Medical Policy

Title: Transcranial Magnetic Stimulation (TMS) as a Treatment of Depression and Other Psychiatric Disorders

See also: Vagus Nerve Stimulation Treatment of Tinnitus

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<sup>a</sup> For example, Alzheimer disease, attention-deficit/hyperactivity disorder, amyotrophic lateral sclerosis, bulimia nervosa, chronic pain, epilepsy, fibromyalgia, migraine headache, obsessive compulsive disorder, panic disorder, Parkinson disease, postpartum depression, posttraumatic stress disorder, schizophrenia, stroke, and substance abuse and craving.
**DESCRIPTION**

Transcranial magnetic stimulation (TMS) is a noninvasive method of delivering electrical stimulation to the brain. TMS involves placement of a small coil over the scalp and passing a rapidly alternating current through the coil wire. The current produces a magnetic field that passes unimpeded through the scalp and bone, resulting in electrical stimulation that affects neuronal function. Repetitive transcranial magnetic stimulation (rTMS) is being evaluated for the treatment of treatment-resistant depression (TRD) and a variety of other psychiatric/neurologic disorders.

**Background**

Transcranial magnetic stimulation (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 individual 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 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 had showed a decrease in activity of the left dorsolateral prefrontal cortex (DLPFC) in depressed patients, and early studies suggested that high frequency (e.g., 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 H1coil,l are also being explored. In contrast to electroconvulsive therapy, TMS does not require anesthesia and does not induce a convulsion.

Repetitive TMS (rTMS) is also being tested as a treatment for a variety of other disorders including alcohol dependence, Alzheimer’s disease, neuropathic pain, obsessive-compulsive disorder (OCD), post-partum depression, depression associated with Parkinson’s disease, stroke, posttraumatic stress disorder, panic disorder, epilepsy, dysphagia, Tourette’s syndrome, schizophrenia, migraine, spinal cord injury, fibromyalgia, and tinnitus. In addition to the potential for altering interhemispheric imbalance, it has been proposed that high frequency rTMS may facilitate neuroplasticity.

**Regulatory Status**

Devices for transcranial stimulation have received clearance by the U.S. Food and Drug Administration (FDA) for diagnostic uses. One device, Neopulse® (Neuronetics, Atlanta,
GA), received approval in Canada, Israel, and the United States as a therapy 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 who have failed one 6-week course of antidepressant medication. 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 to the risk-to-benefit profile of predicate electroconvulsive therapy (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 medication overuse headaches.
- 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.
POLICY
A. 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 (e.g., in cases with psychosis, acute suicidal risk, catatonia or life-threatening inanition 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.

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

C. Continued treatment with rTMS of the brain as maintenance therapy is considered **experimental / investigational**.

D. Transcranial magnetic stimulation of the brain is considered **experimental / 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**

1. Repetitive transcranial magnetic stimulation should be performed using an 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 a week for 6 weeks (total of 30 sessions), followed by a 3-week taper of 3 TMS treatments in week 1, 2 TMS treatments the next week, and 1 TMS treatment in the last week.

2. Contraindications to rTMS include:
   a. Seizure disorder or any history of seizure with increased risk of future seizure; OR
   b. Presence of acute or chronic psychotic symptoms or disorders (such as schizophrenia, schizophreniform or schizoaffective disorder) in the current depressive episode; OR
   c. Neurologic conditions that include epilepsy, cerebrovascular disease, dementia, increased intracranial pressure, having 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.

3. 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 on at least a one year basis and include mock drills.

**RATIONALE**

This policy is updated periodically with searches of the MEDLINE database, with the most recent literature update performed through November 9, 2015. 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. In October 2008, the NeuroStar® TMS received U.S. Food and Drug Administration (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**

Note that over the last decade, there has been a trend to increase the intensity, trains of pulses, total pulses per session, and number of sessions.1 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 2008.2

The Blue Cross and Blue Shield Technology Evaluation Center (TEC) published assessments of repetitive TMS (rTMS) for depression in 2009, 2011, and 2013.3-5 These TEC Assessments concluded that the available evidence does not permit conclusions regarding the effect of TMS on health outcomes.

The Agency for Healthcare Research and Quality published a comparative effectiveness review on nonpharmacologic interventions for TRD in adults in 2011.6 The authors concluded that comparative clinical research on nonpharmacologic interventions in a TRD population is early in its infancy, and many clinical questions about efficacy and effectiveness remain unanswered. The finding of low strength of evidence is most notable in 2 cases: electroconvulsive therapy (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 to Friday for 6 weeks) of DLPFC.7 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 postbaseline 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. 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 outcome 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 two 6-week courses of antidepressant medications into 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 nonsignificant 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 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, 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 reduction in 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 moderate 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 disability.

