered by varying definitions of TRD and the paucity of relevant studies. The greatest volume of evidence is for ECT and rTMS. However, even for the few comparisons of treatments that are supported by some evidence, the strength of evidence is low for benefits, reflecting low confidence that the evidence reflects the true effect and indicating that further research is likely to change our confidence in these findings. This finding of low strength is most notable in 2 cases: ECT and rTMS did not produce different clinical outcomes in TRD, and ECT produced better outcomes than pharmacotherapy. No trials directly compared the likelihood of maintaining remission for nonpharmacologic interventions. The few trials addressing adverse events, subpopulations, subtypes, and health-related outcomes provided low or insufficient evidence of differences between nonpharmacologic interventions. The most urgent next steps for research are to apply a consistent definition of TRD, to conduct more head-to-head clinical trials comparing nonpharmacologic interventions with themselves and with pharmacologic treatments, and to delineate carefully the number of treatment failures following a treatment attempt of adequate dose and duration in the current episode.

**High-Frequency rTMS of the Left DLPFC for TRD**
There is a large body of evidence for the use of rTMS in the treatment of depression. The largest study (23 study sites) to date is a double-blind multicenter trial with 325 TRD patients randomly assigned to daily sessions of high-frequency active or sham rTMS (Monday through Friday for 6 weeks) of DLPFC. TRD was defined as failure of at least 1 adequate course of antidepressant treatment. Patients had failed an average of 1.6 treatments in the current episode, with approximately half of the study population failing to benefit from at least 2 treatments. Loss to follow-up was similar in the 2 groups, with 301
(92.6%) patients completing at least 1 post-baseline assessment and an additional 8% of patients from both groups dropping out before the 4-week assessment. Intention-to-treat (ITT) analysis showed a trend favoring the active rTMS group in the primary outcome measure (2 points on the Montgomery-Asberg Depression Rating Scale [MADRS]; p=0.057) and a modest (2-point) but significant improvement over sham treatment on the HAM-D. The authors reported that after 6 weeks of treatment, subjects in the active rTMS group were more likely to have achieved remission than the sham controls (14% vs 5%, respectively), although this finding is limited by loss to follow-up.

In 2010, George et al reported a randomized, sham-controlled trial that involved 199 patients treated with left-prefrontal rTMS.8 This was a multicenter study involving patients with a moderate level of treatment resistance. The response rate using an ITT analysis was 14% for rTMS and 5% for sham (p=0.02). In this study, the site for stimulation was determined through pretreatment magnetic resonance imaging. Results from phase 2 (open treatment of nonresponders) and phase 3 (maintenance and follow-up) will be reported in the future.

Comparison with ECT
A 2013 systematic review by Berlim et al identified 7 RCTs with a total of 294 patients that directly compared rTMS and ECT treatment for patients with depression. After an average of 15.2 sessions of high-frequency rTMS over the left DLPFC, 33.6% of patients were classified as remitters. This compared with 52% of patients who were classified as remitters following an average of 8.2 ECT sessions. The pooled odds ratio was 0.46, indicating a significant difference in outcomes favoring ECT. There was no significant difference in dropout rates for the 2 treatments.

Deep TMS of the Left DLPFC for TRD
The RCT leading to 510(k) clearance of the Brainsway deep TMS system was conducted at 20 centers in the United States (n=13), Israel (n=4), Germany (n=2), and Canada (n=1). The study included 229 patients with major depressive disorder who had not received benefit from 1 to 4 antidepressant trials or were intolerant to at least 2 antidepressant treatments. Per protocol analysis, which excluded 31 patients who did not receive adequate TMS treatment and 17 patients who did not meet the inclusion and exclusion criteria, the RCT showed a significant benefit for both response rate (38.4% vs 21.4%) and remission rate (32.6% vs 14.6%). Modified ITT analysis, which excluded the 17 patients who did not meet the inclusion/exclusion criteria, showed a significant benefit in both response rate (37% vs 22.8%) and remission rate (30.4% vs 15.8%). At the end of the maintenance period (16-week follow-up), the response rate remained significantly improved by deep TMS. Remission rates were not reported. ITT analysis found no significant benefit of treatment at 4 or 16 weeks.

Low-Frequency rTMS of the Right DLPFC or Bilateral Stimulation for TRD
Fitzgerald et al randomly assigned 60 patients who had failed a minimum of at least 2 6-week courses of antidepressant medications to 1 of 3 groups; high-frequency left rTMS, low-frequency right rTMS, or sham stimulation over 10 sessions. All patients who entered the study completed the double-blind randomized phase, which showed no difference between the 2 active treatments (left, 13.5% reduction; right, 15% reduction) and greater improvements in the MADRS scores compared with the sham group (0.76% reduction). Only 1 patient achieved 50%
improvement during the initial 2 weeks. Then, only the subjects who showed at least 20% improvement at the end of the 10 sessions (15 active, 2 sham) continued treatment. Patients who did not respond by at least 20% were switched to a different active treatment. From week 2 to week 4, there was greater improvement in the low-frequency right rTMS group compared with the high-frequency left rTMS group (39% vs 14% improvement in MADRS, respectively). Seven patients (18% of 40) showed a clinical response of greater than 50% by the end of the 4 weeks.

