Magnetic Resonance-Guided Focused Ultrasound

Policy # 00180
Original Effective Date: 09/22/2005
Current Effective Date: 11/21/2018

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services Are Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider magnetic resonance–guided high-intensity ultrasound ablation for pain palliation in adult patients with metastatic bone cancer who failed or are not candidates for radiotherapy to be **eligible for coverage.**

Based on review of available data, the Company may consider magnetic resonance-guided high-intensity ultrasound ablation for the treatment of medicine-refractory essential tremors to be **eligible for coverage.**

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers magnetic resonance-guided high-intensity ultrasound ablation to be **investigational*** in all other situations including but not limited to:

- Treatment of uterine fibroids; and
- Treatment of other tumors (eg, brain cancer, prostate cancer, breast cancer, desmoid).

Background/Overview

UTERINE FIBROIDS
Uterine fibroids are one of the most common conditions affecting women in the reproductive years. Symptoms of uterine fibroids include menorrhagia, pelvic pressure, or pain.

Treatment
Several approaches currently available to treat symptomatic uterine fibroids include hysterectomy, abdominal myomectomy, laparoscopic and hysteroscopic myomectomy, hormone therapy, uterine artery embolization, and watchful 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 (eg, massage, exercise) and pharmacologic agents (eg, 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. ET most often affects the hands and arms, may affect head and voice, and rarely includes the face, legs, and trunk. ET 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 (β-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.

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 nm in diameter and 15 nm in height/length. This causes a rapid rise in temperature (ie, to 65°C-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 2 indications: treatment of uterine fibroids (leiomyomata) and palliation of pain associated with tumors metastatic to bone. 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.

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FDA or Other Governmental Regulatory Approval

In October 2004, the ExAblate®‡ 2000 System (InSightec) was approved by 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 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. FDA required a postapproval study with 70 patients to evaluate the effectiveness of the system under actual clinical conditions.

In July 2016, FDA approved the use of the ExAblate®‡ Neuro System for the treatment of essential tremors in patients who have not responded to medication (β-blockers or anticonvulsant drugs) through the premarket approval process.

FDA product codes: NRZ, POH.

Centers for Medicare and Medicaid Services (CMS)
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

Rationale/Source

This review was informed by a TEC Assessment (2005) on magnetic resonance–guided focused ultrasound (MRgFUS) for symptomatic uterine leiomyomata, which found the evidence of efficacy insufficient compared with conventional therapies.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled

trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

MAGNETIC RESONANCE–GUIDED FOCUSED ULTRASOUND
Clinical Context and Test Purpose
The purpose of MRgFUS in patients with uterine fibroids, metastatic bone cancer, other tumors, or essential tremors is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of MRgFUS to treat patients with uterine fibroids, metastatic bone cancer, other tumors, or essential tremors improve the net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant populations of interest are patients with:
- Uterine fibroids
- Metastatic bone cancer who have failed radiotherapy or who are not candidates for radiotherapy
- Other tumors
- Essential tremors who are medication-refractory.

Interventions
The therapy being considered is MRgFUS, which is a thermoablative procedure to heat targeted tissue in small volume increments, under constant magnetic resonance imaging guidance.

Comparators
Comparators of interest, by indication, include:
- For uterine fibroids, alternatives nonsurgical treatment or surgery
- For metastatic bone cancer, supportive care
- For other tumors, standard of care
- For essential tremors, neurosurgery or standard of care.

Outcomes
The following therapies and practices are currently being used, by indication:
- For uterine fibroids, the goal is to reduce or eliminate fibroid-related symptoms by reducing fibroid size. Measures to assess the effect of treatment include quality of life (QOL), change in uterine and fibroid volume, pain levels, and pain medication use.
- For metastatic bone cancer, the goal is to alleviate pain. Measures to assess the effect of treatment include pain levels and pain medication use.
- For other tumors, the goal is tumor ablation. Outcomes include reductions in tumor size.

- For essential tremors, the goal is to decrease the frequency of tremors and improve QOL.

Timing
Outcome measures can be assessed at several months to several years postprocedure.

Setting
The procedure, which can be performed on an outpatient basis, is performed in a specialized treatment center.