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

**Durability and Maintenance Therapy**

A 2015 meta-analysis examined durability of the antidepressant effect of high-frequency rTMS of the left DLPFC in the absence of maintenance treatment. Included were 16 double-blind, sham-controlled RCTs with a total of 495 patients. The range of follow-up was 1 to 16 weeks, but most studies only reported follow-up to 2 weeks. The overall effect size was small with a standardized mean difference (SMD; Cohen’s d) of -.48, and the effect sizes were lower in RCTs with 8- to 16-
week follow-up \((d = -0.42)\) than with 1- to 4-week follow-up \((d = -0.54)\). The effect size was higher when antidepressant medication was initiated concurrently with rTMS \((5 \text{ RCTs, } d = -0.56)\) than when patients were on a stable dose of medication \((9 \text{ RCTs, } d = -0.43)\) or were unmedicated \((2 \text{ RCTs, } d = -0.26)\).

In 2014, Dunner et al reported 1-year follow-up with maintenance therapy from a large multicenter observational study \((42 \text{ sites})\) of rTMS for patients with TRD.\(^{18}\) A total of 257 patients agreed to participate in the follow-up study of 307 who were initially treated with rTMS. 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 \(\text{(mean, 16.2 sessions)}\). Seventy-five of the 120 patients \((62.5\%)\) who met response or remission criteria at the end of the initial treatment phase \((\text{including a 2 month taper phase})\) 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 \((\text{from 3 times per week to once a month})\) had a significantly reduced relapse rate compared with patients who had no additional treatment \((37.8\% \text{ vs } 81.8\%)\).\(^{19}\) 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\%.\(^{20}\) At 6 months after the initial rTMS treatment, 26 of 42 patients \((62\%)\) who received tapered maintenance therapy \((\text{from 2 sessions per week for the first 3 weeks to monthly})\) 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.\(^{21}\) During the 24-week follow-up, 10 of 99 patients relapsed, 38 had symptom worsening, 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.\(^{22}\) 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 \((\text{Friday evening, Saturday, and Sunday})\). Of 35 patients, 25 \((71\%)\) relapsed at a mean of 10.2 months \((\text{range, 2-48 months})\).

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

**Alzheimer’s 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.\(^{23}\) 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. At 3 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 State 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's 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, Walpol 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.

**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).
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.

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 an 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, 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).\textsuperscript{32}

**Obsessive-Compulsive Disorder**

A 2013 meta-analysis included 10 small RCTs totaling 282 patients with obsessive-compulsive disorder.\textsuperscript{33} 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 (i.e., 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.\textsuperscript{34} The larger of the 2 studies was a randomized, double-blind, sham-controlled trial in 21 patients with panic disorder with comorbid major depression.\textsuperscript{35} 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's Disease**

A meta-analysis from 2015 included 20 sham-controlled RCTs with a total of 470 patients with Parkinson's disease.\textsuperscript{36} Sample sizes ranged from 8 to 102 patients. The total effect size of rTMS on Unified Parkinson's Disease Rating Scale (UPDRS) part III score was 0.46, which is considered a small-to-medium effect size, and the mean change in the UPDRS-III score (-6.42) was considered a clinically important difference. The greatest effect on motor symptoms was from high-frequency rTMS over the primary motor cortex (SMD=0.77, \textit{p}<0.001) and low-frequency rTMS over other frontal regions (SMD=0.50, \textit{p}=0.008). High-frequency rTMS at other frontal regions and low-frequency rTMS over the primary motor cortex did not have a statistically significant benefit. The largest study included in the systematic review was an exploratory, multicenter, double-blind trial that randomized 106 patients to 8 weeks of 1-Hz rTMS, 10-Hz rTMS, or sham stimulation over the supplementary motor area.\textsuperscript{37} At 9 weeks, all groups showed a similar amount of improvement. It cannot be determined from these results whether the negative results of the largest trial were due to a lack of effect of rTMS on motor symptoms in general or to the location of stimulation. Additional study with a larger number of subjects and longer follow-up is needed to determine if high-frequency rTMS over the primary motor cortex improves motor symptoms in patients with Parkinson's 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.\textsuperscript{38} 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 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 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 posttreatment 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: Posttraumatic Stress Disorder
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. The Assessment concluded that the available evidence is insufficient to demonstrate that TMS is effective in the treatment of schizophrenia.

