BlueCross BlueShield Federal Employee Program.

FEP Medical Policy Manual

FEP 7.01.109 Magnetic Resonance Imaging-Guided Focused Ultrasound

Effective Policy Date: October 1, 2023

Original Policy Date: December 2011

Related Policies:

4.01.19 - Laparoscopic, Percutaneous, and Transcervical Techniques for Uterine Fibroid Myolysis
7.01.95 - Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors

Magnetic Resonance Imaging-Guided Focused Ultrasound

Description

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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.

OBJECTIVE

The objective of this evidence review is to evaluate whether magnetic resonance-guided focused ultrasound improves the net health outcome in patients with uterine fibroids, metastatic bone cancer, other tumors, medication-refractory essential tremors, or medication-refractory tremor dominant Parkinson's disease.

POLICY STATEMENT

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 **not medically necessary** in the treatment of uterine fibroids.

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

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

POLICY GUIDELINES

None

BENEFIT APPLICATION

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

Magnetic resonance-guided high-intensity ultrasound ablation of uterine fibroids is currently performed at a limited number of institutions; therefore, an out-of-network referral may be requested.

FDA 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.

In November 2021, the FDA approved the use of the Exablate Prostate System for prostate tissue ablation through the premarket approval process.

FDA product codes: NRZ, POH, PLP.

RATIONALE

Summary of Evidence

For individuals who have uterine fibroids who receive magnetic resonance-guided focused ultrasound (MRgFUS), the evidence includes systematic reviews, 2 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 (UAE), 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 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 re-intervention rate of the 3 regimens (myomectomy vs UAE vs MRgFUS) in all time points assessed, while the MRgFUS had the highest re-intervention rate. 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 (eg, breast cancer, brain cancer, prostate cancer, desmoid, nonspinal osteoid osteoma) who receive MRgFUS, the evidence includes nonrandomized, uncontrolled phase II trials 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. Another nonrandomized, phase II trial in patients with prostate cancer reported that at 24 months, 88% (78 out of 89) of patients had no evidence of grade group 2 or higher prostate cancer in the treated area. Use of MRgFUS for the treatment of nonspinal osteoid osteoma consists of several larger case series, 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 medicine-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 (PD) 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 (N=27) 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.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Radiology

In 2018, the American College of Radiology published appropriateness criteria for the radiological management of uterine leiomyomas (fibroids).[34] The clinical guidance states that "MR [magnetic resonance]-guided high-intensity focused US [ultrasound] (MRgFUS) is another uterine-sparing option to treat focal leiomyomas. It is noninvasive, though each treatment may take several hours to complete. Its use currently is restricted to patients with fewer than six leiomyomas or leiomyoma volume < 900 cm^3," and "although a reasonable alternative for patients unable or unwilling to tolerate sedation or anesthesia, long-term data and viability results are still lacking."

American Society for Radiation Oncology et al

In 2017, the American Society for Radiation Oncology (ASTRO) published guidelines on palliative radiotherapy for bone metastases, which stated that external-beam radiotherapy continues to be the primary therapy for treating painful uncomplicated bone metastases.[35] The guidelines did not mention magnetic resonance-guided focused ultrasound. If patients experience persistent or recurrent pain more than 1 month after initial treatment, the guidelines recommended retreatment with external-beam radiotherapy. As for advanced radiotherapy such as stereotactic body radiotherapy for retreatment of recurrent pain in spine bone lesions, these "may be feasible, effective, and safe, but the panel recommends that this approach should be limited to clinical trial participation or on a registry given limited data supporting routine use."

In 2022, the American Urological Association (AUA)/ ASTRO published guidance on the management of clinically localized prostate cancer.[36] The guidance states that "there is a lack of data to date to support the use of whole gland or focal ablation for the treatment of clinically localized prostate cancer."

National Comprehensive Cancer Network

Guidelines from the National Comprehensive Cancer Network (NCCN) on bone cancer (v. 3.2023),[37] breast cancer (v. 4.2023),[38] and brain cancer (v.1.2023),[39] do not mention magnetic resonance-guided ultrasound as a treatment option. The NCCN guideline for prostate cancer (v 1.2023) states that "Cryotherapy or other local therapies are not recommended as routine primary therapy for localized prostate cancer due to lack of long-term data comparing these treatments to radiation. At this time, the panel recommends only cryosurgery and high-intensity focused ultrasound (HIFU; category 2B) as local therapy options for RT [radiotherapy] recurrence in the absence of metastatic disease". [40]

National Institute for Health and Care Excellence

Guidance from NICE (2018) on unilateral magnetic resonance-guided ultrasound for treatment-resistant essential tremor states "the evidence on the safety of unilateral MRI [magnetic resonance imaging]-guided focused ultrasound thalamotomy for treatment-resistant essential tremor raises no major safety concerns. However, current evidence on its efficacy is limited in quantity. Therefore, this procedure should not be used unless there are special arrangements for clinical governance, consent, and audit or research."[41]

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
December 2011	New policy	
June 2012	Replace policy	Policy statement changed to not medically necessary. Related policy added. URL corrected in Reference 1. Policy updated with literature review; reference numbers 8, 18 added; references re-numbered.
June 2013	Replace policy	Policy updated with literature review and references. Policy changed to single not medically necessary statement; no change to intent of policy. Policy title changed to MRI-Guided Focused Ultrasound (MRgFUS).
June 2014	Replace policy	Policy updated with literature review, References 2, 6, and 14 added; other references renumbered or removed. No change in policy statement.
June 2015	Replace policy	Policy updated with literature review. Statement added that MRgFUS may be considered medically necessary for pain palliation in adult patients with metastatic bone cancer who failed or are not candidates for radiotherapy. Bullet point on bone metastases removed from not medically necessary statement. References 12 and 21-22 added.
June 2016	Replace policy	Policy updated with literature review through December 15, 2015; references 2 and 23 added. Policy statements unchanged. Global change to policy to remove "imaging, (eg, title, policy statement) to standardize terminology to magnetic resonance guided focused ultrasound (MRgFUS).
September 2018	Replace policy	Policy updated with literature review through May 7, 2018; references 23-26 and 28 added. A policy statement added that MRgFUS ablation may be considered medically necessary for the treatment of medicine-refractory essential tremors. Policy statement clarified that "treatment of other tumors..., is investigational (instead of not medically necessary) as this is a non-approved indication.
September 2019	Replace policy	Policy updated with literature review through May 14, 2019; references on NCCN updated. Policy statements unchanged.
September 2020	Replace policy	Policy updated with literature review through May 18, 2020; no references added. Policy statements unchanged
September 2021	Replace policy	Policy updated with literature review through May 24, 2021; references added. Investigational statement added on tremor-dominant Parkinson disease to the policy statement.
September 2022	Replace policy	Policy updated with literature review through June 3, 2022; references added. Policy statements unchanged
September 2023	Replace policy	Policy updated with literature review through May 22, 2023; references added. Policy statements unchanged