In a subsequent study, Fitzgerald et al randomly assigned 50 patients with TRD to sequential bilateral active or sham rTMS. After 2 weeks of treatment, 3 subjects had dropped out of the sham treatment group, and there was a slight but insignificant improvement favoring the active group for the MADRS (26.2 vs 30.9, respectively) and the Beck Depression Inventory (BDI; 18.3 vs 21.6, respectively).

At this time point, 60% of subjects receiving active rTMS and 50% of subjects receiving sham treatment guessed that they were in the active group. The clinical response was reported by subjects as the major reason for their guess, with 11 of 13 responders (9 active, 2 sham) guessing that they were in the active group. As in the earlier study, only the subjects who showed at least 20% improvement at the end of each week continued treatment. Treatment on week 3 was continued for 15 subjects in the active group and 7 subjects in the sham group. By week 6, 11 subjects in the active rTMS group remained in the study, with no control subjects remaining. Final ratings for the 11 subjects who continued to respond through week 6 were 8.9 on the MADRS and 9.2 on the BDI.

Another multicenter double-blind trial randomly assigned 130 patients with TRD to 5 sessions per week of either 1- or 2-Hz rTMS over the right DLPFC. Sixty-eight patients (52%) completed 4 weeks of treatment; there was an approximate 30% improvement in depression scales outcomes, with no differences between the 1- or 2-Hz groups. Due to the potential for placebo effects for this type of intervention, the absence of a sham control group limits interpretation.

A small, randomized, sham-controlled trial was published in 2010 that involved either right or left rTMS in 48 patients with TRD. Overall reductions in the HAM-D-24 from baseline to 3 months were not significantly different between rTMS and sham treatment groups. In this small study, right cranial stimulation was significantly more effective than left cranial stimulation (sham or rTMS).

rTMS as an Adjunctive Treatment for Moderate-to-Severe Depression

Berlim et al reported a 2013 meta-analysis on the effect of rTMS for accelerating and enhancing the clinical response to antidepressants. Data were obtained from 6 double-blind RCTs with a total of 392 patients. Response was defined as a 50% or greater decrease in scores on the HDRS or the MADRS. At an average of 2.7 weeks after the start of the combined treatments, response rates were significantly higher with rTMS plus antidepressant treatment compared with sham rTMS (43.3% vs 26.8%; odds ratio [OR], 2.50); remission rates were not significantly different. At the end of the studies (average, 6.8 weeks), response and remission rates were significantly higher with combined high-frequency rTMS plus antidepressant treatment compared with sham rTMS (response, 62% vs 46%; OR= -1.9; remission, 53.8% vs 38.6%; OR=2.42).

A 2012 study examined the efficacy of ultra-high-frequency (30 Hz) rTMS over the left prefrontal cortex in moderately to severely depressed patients who were taking medication. Sham treatment consisted of low-frequency stimulation to the left
prefrontal cortex. No benefit of rTMS for depressive symptoms was found when lithium was added as a covariate. Ultra-high-frequency rTMS was found to improve performance on the Trail-Making Test, which covaried with improvement of psychomotor ability.

Additional research on whether adjunctive rTMS can improve response to pharmacologic treatment as a first-line therapy is needed.

Maintenance Therapy
In 2014, Dunner et al reported 1-year follow-up with maintenance therapy from a large multicenter observational study (42 sites) of rTMS for patients with TRD.17 The 307 patients initially treated with rTMS, 257 agreed to participate in the follow-up study. Of these, 205 completed the 12-month follow-up, and 120 patients had met the Inventory of Depressive Symptoms-Self Report response or remission criteria at the end of treatment. Ninety-three of the 257 patients (36.2%) who enrolled in the follow-up study received additional rTMS (mean, 16.2 sessions). Seventy-five of the 120 patients (62.5%) who met response or remission criteria at the end of the initial treatment phase (including a 2 month taper phase) continued to meet response criteria through follow-up.

A variety of maintenance schedules are being studied. Richieri et al used propensity-adjusted analysis of observational data and found that the group of patients who had maintenance rTMS tapered over 20 weeks (from 3 times per week to once per month) had a significantly lower relapse rate compared with patients who had no additional treatment (37.8% vs 81.8%). Connolly et al reported that in the first 100 cases treated at their institution, the response rate was 50.6% and the remission rate was 24.7%. At 6 months after the initial rTMS treatment, 26 of 42 patients (62%) who received tapered maintenance therapy (from 2 sessions per week for the first 3 weeks to monthly) maintained their response. In another study, patients who met criteria for partial response during either a sham-controlled or open-label phase of a prior study were tapered from rTMS and simultaneously started on maintenance antidepressant monotherapy. During the 24-week follow-up, 10 of 99 patients relapsed, 38 reported worsening symptoms, and of these 32 (84%) had symptomatic benefit with adjunctive rTMS.