UTERINE FIBROIDS
Evidence for the use of MRgFUS for the treatment of uterine fibroids consists of 2 small RCTs and many observational studies.

Randomized Controlled Trials
Barnard et al (2017) published preliminary results from Fibroid Interventions: Reducing Symptoms Today and Tomorrow trial, a parallel RCT and cohort study comparing MRgFUS with fibroid embolization to treat uterine fibroids. For the RCT, patients were randomized to uterine artery embolization (UAE; n=22) or to MRgFUS (n=27). Patients and investigators were not blinded. Women who did not want to be randomized were enrolled in the cohort study; 16 underwent UAE and 16 underwent MRgFUS. Patients were instructed to keep diaries with the following information: medication use, return to normal activities, and symptoms. After 6 weeks of follow-up for the RCT patients, there were no differences between groups in symptoms such as fatigue, hot flashes, discomfort urinating, vaginal discharge, or constipation. Recovery was significantly faster in the MRgFUS group, as measured by the first day back to work and first day back to normal. Medication use (ie, opioids, nonsteroidal anti-inflammatory drugs, acetaminophen or aspirin, nausea medication, bowel medication) was also significantly lower in the MRgFUS group. Analyses combining the RCT and cohort patients showed similar results. The MRgFUS procedure took significantly longer than the UAE procedure. A trial limitation was the inability to recruit more patients. Long-term follow-up results will be forthcoming.

A pilot sham-controlled randomized trial evaluating MRgFUS for the treatment of uterine fibroids was published by Jacoby et al (2016). The trial included 20 premenopausal women with symptomatic uterine fibroids (women who were pregnant or had a desire for future children were excluded). Patients were randomized to MRgFUS with the ExAblate 2000 System (n=13) or to a sham treatment not using thermal energy (n=7). The investigators did not specify primary outcomes. The sample size was calculated to assess the feasibility of a larger trial, not to provide sufficient statistical power. All patients who were assigned to the MRgFUS group and 6 of 7 in the placebo group received their allocated treatment; all patients who were treated completed 3 months of follow-up. Patients were unblinded at 3 months, and those in the sham group were given the option of active treatment.

QOL outcomes included the Uterine Fibroid Symptom and Quality of Life Questionnaire, which has scales that include the symptom severity score and health-related quality of life score. The 36-Item Short-Form

Health Survey, which includes the Mental Component Summary and Physical Component Summary, was also used. At 4- and 12-week follow-ups, there were no statistically significant differences between the MRgFUS and the sham groups in the symptom severity score, the health-related QOL score, and the 36-Item Short-Form Health Survey Physical Component Summary or Mental Component Summary scores. Change in uterine and fibroid volume, however, differed significantly between groups at 12 weeks. Uterine volume decreased by 17% in the MRgFUS group and by 3% in the sham group (p=0.04). Total fibroid volume decreased by 18% in the MRgFUS group and did not change in the sham group (p=0.03). The trialists concluded that a larger sham-controlled randomized trial of MRgFUS was feasible.

Systematic Reviews
The remaining published studies are nonrandomized. A systematic review, published by Gizzo et al (2014), conducted a literature search through February 2013 and identified 38 uncontrolled studies with a total of 2500 patients who underwent MRgFUS for the treatment of uterine fibroids. All published studies included women 18 years or older with symptomatic uterine fibroids, and most excluded patients who desired future pregnancies. Reviewers did not pool study findings due to the heterogeneity of outcomes but concluded that, overall, MRgFUS appeared to be a safe, noninvasive option for treating uterine fibroids. Future research, particularly RCTs were recommended to compare MRgFUS with other noninvasive procedures and to explore the fertility-sparing potential further.

Nonrandomized Studies
The following studies were published after the Gizzo (2014) systematic review.

Chen et al (2016) evaluated 107 women undergoing MRgFUS for the treatment of uterine fibroids. Efficacy was defined as the proportion of patients with at least 10% fibroid shrinkage from baseline, as measured by magnetic resonance imaging. At the 6-month follow-up, 93% efficacy was reported.

