CLINICAL MEDICAL POLICY	
Policy Name:	Magnetic Resonance-Guided Focused Ultrasound (MRgFUS)
Policy Number:	MP-094-MD-DE
Responsible Department(s):	Medical Management
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Revision Date:	N/A
Products:	Highmark Health Options Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 8

DISCLAIMER

Highmark Health Options medical policy is intended to serve only as a general reference resource regarding coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT

Highmark Health Options does not provide coverage under the medical-surgical benefits of the Company's Medicaid products for medically necessary Magnetic Resonance Imaging (MRI)-Guided Focused Ultrasound (MRgFUS).

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

The qualifications of the policy will meet the standards of the National Committee for Quality Assurance (NCQA) and the Delaware Department of Health and Social Services (DHSS) and all applicable state and federal regulations.

DEFINITIONS

Essential Tremors – A chronic, incurable condition with unknown cause characterized by involuntary, rhythmic tremor of a body part, most typically the hands and arms.

Uterine Fibroids – (also called leiomyomata or myomas) are benign tumors of the myometrium, the smooth muscle layer of the uterus.

PROCEDURES

1. Magnetic Resonance (MR)-Guided Focused Ultrasound (MRgFUS) is considered investigational and not medically necessary for all indications, including but not limited to treatment of the following indications:
    A. Medicine-refractory essential tremors; OR
    B. Uterine fibroids; OR
    C. All tumors, including but not limited to brain, breast, prostate, and renal; OR
    D. Bone Metastases for palliation of pain.

2. Post-payment Audit Statement
   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Health Options at any time pursuant to the terms of your provider agreement.

GOVERNING BODIES APPROVAL

There are several devices that have received U.S. FDA approval via De Novo and Premarket Application (PMA) processes:

- The ExAblate® 2000 System (InSightec, Inc.) was approved for two indications: "ablation of uterine fibroid tissue in pre- or perimenopausal women with symptomatic uterine fibroids who desire a uterine sparing procedure" and for palliation of pain associated with tumors metastatic to bone.
- The ExAblate® 2100 System also received approval through the PMA process. Approval remains limited to treatment of patients with metastatic bone cancer who failed or are not candidates for radiation therapy or in patient with symptomatic uterine fibroids with a uterine size of less than 24 weeks and those who have completed child bearing.
- In October 2012, the FDA approved the ExAblate® System, Model 2000/2100/2100 VI for pain palliation via the PMA process. For pain palliation, the intended use of the device is in adult patients with metastatic bone cancer who failed or are not candidates for radiation therapy. The device was evaluated through an expedited review process, but the FDA required a post-approval study with 70 patients to evaluate the effectiveness of the system under actual clinical conditions.
- The Sonablate® 450 (SonaCare Medical) is the first high intensity ultrasound system for prostate tissue ablation to receive FDA approval, and therefore underwent the de novo application process, obtaining clearance in 2015.
- Shortly thereafter, Ablatherm Integrated Imaging® (EDAP TMS) received PMA approval.

Additional information is available at:
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm124105.htm.

CODING REQUIREMENTS

Non-covered Procedure Codes
These procedure codes are noncovered and can only be approved upon medical director review

CPT/HCPCS Codes	Description
0071T	Focused ultrasound ablation of uterine leiomyomata, including MR guidance; total leiomyomata volume of less than 200 cc of tissue.
0072T	Focused ultrasound ablation of uterine leiomyomata, including MR guidance; total leiomyomata volume greater or equal to 200 cc of tissue
0398T	Magnetic resonance image guided high intensity focused ultrasound (MRgFUS), stereotactic ablation lesion, intracranial for movement disorder including stereotactic navigation and frame placement when performed
C9734	Focused ultrasound ablation/therapeutic intervention, other than uterine leiomyomata, with or without magnetic resonance (MR) guidance

*These procedure codes are noncovered and can only be approved upon medical director review.