Fitzgerald et al reported a prospective open-label trial of clustered maintenance rTMS for patients with TRD. All patients had received a second successful course of rTMS following relapse and were then treated with monthly maintenance therapy consisting of 5 rTMS treatments over a 2.5-day period (Friday evening, Saturday, and Sunday). Of 35 patients, 25 (71%) relapsed at a mean of 10.2 months (range, 2-48 months).

Additional data are needed related to durability of effect and to maintenance therapy.

Alzheimer Disease
Ahmed et al randomized 45 patients with probable Alzheimer disease to 5 sessions of bilateral high-frequency rTMS, bilateral low-frequency rTMS, or sham TMS over the DLPFC. Thirty-two patients had mild to moderate dementia and 13 had severe dementia. There were no significant differences between groups at baseline. Measures of cortical excitability immediately after the last treatment session showed that treatment with high-frequency rTMS reduced the duration of transcallosal inhibition. Three months after treatment, the high-frequency rTMS group improved significantly more than the other 2 groups in standard rating
scales, and subgroup analysis showed that this was due primarily to improvements in patients with mild/moderate dementia. Patients in the subgroup of mild to moderate dementia who were treated with high-frequency rTMS improved from 18.4 to 22.6 on the Mini-Mental Status Examination, from 20.1 to 24.7 on the Instrumental Daily Living Activity scale, and from 5.9 to 2.6 on the Geriatric Depression Scale.

Rabey et al reported an industry-sponsored randomized double-blind trial of rTMS with cognitive training (NeuroAD system) in 15 patients with probable mild to moderate Alzheimer disease. Patients received 5 sessions per week for 6 weeks over 6 different brain areas, followed by biweekly sessions for 3 months. Specific cognitive tasks were designed for the 6 targeted brain regions. These included syntax and grammar for Broca area, comprehension and categorization for Wernicke area, action naming, object naming and spatial memory tasks for the right and left DLPFC, and spatial attention tasks for the right and left somatosensory association cortex. After 6 weeks of treatment, there was an improvement in the average Alzheimer Disease Assessment Scale, cognitive subsection (ADAS-cog) score of 3.76 points in the rTMS group compared with 0.47 in the placebo group. After 4.5 months of treatment, the ADAS-cog score in the rTMS group had improved by 3.52 points compared with a worsening of 0.38 in the placebo group. The Clinical Global Impression of Change improved significantly by an average of 3.57 after 6 weeks and 3.67 after 4.5 months compared with 4.25 and 4.29, respectively, in the placebo group.

Attention-Deficit/Hyperactivity Disorder
In 2012, Weaver et al reported a randomized, sham-controlled crossover study of rTMS in 9 adolescents/young adults with attention deficit/hyperactivity disorder (ADHD). rTMS was administered in 10 sessions over 2 weeks, with 1 week of no TMS between the active and sham phases. The clinical global impression and ADHD-IV scales improved in both conditions over the course of the study, with no significant differences between the active and sham phases.

Amyotrophic Lateral Sclerosis or Motor Neuron Disease
A Cochrane review from 2013 identified 3 RCTs with a total of 50 participants with amyotrophic lateral sclerosis (ALS) that compared rTMS with sham TMS. All of the trials were considered to be of poor methodologic quality. Heterogeneity prevented pooling of results, and the high rate of attrition further increased the risk of bias. The review concluded that evidence is currently insufficient to draw conclusions about the efficacy and safety of rTMS in the treatment of ALS.

Bulimia Nervosa
In 2008, Walpoth et al reported no evidence of efficacy of rTMS in a small trial (n=14) of patients with bulimia nervosa.

Chronic Pain
A 2014 Cochrane review on noninvasive brain stimulation techniques identified 30 RCTs (528 patients) on TMS for chronic pain. There was low to very low quality evidence that low- frequency rTMS or rTMS to the DLPFC is ineffective. Studies on high-frequency rTMS to the motor cortex were heterogeneous, of low quality, and did not demonstrate a significant effect. Due the low quality of the identified studies, future studies could have a substantial impact on the conclusions.

Dysphagia
rTMS for the treatment of dysphagia following stroke has been examined in small RCTs. One study randomized 26 patients to rTMS or sham over the affected esophageal motor area of the cortex. Ten minutes of rTMS over 5 days reduced both dysphagia on the Dysphagic Outcome and Severity Scale and disability measured by the Barthel Index. There was a trend for improved hand grip strength in the rTMS group. Blinded assessment showed that the effects were maintained at 1-month and 2-month follow-up. Another study randomized 30 patients with dysphagia following stroke or traumatic brain injury to high-frequency rTMS, low-frequency rTMS, or sham stimulation. Active or sham rTMS was administered bilaterally over the anterolateral scalp over a period of 2 weeks. Swallowing scale scores improved in both the low-frequency and sham groups. Improvement in videofluoroscopic evaluation was greater in the low-frequency rTMS group than the other 2 groups. Blinding of evaluators was not described.