Froeling et al (2013) reported on 121 women with symptomatic uterine fibroids who were eligible for treatment with MRgFUS and UAE. Forty-four (36%) women were lost to follow-up. Follow-up data at 60 months were available for 77 women, 41 in the UAE group, and 36 in the MRgFUS group. The primary outcome was the rate of reintervention (eg, repeat MRgFUS, myomectomy, hysterectomy, endometrial ablation). During follow-up, 5 (12%) women in the UAE group and 24 (67%) women in the MRgFUS group experienced a reintervention (statistical comparison not reported). Health-related QOL scores (secondary outcomes) were significantly better in the UAE group than in the MRgFUS group at follow-up.

Fertility Following MRgFUS for Treatment of Uterine Fibroids
A prospective registry of pregnancies after MRgFUS had been maintained by the manufacturer of the ExAblate device. Rabinovici et al (2010) reported on 54 known pregnancies a mean of 8 months after treatment. They included 8 pregnancies from clinical trials designed for women who did not desire pregnancy, 26 pregnancies after commercial treatment, and 20 pregnancies in 17 patients from an ongoing study of MRgFUS in women trying to conceive. Twenty-two (42%) of the 54 pregnancies resulted in deliveries and 11 were ongoing beyond 20 weeks at the time the article was written. There were 14 (26%)

miscarriages and 7 (13%) elective terminations. Among the 22 live births, mean live birth weight was 3.3 kg, and the vaginal delivery rate was 64%. The article provided initial information on the impact of MRgFUS on uterine fibroids in pregnancy; findings suggested that fertility may be maintained but that the number of cases was too small to draw definitive conclusions. The study also did not address the possible impact of MRgFUS treatment on the future ability to become pregnant.

Section Summary: Uterine Fibroids
For the treatment of uterine fibroids, there are 2 small RCTs, one with 49 women that compared MRgFUS with UAE and the other a feasibility trial assessing 20 women that had a sham control. Several nonrandomized studies have also compared MRgFUS with a different treatment. The sham-controlled randomized trial concluded that a larger trial would be feasible. The trial reported significantly lower fibroid volumes in the active treatment group; however, there were no statistically significant differences in QOL between the groups. The other RCT reported no significant differences in medication use or symptoms between the MRgFUS and UAE groups. Recovery was significantly faster in the MRgFUS group than in the UAE group. A 2014 systematic review, which identified only noncomparative studies, did not pool results due to heterogeneity in outcomes among the studies. While reviewers concluded that MRgFUS may be a safe and effective minimally invasive option for the treatment of fibroids, they noted that RCTs comparing MRgFUS with other noninvasive procedures would be informative. In a 2013 comparative study, outcomes appeared to be better with UAE than with MRgFUS. There is insufficient evidence on the long-term treatment effects, recurrence rates, and impact on future fertility and pregnancy of this therapy.

PALLIATIVE TREATMENT OF BONE METASTASES
Evidence for the use of MRgFUS for the treatment of painful bone metastases consists of a large RCT and many observational studies.

Randomized Controlled Trials
In an RCT evaluating the ExAblate System for the treatment of painful bone metastases, Hurwitz et al (2014) evaluated patients with 3 or more months of life expectancy who had painful bone metastases despite radiotherapy, or who were unsuitable for or declined radiotherapy. Patients rated tumor pain on a 10-point scale numeric rating scale (NRS) at 4 or greater. While they could have up to 5 painful lesions, only 1 lesion was treated, and it had to cause pain at least 2 points greater on the NRS than any other lesion. Also targeted tumors needed to be device-accessible.

Study participants were randomized 3:1 to active (n=122) or sham (n=39) MRgFUS treatment. Ten patients in the treatment group and 4 in the sham group did not receive the allocated treatment. An additional 26 patients in the treatment group and 23 in the sham group did not complete the 3-month follow-up. A larger proportion of the placebo group dropped out: 17 (49%) of 35 who were treated decided to have rescue MRgFUS treatment after a lack of response to placebo. A modified intention-to-treat analysis was used that included patients who had at least 1 MRgFUS or placebo sonication. Missing values were imputed using the last-observation carried forward method.

The primary efficacy end point, assessed at 3 months, was a composite outcome comprised of the change in baseline in worst NRS score and morphine equivalent daily dose (MEDD) intake. Patients were considered responders if their worst NRS score decreased by at least 2 points and if their MEDD intake did not increase more than 25% from baseline to 3 months. NRS scores and MEDD intake were reported separately as secondary outcomes.