A 2015 Cochrane review included 41 studies with a total of 1473 participants. Based on very low-quality evidence, there was a significant benefit of temporoparietal TMS compared to sham
for global state (7 RCTs) and positive symptoms (5 RCTs). The evidence on cognitive state was equivocal. For prefrontal rTMS compared to sham, the evidence on global state and cognitive state was of very low quality and equivocal. The authors concluded that there is insufficient evidence to support or refute the use of TMS to treat symptoms of schizophrenia and, although some evidence suggests that temporoparietal TMS may improve certain symptoms (e.g., auditory hallucinations, positive symptoms of schizophrenia), the results were not robust enough to be unequivocal.

Section Summary: Schizophrenia
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.

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 Hx to 25 Hx for 1 second to 25 min/d), and 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).

A 2015 meta-analysis included 4 RCTs on rTMS over the right pars triangularis for patients (N=137) with aphasia after stroke. All studies used double-blinding, but therapists were not blinded. Every study used a different outcome measure, and sample sizes were small (range, 12-40 patients). Meta-analysis showed a medium effect size for naming (p=0.004), a trend for a benefit on repetition (p=0.08), and no significant benefit for comprehension (p=0.18). Additional study in a larger number of patients is needed to determine with greater certainty the effect of this treatment on aphasia after stroke.

Section Summary: Stroke
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 dependence (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.

In 2014, Dinur-Klein et al reported a double-blind RCT of deep rTMS over the prefrontal cortex and insula in heavy smokers (at least 20 cigarettes per day) who had failed previous antismoking treatment. The volunteers had symptoms of mild chronic obstructive pulmonary disease and were reported to be highly motivated to quit smoking. Participants (N=115) were randomized to receive 13 daily sessions of high-frequency, low-frequency, or sham stimulation after, or without, presentation of smoking cues. Cigarette consumption during treatment was measured by cotinine levels in urine and self-reports. Dropout rates ranged from 24% to 42%; all drop-outs were considered treatment failures. Intention-to-treat analysis showed a greater reduction in cigarette consumption with the high-frequency stimulation (mean of 14.45 fewer cigarettes) than sham (7.01) or low-frequency stimulation (8.56). Cotinine levels in completers were also significantly lower in the high-frequency rTMS group than in the sham and low-frequency groups. The group that had high-frequency rTMS plus smoking cues had an abstinence rate of 44% at the end of the treatment and 33% at 6 months after treatment. Interpretation of this study is limited by the high dropout rate and short duration of follow-up.

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in November 2015 identified over 300 ongoing trials on rTMS.

Summary of Evidence
The evidence for repetitive transcranial magnetic stimulation (rTMS) in patients who have treatment-resistant depression (TRD) includes numerous double-blind, randomized sham-controlled short-term trials. Relevant outcomes are symptoms, functional outcomes, and quality of life. Results of these trials show small mean improvements 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 and the lack of alternative treatments, aside from electroconvulsive therapy in patients with TRD, rTMS may be considered a treatment option in patients with TRD who meet specific criteria. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for rTMS in patients who have other psychiatric or neurologic conditions includes numerous small randomized trials. Relevant outcomes are symptoms, functional outcomes, and quality of life. These other conditions include Alzheimer disease, attention-deficit/hyperactivity disorder, amyotrophic lateral sclerosis, bulimia nervosa, chronic pain, epilepsy, fibromyalgia, migraine headache, obsessive compulsive disorder, panic disorder, Parkinson disease, postpartum depression, posttraumatic stress disorder, schizophrenia, stroke, and substance abuse and craving. The available clinical trials are small and report mixed results. There are no
large, high-quality trials for any of these conditions. The evidence is insufficient to determine the effects of the technology on health outcomes.

**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.

**Practice Guidelines and Position Statements**

**American Psychiatric Association**

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].

**International Federation of Clinical Neurophysiology**

A group of European experts was commissioned to establish evidence-based guidelines on the therapeutic use of rTMS. The guidelines included evidence published up until 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.

**American Academy of Child and Adolescent Psychiatry**

In 2013, the American Academy of Child and Adolescent Psychiatry (AACP) Committee on Quality Issues published practice parameters on the assessment and treatment of children and adolescents with tic disorders. AACP does not recommend rTMS, citing the limited evidence regarding safety, ethics, and long-term impact on development.