REIMBURSEMENT

Participating facilities will be reimbursed per their Highmark Health Options contract.

SUMMARY OF LITERATURE

Magnetic Resonance-Guided Focused Ultrasound (MRgFUS) is a noninvasive treatment that combines focused ultrasound and magnetic resonance imaging (MRI). The ultrasound beam penetrates through the soft tissues, and the beam can be focused on targeted sites. This causes a local increase in temperature in the target tissue, resulting in coagulation necrosis while sparing the surrounding normal structures. Broadly, the MRgFUS uses an integrated imaging system to take measurements, confirm the treatment area, and monitor thermal destruction in real time. The device is proposed as a less invasive approach, rather than surgery, for the treatment of localized tumors (e.g., prostate cancer), uterine fibroids, pain palliation on bone metastases, and medicine-refractory essential tremors.

The Pennsylvania Department of Human Services Technology Assessment Group gave MRgFUS an option #4 decision for Metastatic Bone Disease, Uterine Fibroids, and Essential Tremors.

Essential Tremors
Essential tremor (ET) is a common movement disorder characterized by postural tremor of the outstretched upper limbs that is absent at rest, not worsened by movement, and not associated with extrapyramidal or cerebellar signs. ET symptoms can be managed with medication (e.g., propanolol and primidone) for most patients, but 10% of ET patients have medically refractory ET which can be debilitating.

The MRgFUS thalamotomy may be indicated for patients with medically refractory ET. MRgFUS creates a thalamic lesion which can reduce tremor, but can also result in permanent neurologic deficits (Elias, 2016). While creation of a lesion does reduce tremor, and larger lesions can result in more enduring efficacy, larger lesions have a higher incidence of side effects (Elias, 2016). In July 2016, MRgFUS (i.e., Exablate Neuro) was FDA-approved for patients with severe, chronic and medically intractable ET as an alternative to deep brain stimulation or surgical interventions (e.g., thalamotomy and pallidotomy) (InSightec, Inc., Dallas, TX). Preliminary uncontrolled studies have shown improvement compared with baseline scores for

contralateral hand tremor, disability, and quality of life. However, large, randomized, controlled trials are needed to determine the proper patient populations that may benefit from this therapy and assess the long-term efficacy and safety of MRgFUS for this indication. Adverse effects included transient sensory and cerebellar symptoms, and persistent paresthesia.

According to Tarsy et al. (2018), unilateral thalamotomy with magnetic resonance imaging (MRI)-guided focused ultrasound is a newer technique that may be a reasonable alternative for treating contralateral limb tremor associated with ET. This is the only form of thalamotomy approved for ET by the US Food and Drug Administration (FDA), although long-term studies are currently lacking.

In an initial pilot investigation, Bond and associates (2017) evaluated the safety and efficacy of focused ultrasound thalamotomy for the treatment of medically refractory, tremor-dominant Parkinson disease (TDPD). The investigation concluded MRgFUS as a promising new treatment approach for ET, but additional long-term effectiveness and safety data was needed to make a conclusion.

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. Several approaches currently available to treat symptomatic uterine fibroids include hysterectomy, abdominal myomectomy, laparoscopic and hysteroscopy myomectomy, hormone therapy, uterine artery embolization, and watchful waiting. Hysterectomies and various myomectomy procedures are considered the standard treatment. All current surgical treatments are invasive, and all treatments have limitations. MRgFUS is indicated to ablate uterine fibroid tissue in premenopausal or perimenopausal women with symptomatic uterine fibroids who desire a uterine-sparing procedure and whose uterine size is less than 24 weeks gestation size (Hayes, 2018).

In 2015, the Society of Obstetricians and Gynaecologists of Canada published practice guidelines on the management of uterine fibroids in women with otherwise unexplained infertility. The guidelines found no studies comparing magnetic resonance–guided focused ultrasound (MRgFUS) with myomectomy or in women with fibroids who have infertility as their primary complaint, and thus additional data would be needed before the treatment could be offered to this patient population.