Seventy-two (64%) of 112 patients in the MRgFUS group and 7 (20%) of 35 patients in the control group were considered responders, as previously defined. The difference was statistically significant (p=0.01), favoring active treatment. When the 2 measures comprising the primary end point were analyzed separately, there was a statistically significant difference between groups in change in worst NRS score and a nonsignificant difference in change from baseline in pain medication. The NRS score decreased by a mean (standard deviation) of 3.6 (3.1) points in the MRgFUS group and by a mean of 0.7 (2.4) in the placebo group (p<0.01). Change in MEDD from baseline was 3.7 in the MRgFUS group and 15.3 in the placebo group. Fifty-one (46%) patients in the MRgFUS group and 1 (3%) in the placebo group experienced at least 1 adverse event. Most adverse events were transient, with the most common being sonication pain, experienced by 36 (32%) patients in the MRgFUS group. In 17 (15%) patients, sonication pain was severe; 3 patients did not complete treatment due to pain. The most clinically significant adverse events that lasted more than a week were third-degree skin burns in 1 patient (associated with noncompliance with the treatment protocol) and fracture in 2 patients (one of which was outside the treatment location). Potential trial limitations included a nonconventional primary outcome measure and the small initial size of the sham group. Moreover, a large number of sham patients (66%) did not complete the 3-month follow-up; the trialists indicated that this low completion rate was due to lack of response to placebo treatment.

Observational Studies
Liberman et al (2009) conducted a multicenter prospective study in Canada, Israel, and Germany. The study included 31 patients with painful bone metastases who had failed or refused other treatment options; 25 (81%) patients were available for 3-month follow-up. Mean visual analog scale score decreased from 5.9 at baseline to 1.8 three months after treatment. Thirteen of 25 patients who used nonopioid analgesics and 6 of 10 who used opioids decreased medication use after treatment. Neither group reported treatment-related adverse events.

Arrigoni et al (2017) evaluated use of MRgFUS in a case series of 14 patients with intra-articular benign bone lesions who were followed for 12 months. Pain was measured by a visual analog scale and all patients underwent computed tomography and magnetic resonance imaging. Mean pain scores significantly decreased from 7.8 pretreatment to 2.0 at 6-month follow-up to 0.6 at 12-month follow-up (p<0.001). No patients reported worse symptoms and none reported the procedure unsuccessful. Diagnostic imaging supported the clinical findings and showed calcification of the lesion, lack of contrast enhancement, and resolution of bone edema.

Section Summary: Palliative Treatment of Bone Metastases
The evidence consists of a single industry-sponsored RCT that found significant improvement after MRgFUS in a composite outcome comprised of a reduction in pain and morphine use, and in pain reduction as a stand-alone outcome. This trial was appropriately sham-controlled. A substantial proportion of patients in the treatment group experienced adverse events, but most adverse events were transient and not severe. Several case series have also reported improvements in pain and patient satisfaction with MRgFUS.

TREATMENT OF OTHER TUMORS
Only small case series have assessed the safety and/or efficacy of MRgFUS for treating tumors related to breast cancer, brain cancer, prostate cancer, and nonspinal osteoid osteoma.

The most recent case series on the use of MRgFUS for breast cancer ablation was published by Merckel et al (2016). Ten patients with early-stage invasive breast cancer underwent MRgFUS prior to surgical resection. Ablation was confirmed histopathologically in 6 of these patients. The investigators concluded that MRgFUS is safe and feasible. A noted limitation is the long procedure time (average, 145 minutes), due to waiting time after contrast injection and time to find a proper magnetic resonance navigator signal.

In addition, several case series have investigated the use of MRgFUS for desmoid tumors. Avedian et al (2016) used MRgFUS to treat 9 patients with desmoid tumors. Five patients were available for follow-up for at least 12 months. Mean decrease in tumor size was 36% (95% CI, 7% to 66%). Bucknor et al (2017) described the use of MRgFUS to treat 3 patients with large aggressive desmoid tumors within the posterior thigh. Each patient received multiple MRgFUS treatments. In this case series, use of MRgFUS for desmoid tumors required different treatment parameters than those used for fibroids or bone lesions, due to differences in vascularity of the target tissue and the need for effective skin protection when using MRgFUS on extremities. Ghanouni et al (2017) used MRgFUS to treat 15 patients with extra-abdominal desmoid tumors. Treatment times ranged from 0.8 to 8 hours. Results were presented on 9 patients (3 were lost to follow-up before 6 months, 3 received additional treatments). Seven of 9 patients experienced durable clinical benefits, with a median reduction in tumor volume of 98%. Treatment-related adverse events included skin burns, nerve injury, and off-target heating.