Study in a larger number of subjects is needed to determine the efficacy of this treatment with greater certainty.

Epilepsy
In 2012, Sun et al reported a double-blind RCT of low-frequency rTMS to the epileptogenic zone for refractory partial epilepsy. Sixty patients were randomized into 2 groups; one group received 2 weeks of rTMS at 90% of resting motor threshold, and the other group received rTMS at 20% of resting motor threshold. Outcomes were measured for 8 weeks after the end of treatment. With ITT analysis, high-intensity rTMS resulted in a significant decrease in seizures when compared with baseline (from 8.9 per week at baseline to 1.8 per week at follow-up) and when compared with low-intensity rTMS (from 8.6 at baseline to 8.4 per week at follow-up). High-intensity rTMS also decreased interictal discharges (from 75.1 to 33.6 per hour) and improved ratings on the Symptom Checklist–90. These initial results are promising, but require substantiation in additional trials.

Fibromyalgia
A 2012 systematic review included 4 studies on transcranial direct current stimulation and 5 on rTMS for treatment of fibromyalgia pain. Three of the 5 trials were considered to be high quality. Four of the 5 were double-blind RCTs; the fifth included study was a case series of 4 patients who were blinded to treatment. Quantitative meta-analysis was not conducted due to variability in brain site, stimulation frequency/intensity, total number of sessions, and follow-up intervals, but 4 of the 5 studies on rTMS reported significant decreases in pain. Greater durability of pain reduction was observed with stimulation of the primary motor cortex compared with the DLPFC.

One of the studies included in the systematic review was a small 2011 trial that was conducted in the United States by Short et al. Twenty patients with fibromyalgia, defined by the American College of Rheumatology criteria, were randomized to 10 sessions of left prefrontal rTMS or sham TMS along with their standard medications. At 2 weeks after treatment, there was a significant change from baseline in average visual analog scale for pain in the rTMS group (from 5.60 to 4.41) but not in the sham-treated group (from 5.34 to 5.37). There was also a significant improvement in depression symptoms in the active group compared with baseline (from 21.8 to 14.10) but not in the sham group (from 17.6 to 16.4). There were no statistically significant differences between the groups in this small trial.
A 2013 report evaluated the effect of very low-intensity rTMS in a randomized sham-controlled double-blinded trial of 54 patients with fibromyalgia. Six weeks of rTMS (once per week) with 33 magnetic coils around the head resulted in a significant improvement in pain thresholds (+28%) across the 8 sessions and in the ability to perform daily activities (11%), perceived chronic pain (-39%) and sleep quality (75%) beginning at week 6. Fatigue, anxiety, depression, and severity of headaches were unaffected by treatment.

Additional study is needed to determine effective treatment parameters in a larger number of subjects and to evaluate durability of the effect.

**Migraine Headache**
A pivotal randomized, double-blind, multicenter, sham-controlled trial was performed with the Cerena™ TMS device to demonstrate safety and effectiveness for the de novo application. Enrolled in the study were 201 patients with a history of aura preceding more than 30% of headaches with moderate or severe headache severity for approximately 90% of migraine attacks. Following a month baseline phase to establish the frequency and severity of migraine, patients were randomized to a treatment phase consisting of 3 treatments or 3 months, whichever occurred first. Patients were instructed to treat their migraine headache during the aura phase and to record their pain severity (0-3), severity of associated migraine symptoms (photophobia, phonophobia, nausea), presence of vomiting, and use of rescue medications at the time of treatment and at 1, 2, 24, and 48 hours after treatment. The primary end point was the proportion of patients who were pain-free 2 hours after treatment. Of the 201 patients enrolled, 164 recorded at least 1 treatment and 113 recorded at least 1 treatment when there was pain. Post hoc analysis of these 113 patients showed a benefit of the device for the primary end point (37.74% pain free after 2 hours for Cerena™ and 16.67% for sham, p=0.018) and for the proportion of subjects who were pain free after 24 hours (33.96% for Cerena™, 10% for sham; p=0.002). Active treatment was not inferior to sham for the proportion of subjects free of photophobia, suggesting that the device does not worsen photophobia. However, the device was not noninferior to sham for the proportion of subjects free of nausea and phonophobia.

These results are limited by the 46% dropout rate and post hoc analysis. According to the FDA labeling, the device has not been demonstrated as safe or effective when treating cluster headache, chronic migraine headache, or when treating migraine headache during the aura phase. The device has not been demonstrated as effective in relieving the associated symptoms of migraine (photophobia, phonophobia, nausea).

**Obsessive-Compulsive Disorder**
A 2013 meta-analysis included 10 small RCTs totaling 282 patients with obsessive-compulsive disorder. Response rates of rTMS augmentation therapy were 35% for active and 13% for sham rTMS. The pooled odds ratio was 3.39, and the number needed to treat was 5. There was no evidence of publication bias. Exploratory subgroup analysis suggested that the 2 most promising stimulation parameters were low-frequency rTMS and non-DLPFC regions (ie, orbitofrontal cortex or supplementary motor area). Further study focusing on these stimulation parameters is needed.

