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<b>Preauthorization</b>	No	<b>Review Dates:</b> 05/09, 05/10, 05/11, 05/12, 05/13, 05/14, 05/15, 05/16, 05/17, 05/18, 09/18, 09/19, 09/20, 09/21, 09/22	

***This protocol considers some applications of this test or procedure investigational. If the physician feels this service is medically necessary, preauthorization is recommended.***

*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.*

### RELATED PROTOCOL

Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors

Populations	Interventions	Comparators	Outcomes
Individuals: • With uterine fibroids	Interventions of interest are: • Magnetic resonance-guided focused ultrasound	Comparators of interest are: • Alternative nonsurgical treatment • Surgery	Relevant outcomes include: • Symptoms • Quality of life • Resource utilization • Treatment-related morbidity
Individuals: • With metastatic bone cancer who have failed or are not candidates for radiotherapy	Interventions of interest are: • Magnetic resonance-guided focused ultrasound	Comparators of interest are: • Supportive care	Relevant outcomes include: • Symptoms • Functional outcomes • Health status measures • Quality of life • Treatment-related morbidity
Individuals: • With other tumors (e.g., brain cancer, prostate cancer, breast cancer, desmoid, nonspinal osteoid osteoma)	Interventions of interest are: • Magnetic resonance-guided focused ultrasound	Comparators of interest are: • Standard care	Relevant outcomes include: • Symptoms • Health status measures • Treatment-related morbidity
Individuals: • With medication-refractory essential tremors	Interventions of interest are: • Magnetic resonance-guided focused ultrasound	Comparators of interest are: • Neurosurgery • Standard of care	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of Life • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> <li>• With medication-refractory tremor-dominant Parkinson disease</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>• Magnetic resonance-guided focused ultrasound</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>• Neurosurgery</li> <li>• Standard of care</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>• Symptoms</li> <li>• Functional outcomes</li> <li>• Quality of Life</li> <li>• Treatment-related morbidity</li> </ul>

## DESCRIPTION

An integrated system providing magnetic resonance-guided focused ultrasound (MRgFUS) treatment is proposed as a noninvasive therapy for uterine fibroids and pain palliation of bone metastases. MRgFUS is also being investigated as a treatment of other benign and malignant tumors as well as essential tremors.

## SUMMARY OF EVIDENCE

For individuals who have uterine fibroids who receive MRgFUS, the evidence includes 2 small randomized controlled trials (RCTs), nonrandomized comparative studies, and case series. Relevant outcomes are symptoms, quality of life, resource utilization, and treatment-related morbidity. One RCT (N=20) has reported some health outcomes but its primary purpose was to determine the feasibility of a larger trial. It did not find statistically significant differences in quality of life outcomes between active and sham treatment groups but it did find lower fibroid volumes after active treatment. This trial did not have an active comparator, the clinical significance of the primary outcome was unclear, and there were no follow-up data beyond 1 year. The second RCT (N=49) had preliminary results at 6 weeks posttreatment, comparing MRgFUS with uterine artery embolization, and demonstrated that the 2 groups are comparable in medication use and symptom improvement following treatments. Patients in the MRgFUS group reported recovering significantly faster than patients in the uterine artery embolization (UAE) group, as measured by time to return to work and time to normal activities. Long-term follow-up results reported that there was lower reintervention rate and greater improvement in symptoms after UAE compared to MRgFUS. A 2021 meta-analysis reported that, comparatively, myomectomy had the lowest reintervention rate of the 3 regimens (myomectomy vs. UAE vs. MRgFUS) in all time points assessed while the MRgFUS had the highest re-intervention rate. In a 2013 comparative study, outcomes appeared to be better with UAE than with MRgFUS. Long-term data on the treatment effects, recurrence rates, and impact on future fertility and pregnancy are lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with metastatic bone cancer who have failed or are not candidates for radiotherapy who receive MRgFUS, the evidence includes a sham-controlled randomized trial, a systematic review of RCTs and observational studies, and case series. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The RCT found statistically significant improvements after MRgFUS in a composite outcome comprised of a reduction in pain and morphine use, and in pain reduction as a stand-alone outcome. A substantial proportion of patients in the treatment group experienced adverse events but most events were transient and not severe. Pooled efficacy data from a systematic review reported a treatment response to MRgFUS of 79%. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with other tumors (e.g., breast cancer, brain cancer, prostate cancer, desmoid, nonspinal osteoid osteoma) who receive MRgFUS, the evidence includes a nonrandomized, uncontrolled phase II trial and several case series. Relevant outcomes are symptoms, health status measures, and treatment-related morbidity. A nonrandomized, uncontrolled phase II trial evaluating MRgFUS for prostate cancer reported a 93% success rate at 5 months. The use of MRgFUS for the treatment of nonspinal osteoid osteoma consists of several larger case se-

