Preauthorization is required.

The following Protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.

Populations

<table>
<thead>
<tr>
<th>Individuals:</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>With treatment-resistant depression</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td></td>
<td>• Repetitive transcranial magnetic stimulation</td>
<td>• Pharmacotherapy</td>
<td>• Symptoms</td>
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<td></td>
<td></td>
<td>• Electroconvulsive therapy</td>
<td>• Functional outcomes</td>
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<td></td>
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<td></td>
<td>• Quality of life</td>
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</tbody>
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</tr>
</thead>
<tbody>
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<td>With other psychiatric or neurologic disorders&lt;sup&gt;a&lt;/sup&gt;</td>
<td>• Repetitive transcranial magnetic stimulation</td>
<td>• Pharmacotherapy</td>
<td>• Symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Physical and occupational therapy</td>
<td>• Functional outcomes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Quality of life</td>
</tr>
</tbody>
</table>

<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.

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 two to three 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.

Policy
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 four trials of psychopharmacologic agents including two different agent classes and two augmentation trials; OR
   b. Inability to tolerate a therapeutic dose of medications as evidenced by four trials of psychopharmacologic agents with distinct side effects; OR
   c. History of response to rTMS in a previous depressive episode (at least three 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.

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 bi-polar 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 five days a week for six weeks.
(total of 30 sessions), followed by a three-week taper of three TMS treatments in week one, two TMS treatments the next week, and one TMS treatment in the last week.

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. Neurological 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.

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, 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.

Medicare Advantage

For Medicare Advantage transcranial magnetic stimulation (TMS) is considered medically necessary in adults who have a confirmed diagnosis of major depressive disorder (MDD), single or recurrent episode, and meet the following criteria (see Medicare Advantage Policy Guidelines):

• Resistance to treatment as evidenced by a lack of a clinically significant response to four (4) trials of psychopharmacologic agents in the current depressive episode;
  o Two different agent classes, at or above the minimum effective dose and duration and includes trials of at least two (2) evidence-based augmentation therapies; or

• Inability to tolerate psychopharmacologic agents as evidenced by four (4) trials of psychopharmacologic agents with distinct side effects; or

• History of response to TMS in a previous depressive episode; or

• History of response to electroconvulsive therapy (ECT) in a previous or current MDD episode, or inability to tolerate ECT, and TMS is considered a less invasive treatment option; and

• A trial of an evidence-based psychotherapy known to be effective in the treatment of MDD of an adequate frequency and duration without significant improvement in depressive symptoms as documented by standardized rating scales that reliably measure depressive symptoms; and

• The TMS treatment is delivered by a device that is FDA-approved or –cleared for the treatment of MDD in a safe and effective manner. TMS treatment should generally follow the protocol and parameters specified in
the manufacturer’s user manual, with modifications only as supported by the published scientific evidence base; and

- The order for treatment (or retreatment) is written by a physician (MD or DO) who has examined the patient and reviewed the record. The physician must have experience in administering TMS therapy and the treatment must be given under direct supervision of this physician, i.e., he or she must be in the area and be immediately available.

TMS is considered **not medically necessary** for any of the following:

- Presence of psychotic symptoms in the current depressive episode;
- Acute or chronic psychotic disorder such as schizophrenia, schizophreniform disorder, or schizoaffective disorder;
- 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;
- Persons with conductive, ferromagnetic or other magnetic-sensitive metals implanted in their head which are non-removable and within 30 cm of the TMS magnetic coil. Examples include cochlear implants, implanted electrodes/stimulators, aneurysm clips or coils stents, and bullet fragments. (Dental amalgam fillings are not affected by the magnetic field and are acceptable for use with TMS.)
- Maintenance therapy; and
- All other conditions not included in the above list of “Indications.”

Retreatment may be considered **medically necessary** for patients who met the guidelines for initial treatment and subsequently developed relapse of depressive symptoms if the patient responded to prior treatments as evidenced by a greater than 50% improvement in standard rating scale measurements for depressive symptoms or if there were a relapse after remission [e.g., (GDS), PHQ-9, BDI, HAM-D, MADRS, QIDS or IDS-SR score].

**Medicare Advantage Policy Guidelines**

*Limitations*

The benefits of TMS use must be carefully considered against the risk of potential side effect in patients with any of the following:

- Seizure disorder or any history of seizure (except those induced by ECT or isolated febrile seizures in infancy or childhood without subsequent treatment or recurrence). Additional consideration should be given for individuals on medications which may lower the seizure threshold or with conditions rendering the patient more prone to seizures, such as alcoholism;
- Presence of vagus nerve stimulators leads in the carotid sheath;
- Presence of an implanted medical device located less than 30 cm from the TMS magnetic coil, including but not limited to pacemakers, implanted defibrillators, vagus nerve stimulators.

The attending physician must monitor and document the patient’s clinical progress during treatment. The attending physician must use evidence-based validated depression monitoring scales such as the Geriatric Depression Scale (GDS), the Personal Health Questionnaire Depression Scale (PHQ-9), the Beck Depression Scale (BDI) Hamilton Rating Scale for Depression (HAM-D), the Montgomery Asberg Depression Rating Scale (MADRS),
the Quick Inventory of Depressive Symptomatology (QIDS) or the Inventory for Depressive Symptomatology Systems Review (IDS-SR) to monitor treatment response and the achievement of remission of symptoms.

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 five 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 shown 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 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 dependence, 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. (Refer to the Treatment of Tinnitus Protocol for information on rTMS for 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), was approved in Canada, Israel, and the United States as a therapy for depression. Initially examined by FDA under a traditional 510(k) process, the NeoPulse, now known as NeuroStar® TMS, was granted a de novo 510(k) classification by FDA in 2008. NeuroStar® TMS is indicated for the treatment of patients with depression who have failed one six-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 one 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 electroconvulsive therapy 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) was granted a de novo 510(k) classification by FDA 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.

Related Protocols
Treatment of Tinnitus
Vagus Nerve Stimulation

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.

References
We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


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.


57. National Government Services, Inc. Local Coverage Determination (LCD): TRANSCRANIAL MAGNETIC Stimulation (L33398) for services performed on or after 10/01/2015.