**Panic Disorder**
A 2014 Cochrane review identified 2 RCTs with a total of 40 patients that compared low-frequency rTMS with sham rTMS over the right DLPFC. The larger of the 2 studies was a randomized, double-blind, sham-controlled trial in 21 patients with panic disorder with comorbid major depression. Response was defined as a 40% or greater decrease on the Panic Disorder Severity Scale and a 50% or greater decrease on HAM-D. After 4 weeks of treatment, the response rate for panic was 50% with active rTMS and 8% with sham. The study had a high risk of attrition bias. The overall quality of evidence for the 2 studies was considered to be low, and the sample sizes were small, precluding any conclusions about the efficacy of rTMS for panic disorder.

**Parkinson Disease**

A systematic review from 2009 included 10 RCTs with a total of 275 patients with Parkinson disease. Seven of the studies were double-blind, 1 was not blinded, and 2 of the studies did not specify whether the raters were blinded. In studies that used high-frequency rTMS, there was a significant improvement on the Unified Parkinson’s Disease Rating Scale (UPDRS) with a moderate effect size of -0.58. For low-frequency rTMS, the results were heterogeneous and did not significantly reduce the UPDRS. The analyzed studies varied in outcomes reported, rTMS protocol, patient selection criteria, demographics, stages of Parkinson disease and duration of follow-up, which ranged from immediate to 16 weeks after treatment.

In 2012, Benninger et al reported a randomized double-blind sham-controlled trial of brief (6 seconds) very high-frequency (50 Hz) rTMS over the motor cortex in 26 patients with mild to moderate Parkinson disease. Eight sessions of 50-Hz rTMS did not improve gait, bradykinesia, or global and motor scores on the UPDRS compared with the sham-treated group. Activities of daily living were significantly improved a day after the intervention, but the effect was no longer evident at 1 month after treatment. Functional status and self-reported well-being were not affected by the treatment. No adverse effects of the very high-frequency stimulation were identified.

Another study from 2012 randomized 20 patients with Parkinson disease to 12 brief sessions (6 minutes) of high-frequency (5-Hz) rTMS or sham rTMS over the leg area of the motor cortex followed by treadmill training. Blinded evaluation showed a significant effect of rTMS combined with treadmill training on neurophysiologic measures, and change in fast walking speed and the timed up and go task. Mean treadmill speed improved to a similar extent in the active and sham rTMS groups.

A 2013 exploratory, multicenter, double-blind trial randomized 106 patients to 8 weeks of 1-Hz rTMS, 10 Hz rTMS, or sham stimulation over the supplementary motor area. At 9 weeks, all groups showed a similar amount of improvement. At the 20-week follow-up, only the 1 Hz group showed a significant improvement (6.84 points) in the primary outcome measure, the UPDRS part III. There was no significant improvement in other outcome measures.

Additional study with a larger number of subjects and longer follow-up is needed to determine if rTMS improves motor symptoms in patients with Parkinson disease.

**Postpartum Depression**

Myczkowski et al conducted a double-blind, sham-controlled study of 14 patients with postpartum depression randomized to 20 sessions of active or sham rTMS over
the left DLPFC. A positive response to treatment was defined as a reduction of at least 30% in the HAM-D and Edinburgh Postnatal Depression Scale (EPDS). At 2 weeks after the end of treatment, the active rTMS group showed significant improvements in the HAM-D, Global Assessment Scale, Clinical Global Impression and Social Adjustment Scale. The difference in the EPDS (reduction of 39.4% vs 6.2% for sham) did not reach statistical significance in this small study, and there were marginal cognitive and social improvements. In addition, results were presented as mean values, rather than by the proportion of patients who showed clinically meaningful improvement.

**Posttraumatic Stress Disorder**
The efficacy of rTMS for posttraumatic stress disorder (PTSD) has been examined in several small RCTs.

A 2004 study randomized 24 patients with PTSD to 10 sessions of low-frequency (1-Hz), high-frequency (10-Hz), or sham rTMS over the right DLPFC. Blinded assessment 2 weeks after the intervention found that high-frequency rTMS improved scores on the self-reported PTSD checklist (PCL) by 29.3%, the clinician evaluation on the Treatment Outcome PTSD scale by 39.0%, the HAM-D by 25.9%, and the Hamilton Anxiety Rating Scale by 44.1%. Scores for the sham and low-frequency group were not significantly improved.

In 2012, Watts et al reported a double-blind trial with 20 patients randomized to low-frequency rTMS or sham over the right DLPFC. Blinded evaluation at the end of treatment showed clinically significant improvements in scores on the Clinician Administered PTSD Scale (CAPS) and the PCL compared with sham. Depressive and anxiety symptoms also improved in the rTMS group. Six of the 10 rTMS patients showed a degradation of symptoms between the immediate posttreatment assessment and the 2-month post treatment follow-up.