Section Summary: Treatment of Other Tumors
Currently, evidence on the use of MRgFUS for the treatment of other tumors consists of small case series, which is insufficiently robust to draw conclusions about efficacy. Several ongoing trials are evaluating the safety and efficacy of MRgFUS for other tumors, with completion dates in the coming years (see Table 1).

ESSENTIAL TREMORS
Evidence for the use of MRgFUS to treat medicine-refractory essential tremors consists of a technology assessment, a meta-analysis, and a single-arm study published subsequent to the technology assessment.

Systematic Reviews
The technology assessment was published by Health Quality Ontario (2018). The literature search, conducted through April 2017, identified 9 studies for inclusion: 4 single cohort studies, 2 retrospective chart reviews, 2 uncontrolled prospective studies, and an RCT. The RCT compared MRgFUS with sham treatment, the chart reviews compared MRgFUS with deep brain stimulation and radiofrequency thalamotomy. Study quality was evaluated using the GRADE system. The RCT was rated high quality, the uncontrolled comparative studies were rated very low quality, and the remaining studies were rated low quality. All studies reported tremor severity as an outcome. Pooling of results was not conducted due to heterogeneity in study designs, analyses, and outcomes across the studies. Reviewers determined that, overall, MRgFUS decreased tremor severity and improved QOL. The high-quality RCT by Elias et al (2016) is discussed below.

Mohammed et al (2018) conducted a meta-analysis evaluating the use of MRgFUS to treat medicine-refractory essential tremors. The literature search, conducted through August 2017 identified 9 studies (total N=160 patients) for inclusion, 8 of which were also evaluated in the Ontario technology assessment. Pooled analyses found significant improvements in the mean percentage change in Clinical Rating Scale for Tremor scores (62.2%) and Quality of Life in Essential Tremor scores (46.5%). Complications included nausea, vomiting, and ataxia, which decreased during the 12-month follow-up.

Randomized Controlled Trials
A single high-quality study, a double-blind, sham-controlled randomized trial by Elias et al (2016), was identified by the 2 systematic reviews. Trial selection criteria included patients with moderate or severe postural or intention tremor of the hand (≥2 on the Clinical Rating Scale for Tremor) and refractory to at least 2 medical therapies. Patients were randomized to MRgFUS thalamotomy (n=56) or sham treatment (n=20). Outcomes were tremor severity, improvement, and QOL, measured at 3 months postprocedure. Patients in the treatment group were followed for an additional 12 months. Mean score for hand tremor improved significantly from baseline in the treatment group (47%) compared with the sham group (0.1%) at 3 months. Change in mean functional improvement score from baseline differed significantly in the MRgFUS group (62%) compared with the sham group (3%) at 3 months. Change in Quality of Life in Essential Tremor Questionnaire scores also differed significantly in the treatment group compared with the sham group, with the largest improvements experienced in the psychosocial domain. The improvements in hand tremor score, functional improvement, and QOL were maintained at 12 months in the MRgFUS group.
Chang et al (2018) published results from 67 patients who participated in the open-label extension of the RCT. Because 9 patients from the original trial received additional treatment during the 2-year follow-up, they were excluded from the analysis. Improvements in tremor and disability scores were maintained at the 2-year follow-up (tremor, 19.8±4.9 [baseline] to 8.8±5.0 [at 2 years]; disability, 16.4±4.5 [baseline] to 6.5±5.0 [at 2 years]).