**National Institute for Health and Care Excellence**

In 2015, the National Institute for Health and Care Excellence (NICE) provided provisional recommendations, revised from earlier guidance, stating that evidence on the short-term efficacy
of rTMS for depression is adequate, although the clinical response is variable and some patients may not benefit.\textsuperscript{52} rTMS for depression may be used with normal arrangements for clinical governance and audit, “provided that patients are informed about the other treatment options available and they understand the possibility that they may derive little or no benefit from the procedure.” The final recommendation was expected November 2015 but is not yet posted.

In 2014, NICE provided guidance on the use of rTMS for treating and preventing migraine.\textsuperscript{53} The guidance states that evidence on the efficacy of TMS for the treatment of migraine is limited in quantity and for the prevention of migraine is limited in both quality and quantity. Evidence on its safety in the short and medium term is adequate, but there is uncertainty about the safety of long-term or frequent use of TMS. Therefore, this procedure should only be used with special arrangement for clinical governance, consent, and audit or research.

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.\textsuperscript{54}

American Academy of Neurology
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).\textsuperscript{59}

Canadian Network for Mood and Anxiety Treatments
The Canadian Network for Mood and Anxiety Treatments updated their clinical guidelines on neurostimulation therapies for the management of major depressive disorder in adults.\textsuperscript{56} 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.

U.S. Preventive Services Task Force Recommendations
Not applicable.
CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

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 deliver and management, per session
90869 Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; subsequent motor threshold redetermination with delivery and management

- Code 90867 is reported once per course of treatment, and codes 90868 and 90869 cannot be reported for the same session.

ICD-9 Diagnoses

296.23 Major depressive disorder, single episode, severe, without mention of psychotic behavior
296.33 Major depressive disorder, recurrent episode, severe, without mention of psychotic behavior

ICD-10 Diagnoses (Effective October 1, 2015)

F32.2 Major depressive disorder, single episode, severe without psychotic features
F33.2 Major depressive disorder, recurrent severe without psychotic features

REVISIONS

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<tr>
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<tbody>
<tr>
<td>12-07-2012</td>
<td>Policy added to the bcbsks.com web site.</td>
</tr>
<tr>
<td>05-07-2013</td>
<td>Updated Description section.</td>
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<tr>
<td></td>
<td>Updated Rationale section.</td>
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<td>Updated Reference section.</td>
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<tr>
<td>10-15-2014</td>
<td>Updated Description section.</td>
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<td>In Policy section:</td>
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<td>Removed the following, “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.”</td>
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<td>And added:</td>
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<td>A. 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:</td>
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<tr>
<td></td>
<td>1. Confirmed diagnosis of severe major depressive disorder (single or recurrent) documented by standardized rating scales that reliably measure depressive symptoms; AND</td>
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<td>2. Any one of the following (a, b, c, or d):</td>
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<tr>
<td></td>
<td>a. Failure of 4 trials of psychopharmacologic agents including 2 different agent</td>
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</table>
### Transcranial Magnetic Stimulation (TMS) as a Treatment of Depression and Other Psychiatric Disorders

#### 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 (e.g., in cases with psychosis, acute suicidal risk, catatonia or life-threatening inanition rTMS should NOT be utilized); AND

#### Failure of a Trial of a Psychotherapy Known to Be Effective
- 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.

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#### Added Policy Guideline Section.

### Coding Section:
- Added ICD-9 diagnoses: 296.23, 296.33
- Added ICD-10 diagnoses: F32.2, F33.2

### Updated Rationale Section.

### Updated References Section.

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#### 03-18-2015
- Updated Description Section.

### Policy Section:
- Added Item D: "Transcranial magnetic stimulation of the brain is considered experimental / investigational as a treatment of all other psychiatric/neurologic disorders, including but not limited to bipolar disorder, schizophrenia, obsessive-compulsive disorder, or migraine headaches."

### Updated Rationale Section.

### Updated References Section.

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#### 02-17-2016
- Updated Description Section.

### Updated Rationale Section.

### Updated References Section.

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### REFERENCES


33. Berlim MT, Neufeld NH, Van den Eynde F. Repetitive transcranial magnetic stimulation (rTMS) for obsessive-compulsive disorder (OCD): an exploratory meta-analysis of


42. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Transcranial magnetic stimulation for the treatment of schizophrenia. TEC Assessments. 2011;Volume 26, Tab 6.


Other References
1. Blue Cross and Blue Shield of Kansas Behavioral Health Liaison Committee, June 2012; June 2014; June 2015.
2. BCBSKS Medical Consultant, Practicing Board Certified Psychiatrist, November 2012.