In another double-blind trial, 30 patients with PTSD were randomized to deep, high-frequency rTMS after brief exposure to a script of the traumatic event, rTMS after a script of a nontraumatic event, or sham stimulation after a brief script of the traumatic event. Patients received 3 treatment sessions per week for 4 weeks, and response was defined as a 50% or greater improvement in CAPS score. ITT analysis showed a significant improvement in the total CAPS score in the exposure plus stimulation group (24.3) compared with rTMS alone (7.9) or traumatic exposure with sham rTMS (9.1). The greatest improvement was in the intrusive component of CAPS. Heart rate responses to the traumatic script were also reduced over the 4 weeks of treatment. The proportion of patients who showed a response to treatment was not reported and the durability of the response was not assessed.

**Section Summary**
Several small RCTs have reported improvement of PTSD with rTMS over the right dorsolateral cortex. Results of high-frequency versus low-frequency stimulation are conflicting, and durability of the response has not been assessed. Additional study is needed.

**Schizophrenia**
One of the largest areas of TMS research outside of depressive disorders is the treatment of auditory hallucinations in schizophrenia resistant to pharmacotherapy. In 2011, TEC published an Assessment of TMS as an adjunct treatment for
schizophrenia. Five meta-analyses were reviewed, along with RCTs in which measurements were carried out beyond the treatment period. A meta-analysis of the effect of TMS on positive symptoms of schizophrenia (hallucinations, delusions, disorganized speech and behavior) did not find a significant effect of TMS. Four meta-analyses that looked specifically at auditory hallucinations showed a significant effect of TMS. It was noted that outcomes were evaluated at the end of treatment, and the durability of the effect is unknown. The Assessment concluded that the available evidence is insufficient to demonstrate that TMS is effective in the treatment of schizophrenia.

A 2012 meta-analysis included 17 randomized, double-blind, sham-controlled trials (N=337) of the effect of rTMS on auditory hallucinations. When measured at the end of treatment, the mean effect size of rTMS directed at the left temporoparietal area was 0.40 (moderate), and the effect size of rTMS directed at all brain regions was 0.33 (small). For the 5 trials that examined outcomes of rTMS 1 month after treatment, the effect was no longer significant.

A 2013 meta-analysis included 17 RCTs (N=398) that evaluated low-frequency rTMS of the left temporoparietal cortex for the treatment of auditory hallucinations. The mean effect size for severity of auditory hallucinations (all studies) was -0.42. The odds ratio for the response to treatment, defined as a 30% or greater reduction, was 2.94 (6 trials, N=181).

A small (N=18) double-blind, randomized, sham-controlled trial from 2012 found no significant effect of deep rTMS with an H1 coil on auditory hallucinations.

**Section Summary**
The evidence on rTMS for the treatment of auditory hallucinations in schizophrenia consists of a number of small RCTs. Evidence to date shows small-to-moderate effects on hallucinations when measured at the end of treatment, but evidence suggests that the effect is not durable.

**Stroke**
There are a number of RCTs and systematic reviews that have evaluated rTMS for recovery from stroke.

A 2013 Cochrane review included 19 RCTs with a total of 588 participants on the effect of TMS for improving function after stroke. The 2 largest trials (N=183) showed that rTMS was not associated with a significant improvement in the Barthel Index. Four trials (N=73) found no significant effect for motor function. Subgroup analysis for different stimulation frequencies or duration of illness also did not show a significant benefit of rTMS when compared with sham rTMS or no treatment. The review concluded that current evidence does not support the routine use of rTMS for the treatment of stroke.

Hsu et al reported a meta-analysis of the effect of rTMS on upper-limb motor function in patients with stroke in 2012. Eighteen RCTs with a total of 392 patients were included in the meta-analysis. Most of the studies were double blind (n=11) or single blind (n=3). Eight studies applied low-frequency (1-Hz) rTMS over the unaffected hemisphere, 5 applied high-frequency (5-Hz) rTMS over the affected hemisphere, and 2 used both low- and high-frequency stimulation. Outcomes included kinematic motion analyses (5 trials), hand grip (2 trials), and the Wolf Motor Function Test (2 trials). Meta-analysis of results showed a moderate effect size (0.55) for rTMS on motor outcome, with a greater effect size of rTMS in
patients with subcortical stroke (mean effect size, 0.73) compared with nonspecified lesion sites (mean effect size, 0.45), and for studies applying low-frequency rTMS (mean effect size, 0.69) compared with high-frequency rTMS (effect size, 0.41). Effect size of 0.5 or greater was considered to be clinically meaningful.

A 2014 meta-analysis assessed the effect of rTMS on recovery of hand function and excitability of the motor cortex after stroke. Eight RCTs with a total of 273 participants were included in the review. The quality of the studies was rated moderate to high, although the size of the studies was small. There was variability in the time since stroke (5 days to 10 years), in the frequency of rTMS applied (1 Hz to 25 Hz for 1 second to 25 min/d), and in the stimulation sites (primary motor cortex or premotor cortex of the unaffected hemisphere). Meta-analysis found a positive effect on finger motor ability (4 studies; N=79; standardized mean difference, 0.58) and hand function (3 studies; N=74; standardized mean difference, -0.82), but no significant change in motor evoked potential (n=43) or motor threshold (n=62).