In 2017, the Agency for Healthcare Research and Quality issued a comparative effectiveness review on management of uterine fibroids which concluded six studies assessed high intensity focused ultrasound (HIFU) for fibroid ablation, but only one fair quality pilot study (n=20) used MRgFUS. The other studies were rated as poor quality, primarily due to lack of masking participants and outcome assessors to the intervention received. The strength of evidence is low because of short follow-up and poor quality of overall study design. Therefore, evidence related to patient reported outcomes for MRgFUS in use for uterine fibroids is insufficient.

Hayes (2018) conducted a literature search and identified 9 studies that evaluated MRgFUS for uterine fibroids. Overall, a low-quality body of evidence suggests that MRgFUS reduces fibroid volume in women with symptomatic uterine fibroids. The low quality of evidence is due to the lack of well-designed controlled studies on MRgFUS and the predominance of studies using data from the same patient population. There was only one randomized controlled trial (RCT) which identified that there was a statistically significant decrease in fibroid volume, but patients reported significantly higher levels of abdominal or pelvic pain. Another study compared a cohort of patients that underwent MRgFUS and a cohort that underwent hysterectomies; patients undergoing a hysterectomy reported significant

improvements when compared with patients who received MRgFUS. There are no published data comparing MRgFUS with other uterus-sparing treatments, such as myomectomy or uterine artery embolization (UAE). Additional long-term studies are needed to compare outcomes of MRgFUS with other therapies before definitive conclusions about the effectiveness of this technology can be made. Therefore, Hayes gave a C rating to MRgFUS for indicated symptomatic uterine fibroids (Hayes, 2018).

Palliative Treatment of Bone Metastases

Bones are a common place for metastatic cancer cells to colonize and establish secondary tumor sites. Out of the estimated 1.2 million new cancer diagnoses each year, approximately 50% of the tumor metastases occurs to the skeleton (Hayes, 2018). There are different treatment options for bone metastases, including medications, radiation therapy, and surgical interventions, and each option has potential for side effects and intolerability (Hayes, 2018). All of these treatment options may produce positive results, however, many patients experience inadequate pain control or unwanted side effects, which will prompt alternative therapy considerations. MRgFUS is an alternative therapy that takes pretreatment scans to localize the target bone lesion and construct 3-dimensional treatment plans (Hayes, 2018). MRgFUS energy acts on bone primarily through thermal effects. The exact mechanism for pain palliation from MRgFUS is not fully understood but is thought to involve the indirect ablation of periosteum and tumor tissue in the ultrasound beam path. Nerve fibers in the bone periosteum are considered to be a major source of pain from bone metastases, and ablation of these nerves may result in pain palliation after MRgFUS (Hayes, 2018). According to Hayes (2018), a D2 rating was given to the MRgFUS using the ExAblate system for palliation of metastatic bone pain. The rating reflects a very-low quality insufficient body of evidence. The balance of potential benefits and harms of MRgFUS could not be determined, and there is insufficient evidence of long-term safety.

In 2011, the American Society for Radiation Oncology 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. The guidelines did not mention MRgFUS and did not offer specific recommendations for patients who fail or are not candidates for radiotherapy.

Other Tumors

MRI-guided high-intensity focused ultrasound (MRgFUS) ablation is also being studied as a treatment of other tumors including breast, prostate, brain, and desmoid tumors.

Only small case series have been published on the safety and/or efficacy of MRgFUS for treating tumors related to breast cancer, brain cancer, prostate cancer, and nonspinal osteoid osteoma. Randomized controlled trials are needed to evaluate the long term efficacy and safety of MRgFUS for these indications.

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

The evidence is insufficient for the treatment of tumors, to determine the effects of the technology on net health outcomes.

POLICY SOURCE(S)

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Policy History

Date	Activity
01/02/2019	Initial policy developed
03/12/2019	QI/UM Committee approval
05/06/2019	Provider effective date