ries, including a propensity score-matched retrospective study that reported similar reductions in pain with radiofrequency ablation and MRgFUS. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with medication-refractory essential tremors who receive MRgFUS, the evidence includes a technology assessment, meta-analyses, and a double-blind, sham-controlled randomized trial. Relevant outcomes include symptoms, functional outcomes, quality of life, and treatment-related morbidity. The assessment did not pool study results but concluded that, overall, MRgFUS decreased tremor severity and improved quality of life. One meta-analysis reported significant improvements in hand tremor scores from baseline up to 24 months post-treatment, with evidence of a diminishing treatment benefit over time. Another meta-analysis found similar improvements in tremor severity with MRgFUS to unilateral deep brain stimulation (DBS), but improvements in both were inferior to bilateral DBS. The sham-controlled randomized trial found significant improvements in the treatment group in tremor severity, functional improvement, and quality of life after 3 months of follow-up. The improvements in hand tremor score, function, and quality of life were maintained at the 2-year follow-up. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with medicine-refractory tremor dominant Parkinson disease who receive MRgFUS, the evidence includes a pilot RCT. Relevant outcomes include symptoms, functional outcomes, quality of life, and treatment-related morbidity. The double-blind, sham-controlled, pilot randomized trial found significant improvements in the treatment group in tremor severity after 3 months of follow-up. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

## POLICY

Magnetic resonance-guided high-intensity ultrasound ablation may be considered **medically necessary** for pain palliation in adults with metastatic bone cancer who have failed or are not candidates for radiotherapy.

Magnetic resonance-guided high-intensity ultrasound ablation may be considered **medically necessary** for the treatment of medicine-refractory essential tremors.

Magnetic resonance-guided high-intensity ultrasound ablation is considered **investigational** in all other situations including but not limited to:

- Treatment of uterine fibroids;
- Treatment of other tumors (e.g., brain cancer, prostate cancer, breast cancer, desmoid);
- Treatment of medication-refractory tremor dominant Parkinson disease.

## BACKGROUND

### UTERINE FIBROIDS

Uterine fibroids are one of the most common conditions affecting women in the reproductive years. African American women have a greater lifetime incidence of uterine fibroids compared to other racial groups.<sup>1</sup> Symptoms of uterine fibroids include menorrhagia, pelvic pressure, or pain.

### Treatment

Approaches currently available to treat symptomatic uterine fibroids include hysterectomy, abdominal myomectomy, laparoscopic and hysteroscopic myomectomy, hormone therapy, uterine artery embolization, and watch-

ful waiting. Hysterectomy and various myomectomy procedures are considered the criterion standard treatments.

#### METASTATIC BONE DISEASE

Metastatic bone disease is one of the most common causes of cancer pain.

##### Treatment

Existing treatments include conservative measures (e.g., massage, exercise) and pharmacologic agents (e.g., analgesics, bisphosphonates, corticosteroids). For patients who do not respond to these treatments, standard care is external-beam radiotherapy. However, a substantial proportion of patients have residual pain after radiotherapy, and there is a need for alternative treatments for these patients.

#### ESSENTIAL TREMORS

Essential tremor (ET) is the most common movement disorder, with an estimated prevalence of 5% worldwide. Essential tremor most often affects the hands and arms, may affect head and voice, and rarely includes the face, legs, and trunk. Essential tremor is heterogeneous among patients, varying in frequency, amplitude, causes of exacerbation, and association with other neurologic deficits.

