FEP 2.01.50 Transcranial Magnetic Stimulation as a Treatment of Depression and Other Psychiatric/Neurologic Disorders

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 electrical current produces a magnetic field that passes unimpeded through the scalp and bone that stimulate neuronal function. Repetitive TMS (rTMS) is being evaluated for the treatment of treatment-resistant depression (TRD) and other psychiatric and neurologic disorders.

OBJECTIVE
The objective of this evidence review is to evaluate whether the use of repetitive transcranial magnetic stimulation of the brain improves the net health outcome for individuals with various psychiatric or neurologic conditions.

POLICY STATEMENT
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; further, electroconvulsive therapy would not be clinically superior to rTMS (eg, in cases with psychosis, acute suicidal risk, catatonia or life-threatening inanition rTMS should NOT be used); 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.
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symptoms, as documented by standardized rating scales that reliably measure depressive symptoms.

Repetitive TMS 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.

Repetitive TMS of the brain is considered investigational as a treatment of all other psychiatric and neurologic disorders, including but not limited to bipolar disorder, schizophrenia, obsessive-compulsive disorder, or migraine headaches.

POLICY GUIDELINES

Repetitive transcranial magnetic stimulation (TMS) should be performed using a U.S. Food and Drug Administration–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.

Contraindications to repetitive TMS 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 (eg, 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; 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, pacemaker, vagus nerve stimulator, or metal aneurysm clips or coils, staples, or stents.

The following should be present for the administration of repetitive TMS:

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, eg, suction and oxygen; and

The facility must maintain awareness of response times of emergency services (either fire/ambulance or “code team”), which should be available within 5 minutes. These relationships are reviewed on at least a 1-year basis and include mock drills.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

Devices for transcranial stimulation have been cleared for marketing by the U.S. Food and Drug Administration (FDA) for diagnostic uses. The NeoPulse, now known as NeuroStar® TMS, was granted a de novo 510(k) classification by FDA in 2008. A number of devices subsequently received FDA clearance for the treatment of major depressive disorders in adults who have failed to achieve satisfactory improvement from prior antidepressant medication in the current episode. Some devices are listed in Table 1. FDA product code: OBP.
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Table 1. Repetitive TMS Devices Cleared by FDA for the Treatment of Major Depressive Disorder

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>FDA Clearance No.</th>
<th>FDA Clearance Year</th>
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</thead>
<tbody>
<tr>
<td>NeuroStar® TMS</td>
<td>Neuronetics</td>
<td>DEN070003</td>
<td>2008</td>
</tr>
<tr>
<td>Brainsway™ H-Coil Deep TMS</td>
<td>Brainsway</td>
<td>K122288</td>
<td>2013</td>
</tr>
<tr>
<td>Rapid® Therapy System</td>
<td>Magstim</td>
<td>K162935</td>
<td>2015</td>
</tr>
<tr>
<td>MagVita TMS Therapy System</td>
<td>Tonica Elektronik</td>
<td>K150641</td>
<td>2015</td>
</tr>
<tr>
<td>Neurosoft TMS</td>
<td>TeleEMG</td>
<td>K160309</td>
<td>2016</td>
</tr>
<tr>
<td>MagVita TMS Therapy System with Theta Burst</td>
<td>Tonica Elektronik</td>
<td>K173620</td>
<td>2018</td>
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</table>

FDA: Food and Drug Administration; TMS: transcranial magnetic stimulation.

In 2013, the Cerena™ TMS device (eNeura Therapeutics) was granted a de novo 510(k) classification by FDA for the acute treatment of pain associated with a migraine headache with aura. Warnings, precautions, and contraindications include the following:

- The device is only intended for 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.
  - for medication overuse headaches.
- The device has not been demonstrated as safe and/or effective:
  - when treating cluster headache or a chronic migraine headache.
  - when treating during the aura phase.
  - in relieving the associated symptoms of a migraine (photophobia, phonophobia, and nausea).
  - 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.

In 2014, eNeura Therapeutics received 510(k) marketing clearance for the SpringTMS® for the treatment of migraine headache. The device differs from the predicate Cerena™ TMS device with the addition of an LCD screen, a use authorization feature, lithium battery pack, and smaller size. The stimulation parameters are unchanged. The sTMS Mini (eNeura Therapeutics) received marketing clearance by the FDA in 2016. FDA product code: OKP.

In August 2018, the Deep TMS System (Brainsway) was granted a de novo 510(k) classification by FDA (DEN170078). The new classification applies to this device and substantially equivalent devices of this generic type. The Brainsway Deep TMS System is cleared for treatment of adults with obsessive-compulsive disorder. FDA product code: QCI.