Section Summary: Essential Tremors
Evidence for the use of MRgFUS in the treatment of medicine-refractory essential tremors consists of a technology assessment that included a high-quality RCT; a meta-analysis; and a noncomparative study

published after the technology assessment. The assessment did not pool results from the studies but concluded, overall, MRgFUS decreased tremor severity and improved QOL. The meta-analysis, which included 9 studies total (8 were also in the technology assessment), found that MRgFUS significantly improved Clinical Rating Scale for Tremor scores as well as QOL measures. The sham-controlled randomized trial which was considered high quality, found significant improvements in the treatment group in tremor severity, functional improvement, and QOL after 3 months of follow-up, and these results were maintained through 2 years of follow-up.

SUMMARY OF EVIDENCE

For individuals who have uterine fibroids who receive MRgFUS, the evidence includes 2 small 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) is ongoing; preliminary results at 6 weeks posttreatment, comparing MRgFUS with uterine artery embolization have shown 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 group, as measured by time to return to work and time to normal activities. In a separate 2013 comparative study, outcomes appeared to be better with uterine artery embolization 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 the effects of the technology on health outcomes.

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 and several 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. The case series reported reductions in pain following MRgFUS treatment, consistent with the RCT. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with other tumors (eg, breast cancer, brain cancer, prostate cancer, desmoid, nonspinal osteoid osteoma) who receive MRgFUS, the evidence includes small case series. Relevant outcomes are symptoms, health status measures, and treatment-related morbidity. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with medicine-refractory essential tremors who receive MRgFUS, the evidence includes 2 systematic reviews that identified an RCT and several observational studies. 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. 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 a meaningful improvement in the net health outcome.

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Policy History

Original Effective Date: 09/22/2005
Current Effective Date: 11/21/2018

09/07/2005	Medical Director review
09/20/2005	Medical Policy Committee review
09/22/2005	Quality Care Advisory Council approval
07/07/2006	Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
09/05/2007	Medical Director review
09/19/2007	Medical Policy Committee approval. Coverage eligibility unchanged.

09/03/2009	Medical Policy Committee approval
09/16/2009	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/09/2010	Medical Policy Committee review
09/15/2010	Medical Policy Implementation Committee approval. Added that magnetic resonance imaging (MRI)-guided ablation of other tumors, including but not limited to breast, brain, prostate cancer, and palliative treatment of bone metastases, is considered to be investigational.
09/01/2011	Medical Policy Committee review
09/14/2011	Medical Policy Implementation Committee approval. Title changed from "MRI-Guided High Intensity Ultrasound Ablation of Uterine Fibroids" to "MRI-Guided Focused Ultrasound (MRgFUS) for the Treatment of Uterine Fibroids and Other Tumors." Coverage eligibility unchanged.
10/11/2012	Medical Policy Committee review
10/31/2012	Medical Policy Implementation Committee approval
10/03/2013	Medical Policy Committee review
10/16/2013	Medical Policy Implementation Committee approval. Policy title changed from "MRI-Guided Focused Ultrasound (MRgFUS) for the Treatment of Uterine Fibroids and Other Tumors" to "MRI-Guided Focused Ultrasound (MRgFUS)". Policy changed to a single investigational statement with no change to coverage eligibility.
11/06/2014	Medical Policy Committee review
11/21/2014	Medical Policy Implementation Committee approval. No change to coverage. Title changed from MRI-Guided Focused Ultrasound (MRgFUS) to Magnetic Resonance Imaging-Guided Focused Ultrasound.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
10/29/2015	Medical Policy Committee review
11/16/2015	Medical Policy Implementation Committee approval. Added "Based on review of available data, the Company may consider magnetic resonance imaging (MRI)–guided high-intensity ultrasound ablation for pain palliation in adult patients with metastatic bone cancer who failed or are not candidates for radiotherapy to be eligible for coverage."
11/03/2016	Medical Policy Committee review
11/16/2016	Medical Policy Implementation Committee approval. Title change, "imaging" removed from policy statements.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. No change to coverage.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. A policy statement added that MRgFUS ablation may be considered eligible for coverage for the treatment of medicine-refractory essential tremors.

Next Scheduled Review Date: 11/2019

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2017 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

Magnetic Resonance-Guided Focused Ultrasound

Policy # 00180
Original Effective Date: 09/22/2005
Current Effective Date: 11/21/2018

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	0071T, 0072T
HCPCS	C9734
ICD-10 Diagnosis	All related diagnoses

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association TEC or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.