**Section Summary**

Evidence consists of a number of RCTs and meta-analyses of the effect of rTMS on recovery from stroke. Results are conflicting, and efficacy may depend on the location of the stroke and frequency of the rTMS. Additional study is needed to determine whether rTMS facilitates standard physical therapy in patients with stroke.

**Substance Abuse and Craving**

Jansen et al reported a 2013 meta-analysis of the effect of rTMS and transcranial direct current stimulation (tDCS) of the DLPFC on substance use disorder (alcohol, nicotine, cocaine, marijuana) or craving for high palatable food. Seventeen double-blind, sham-controlled RCTs that used high-frequency stimulation were included in the analysis. The standardized effect size was 0.476, indicating a medium effect size for active stimulation over sham, although there was significant heterogeneity in the included studies. No significant differences were found in the effectiveness of rTMS versus tDCS, the different substances, or the side of stimulation.

**Clinical Input Received From Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 1 physician specialty society and 3 academic medical centers while this policy was under review in 2014. The reviewers considered rTMS to be medically necessary for TRD. Input agreed with the proposed criteria for treatment of TRD with rTMS, as included in the policy statement.

**Summary of Evidence**

The literature on repetitive TMS (rTMS) for treatment-resistant depression (TRD) includes numerous double-blind, randomized sham-controlled short-term trials. Results of these trials show mean improvements of uncertain clinical significance.
across groups as a whole. The percentage of subjects who show a clinically significant response is reported at approximately 2 to 3 times that of sham controls, with approximately 15% to 25% of patients meeting the definition of clinical response. Based on the short-term benefit observed in randomized controlled trials, clinical input, and the lack of alternative treatments aside from electroconvulsive therapy (ECT) in patients with TRD, rTMS may be considered medically necessary in patients with TRD who meet specific criteria.

For other psychiatric/neurologic conditions, the evidence is insufficient to determine whether rTMS leads to improved outcomes. The available clinical trials are small and report mixed results for a variety of conditions other than depression. There are no large, high-quality trials for any of these other conditions. Therefore, rTMS is considered investigational for other psychiatric/neurologic conditions.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements
The American Psychiatric Association (APA) 2010 practice guidelines for the treatment of patients with major depressive disorder states that treatment in the acute phase should be aimed at inducing remission of the major depressive episode and achieving a full return to the patient’s baseline level of functioning [I, Recommended with substantial clinical confidence]. Acute phase treatment may include pharmacotherapy, depression-focused psychotherapy, the combination of medications and psychotherapy, or other somatic therapies such as ECT, TMS, or light therapy. APA states that a number of strategies are available when a change in the treatment plan seems necessary, such as transdermal selegiline, a relatively selective MAO B inhibitor with fewer dietary and medication restrictions, or transcranial magnetic stimulation could also be considered [II, Recommended with moderate clinical confidence].

A group of European experts was commissioned to establish evidence-based guidelines on the therapeutic use of rTMS. The guidelines included evidence published through March 2014. For most indications there was an absence of sufficient evidence, and the committee could provide no recommendation. Indications which had a recommendation of a definite effect were neuropathic pain and depression. Indications which had a recommendation for a possible or probable effect included complex regional pain syndrome, Parkinson disease, motor stroke, hemispatial neglect, epilepsy, tinnitus, anxiety disorders, auditory hallucinations, negative symptom of schizophrenia, addiction and craving.

In 2007 the National Institute for Health and Care Excellence (NICE) published an Interventional Procedure Guideline (IPG) 242, which stated that current evidence suggests no major safety concerns for the use of TMS in the treatment of depression. There was uncertainty related to the clinical efficacy of TMS, which may depend on a number of factors such as higher intensity, greater frequency, bilateral application, and/or longer treatment durations than have appeared in evidence to date. TMS should be performed in research studies designed to evaluate these factors. The opinion was repeated in the NICE 2009 Clinical Guideline 90.
NICE guidance in 2006 on the management of bipolar disorder in adults, children, and adolescents in primary and secondary care states that TMS should not be routinely used for acute depressive episodes in people with bipolar disorder. The guidance states that TMS is not of proven efficacy for bipolar disorder and that when compared with sham TMS, the participants receiving sham treatment had lower end point mania symptom scores.

2006 Practice Guidelines on the evaluation and treatment of depression, psychosis, and dementia in Parkinson disease from the American Academy of Neurology concluded that there is insufficient evidence to support or refute the efficacy of TMS or ECT in the treatment of depression associated with Parkinson disease (level U; data inadequate or conflicting given current knowledge, treatment is unproven).