**RATIONALE**

**Summary of Evidence**

For individuals who have TRD who receive rTMS, the evidence includes a large number of sham-controlled randomized trials and meta-analyses of these trials. Relevant outcomes are symptoms, functional outcomes, and quality of life. The meta-analyses found a clinical benefit associated with rTMS for TRD with improved response rates and rates of remission compared with sham. The most recent meta-analyses have concluded that the effect of rTMS, on average depression scores, is smaller than the effect of ECT on TRD and that the mean improvement in depression scores with rTMS did not reach the minimal clinically important difference; however, clinically meaningful improvements were noted in a subgroup of studies using higher frequency pulses. One potential area of benefit for rTMS is in
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accelerating or enhancing the response to antidepressant medications, and there is some evidence that rTMS, when given in conjunction with the initiation of pharmacologic therapy, improves the response rate compared with pharmacologic therapy alone. The effect of rTMS appears to be less robust when it is given in combination with a stable dose of antidepressant medication. Meta-analyses have also found that the efficacy of rTMS decreases with longer follow-up, though some studies have reported persistent response up to 6 months in some patients. There is limited evidence to compare the effects of these treatments on cognition, although the adverse events of rTMS appear to be minimal. While the most recent meta-analyses have reported that the effect of rTMS is smaller than the effect of ECT on TRD, because rTMS does not require general anesthesia or induce seizures, some individuals may decline ECT so the balance of incremental benefits and harms associated with rTMS may be a reasonable compared with ECT. Based on the short-term benefit observed in RCTs and the lack of alternative treatments, aside from ECT in patients with TRD, rTMS may be considered a treatment option in patients with TRD who meet specific criteria. The evidence for theta burst stimulation includes a large randomized trial showing noninferiority with another method of rTMS; no significant differences were noted in the number of adverse events. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have psychiatric or neurologic disorders other than depression (eg, amyotrophic lateral sclerosis, chronic pain, epilepsy, fibromyalgia, migraine headache, obsessive-compulsive disorder, panic disorder, Parkinson disease, posttraumatic stress disorder, schizophrenia, stroke, substance abuse and craving) who receive rTMS, the evidence includes numerous small RCTs and meta-analyses of these randomized trials. Relevant outcomes are symptoms, functional outcomes, and quality of life. The trials included in the meta-analyses are typically small and of low methodologic quality. In addition, stimulation parameters have not been established, and trial results are heterogeneous. There are no large, high-quality trials for any of these conditions demonstrating efficacy or the durability of any treatment effects. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

American Psychiatric Association
The American Psychiatric Association’s 2010 practice guidelines (reaffirmed in 2015) for the treatment of patients with major depressive disorder have indicated 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 (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 electroconvulsive therapy, transcranial magnetic stimulation (TMS), or light therapy. The Association stated that a number of strategies are available when a change in the treatment plan seems necessary, such as transdermal selegiline, a relatively selective monoamine oxidase B inhibitor with fewer dietary and medication restrictions, or TMS could also be considered (recommended with moderate clinical confidence).

The Association’s guidelines on the treatment of patients with obsessive-compulsive disorder (2007, reaffirmed in 2012) have indicated that “findings of the four published trials of repetitive TMS (rTMS) are inconsistent, perhaps because the studies differed in design, stimulation sites, duration, and stimulation parameters. The available results and the technique’s non-invasiveness and good tolerability should encourage future research, but the need for daily treatment may limit the use of TMS in practice.”

American Academy of Child and Adolescent Psychiatry
In 2013, the American Academy of Child and Adolescent Psychiatry published practice parameters on the assessment and treatment of children and adolescents with tic disorders. The Academy did not...
recommend rTMS, citing the limited evidence on the 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 provided revised 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.43

In 2014, the Institute provided guidance on the use of rTMS for treating and preventing migraine.44 The guidance stated that evidence on the efficacy of TMS for the treatment of a migraine was limited in quantity and for the prevention of a migraine was limited in both quality and quantity. Evidence on its safety in the short and medium term was adequate, but there was uncertainty about the safety of long-term or frequent use of TMS.

American Academy of Neurology
The American Academy of Neurology issued practice guidelines in 2006 on the evaluation and treatment of depression, psychosis, and dementia in Parkinson disease.45 The guidelines found the evidence insufficient to support or refute the efficacy of TMS or electroconvulsive therapy in the treatment of depression associated with Parkinson disease (level U; data inadequate or conflicting given current knowledge, treatment is unproven).

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

Medicare National Coverage
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES
8. Berlim MT, Van den Eynde F, Daskalakis ZJ. Efficacy and acceptability of high frequency repetitive transcranial magnetic stimulation (rTMS) versus electroconvulsive therapy (ECT) for major depression: a systematic review and meta-analysis of randomized trials. *Depress Anxiety*. Jul 2013;30(7):614-623. PMID 23349112


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<thead>
<tr>
<th>Date</th>
<th>Update Policy</th>
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<tbody>
<tr>
<td>December 2018</td>
<td>Policy updated with literature review through August 23, 2018; references 9, 10, 19, 21, 24, 29, 31, 35 and 37 added. Policy statements unchanged except “not medically necessary” revised to “investigational” to align with FDA 510(k) status.</td>
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