##### Treatment

The neuropathology of ET is uncertain, with some evidence suggesting that ET is localized in the brainstem and cerebellum. If patients with ET experience intermittent or persistent disability due to the tremors, initial therapy is with drugs (beta-blockers or anticonvulsants). For medicine-refractory patients, surgery (deep brain stimulation or thalamotomy) may be offered, though high rates of adverse events have been observed.

#### TREMOR-DOMINANT PARKINSON DISEASE

The 3 cardinal features of Parkinson disease (PD) are tremor, bradykinesia, and rigidity. The tremor in PD is a resting tremor that occurs when the body part is not engaged in purposeful activities. Major subtypes of PD include tremor-dominant, akinetic-rigid, and postural instability and gait difficulty. The progression of PD is highly variable and patients can change subtypes as the disease progresses.

##### Treatment

Dopaminergic therapy (i.e., levodopa or a dopamine agonist) is the first-line treatment for PD, which improves tremor. Amantadine and anticholinergics (e.g., trihexyphenidyl) can also be considered as initial treatment for tremor-dominant PD or as add-on therapy in patients who have persistent tremor despite dopaminergic therapy. For medication-refractory patients, surgery (deep brain stimulation or lesioning procedures) may be offered. Lesioning procedures include conventional unilateral thalamotomy and focused ultrasound thalamotomy. Deep brain stimulation is the most frequently performed surgical procedure for the treatment of PD.

#### MAGNETIC RESONANCE-GUIDED FOCUSED ULTRASOUND

Magnetic resonance-guided focused ultrasound (MRgFUS) is a noninvasive treatment that combines 2 technologies: focused ultrasound and magnetic resonance imaging (MRI). The ultrasound beam penetrates through the soft tissues and, using MRI for guidance and monitoring, the beam can be focused on targeted sites. Ultrasound causes a local increase in temperature in the target tissue, resulting in coagulation necrosis while sparing the surrounding normal structures. Ultrasound waves from each sonication are directed at a focal point that has a maximum focal volume of 20 mm in diameter and 15 mm in height/length. This causes a rapid rise in temperature (i.e., to 65°C to 85°C), which is sufficient to ablate tissue at the focal point. In addition to providing guidance, the associated MRI can provide online thermometric imaging, a temperature “map”, to confirm the therapeutic effect of the ablation treatment and allow for real-time adjustment of the treatment parameters.

The U.S. Food and Drug Administration (FDA) approved the ExAblate® MRgFUS system (InSightec) for 4 indications: treatment of uterine fibroids (leiomyomata), palliation of pain associated with tumors metastatic to bone, medication refractory ET, and tremor-dominant PD. The ultrasound equipment is specifically designed to be compatible with magnetic resonance magnets, and it is integrated into standard clinical MRI units; it also includes a patient table, which has a cradle that houses the focused ultrasound transducer in water or a light oil bath. Some models have a detachable cradle; only certain cradle types can be used for palliation of pain associated with metastatic bone cancer. For treating pain associated with bone metastases, the aim of MRgFUS is to destroy nerves in the bone surface surrounding the tumor.

MRgFUS is also being investigated for the treatment of other tumors, including breast, prostate, brain, and desmoid tumors as well as nonspinal osteoid osteoma.

## REGULATORY STATUS

In October 2004, the ExAblate 2000 System (InSightec) was approved by the FDA through the premarket approval process for “ablation of uterine fibroid tissue in pre- or perimenopausal women with symptomatic uterine fibroids who desire a uterine sparing procedure.” Treatment is indicated for women with a uterine gestational size of fewer than 24 weeks who have completed childbearing.

In October 2012, the ExAblate System, Model 2000/2100/2100 VI, was approved by the FDA through the premarket approval process for pain palliation in adults with metastatic bone cancer who have failed or are not candidates for radiotherapy. The device was evaluated through an expedited review process. The FDA required a postapproval study with 70 patients to evaluate the effectiveness of the system under actual clinical conditions.

In July 2016, the FDA approved the use of the ExAblate Neuro System for the treatment of ET in patients who have not responded to medication (beta-blockers or anticonvulsant drugs) through the premarket approval process. In December 2018, the FDA approved the use of the ExAblate Model 4000 (Neuro) for the treatment of tremor-dominant PD with medication-refractory tremor through the premarket approval process.

FDA product codes: NRZ, POH.

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

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