The Canadian Network for Mood and Anxiety Treatments updated their clinical guidelines on neurostimulation therapies for the management of major depressive disorder in adults. The evidence reviewed supported ECT as a first-line treatment under specific circumstances; when used in patients who have failed to respond to 1 or more adequate antidepressant medication trials, ECT response rates have been estimated to be 50% to 60%. The guidelines considered rTMS to be a safe and well-tolerated treatment, with no evidence of cognitive impairment. Based on the 2008 meta-analysis by Lam et al, response (25%) and remission (17%) rates were found to be greater than sham but lower than for other interventions for TRD, leading to a recommendation for rTMS as a second-line treatment. The guidelines indicated that there is a major gap in the evidence base regarding maintenance rTMS, as only 1 open-label case series was identified.

Agency for Healthcare Research and Quality
The Agency for Healthcare Research and Quality (AHRQ) published a comparative effectiveness review on nonpharmacologic interventions for TRD in adults in 2011.6

Findings for the key questions (KQ) of the review follow.

Reference Resources

1. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Transcranial magnetic stimulation for depression. TEC Assessments 2009; Volume 24, Tab 5.
2. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Transcranial magnetic stimulation for depression. TEC Assessments 2011; Volume 26, Tab 3.


47. Yang YR, Tseng CY, Chiou SY et al. Combination of rTMS and Treadmill Training Modulates Corticomotor Inhibition and Improves Walking in Parkinson Disease: A Randomized Trial. Neurorehabil Neural Repair 2012.


66. Blue Cross and Blue Shield Association Medical Policy Manual, Policy Number: 2.01.50. Last Reviewed December 2015

Document Precedence

Blue Cross and Blue Shield of Vermont (BCBSVT) Medical Policies are developed to provide clinical guidance and are based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. The applicable group/individual contract and member certificate language, or employer’s benefit plan if an ASO group, determines benefits that are in effect at the time of service. Since medical practices and knowledge are constantly evolving, BCBSVT reserves the right to review and revise its medical policies periodically. To the extent that there may be any conflict between medical policy and contract/employer benefit plan language, the member’s contract/employer benefit plan language takes precedence.

Audit Information

BCBSVT reserves the right to conduct audits on any provider and/or facility to ensure compliance with the guidelines stated in the medical policy. If an audit identifies instances of non-compliance with this medical policy, BCBSVT reserves the right to recoup all non-compliant payments.
Administrative and Contractual Guidance

Benefit Determination Guidance

Prior approval is required and benefits are subject to all terms, limitations and conditions of the subscriber contract.

An approved referral authorization for members of the New England Health Plan (NEHP) is required. A prior approval for Access Blue New England (ABNE) members is required. NEHP/ABNE members may have different benefits for services listed in this policy. To confirm benefits, please contact the customer service department at the member’s health plan.

Federal Employee Program (FEP): Members may have different benefits that apply. For further information please contact FEP customer service or refer to the FEP Service Benefit Plan Brochure. It is important to verify the member’s benefits prior to providing the service to determine if benefits are available or if there is a specific exclusion in the member’s benefit.

Coverage varies according to the member’s group or individual contract. Not all groups are required to follow the Vermont legislative mandates. Member Contract language takes precedence over medical policy when there is a conflict.

If the member receives benefits through an Administrative Services Only (ASO) group, benefits may vary or not apply. To verify benefit information, please refer to the member’s employer benefit plan documents or contact the customer service department. Language in the employer benefit plan documents takes precedence over medical policy when there is a conflict.

Policy Implementation/Update information

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<tr>
<th>Date</th>
<th>Description</th>
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<tr>
<td>01/2017</td>
<td>Removed ICD 9 codes, Updated ICD Codes added F32.89 deleted F32.8, Updated references, Updated formatting to align to BCBSA MPRM # 2.01.50</td>
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Eligible providers

Qualified healthcare professionals practicing within the scope of their license(s).
Gabrielle Bercy-Roberson, MD, MPH
Senior Medical Director
Chair, Health Policy Committee

Joshua Plavin, MD, MPH
Chief Medical Officer

Attachment I
CPT Code List & Instructions

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Number</th>
<th>Description</th>
<th>Policy Instructions</th>
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<tr>
<td>CPT</td>
<td>90867</td>
<td>Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; initial, including cortical mapping, motor threshold determination, delivery and management</td>
<td>Prior Approval Required</td>
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<td>CPT</td>
<td>90868</td>
<td>Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; subsequent delivery and management, per session</td>
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<td>CPT</td>
<td>90869</td>
<td>Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; subsequent motor threshold re-determination with delivery and management</td>
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### Attachment II
**ICD-10 Code List**

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<th>Code Type</th>
<th>Number</th>
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<tr>
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<td>Major depressive disorder, single episode, moderate</td>
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<td>Major depressive disorder, single episode, severe without psychotic features</td>
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<td>ICD-10</td>
<td>F32.3</td>
<td>Major depressive disorder, single episode, severe with psychotic features</td>
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<td>ICD-10</td>
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<td>Major depressive disorder, recurrent severe without psychotic features</td>
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<tr>
<td>ICD-10</td>
<td>F33.9</td>
<td>Major depressive disorder, recurrent, unspecified</td>
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The following diagnosis codes are considered medically necessary for TMS when applicable criteria is met.