Fibroid Treatment

Number: 0304

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

Policy

Note: POWER MORCELLATION FOR HYSTERECTOMY OR MYOMECTOMY REQUIRES PRECERTIFICATION.

I. Aetna considers radiofrequency ablation (open or laparoscopic) or transcatheter uterine artery embolization (UAE) medically necessary as an alternative to hysterectomy or myomectomy for the treatment of uterine fibroids when the member has persistence of one or more symptoms directly attributed to uterine fibroids (i.e., excessive menstrual bleeding (menorrhagia), bulk-related pelvic pain, pressure or discomfort, urinary symptoms referable to compression of the ureter or bladder, and/or dyspareunia).

Aetna considers other uses of transcatheter UAE experimental and investigational because its effectiveness for indications other than the one listed above has not been established.

II. Aetna considers myomectomy or hysterectomy using power morcellation experimental and investigational for the removal of uterine fibroids because its safety and effectiveness has not been established. An exceptions to this policy, fibroid removal with power morcellation is considered medically necessary for the following indications in women without known or strongly suspected uterine cancer:

Policy History

Last Review 07/25/2018
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Review History

Definitions

Additional Information

Clinical Policy
Bulletin Notes
(i) premenopausal women who wish to maintain fertility and who have no risk factors for uterine sarcoma (e.g., history of 2 or more years of tamoxifen therapy, history of pelvic irradiation, history of childhood retinoblastoma, Lynch syndrome, or personal history of hereditary leiomyomatosis and renal cell carcinoma syndrome); (ii) premenopausal women who have clinical indications for hysterectomy and who have no risk factors for uterine sarcoma, where a vaginal hysterectomy is technically difficult due to the large size of the uterus; or (iii) women with co-morbidities (e.g., cardiovascular, renal, hepatic, pulmonary, endocrine, or morbid obesity) where surgical alternatives to fibroid removal with power morcellation (hysterectomy without power morcellation, radiofrequency ablation, uterine artery embolization) pose an unacceptable risk.

In all cases, the member must be informed of alternative procedures for fibroids and the risks of power morcellation in spreading unsuspected cancerous tissue beyond the uterus.

III. Aetna considers the following treatments for uterine fibroids experimental and investigational because their safety and effectiveness have not been established:

- Acupuncture
- Cryomyolysis
- Laparoscopic uterine artery occlusion
- Cryotherapy, interstitial thermotherapy, lasers, electrical, and ultrasound (focused ultrasound) ablation, with or without magnetic resonance imaging (MRI) guidance.

Note: Precertification of power morcellation for hysterectomy or myomectomy is required of all Aetna participating providers and members in applicable plan designs.

Background

Uterine fibroids (i.e., leiomyomas or myomas) are noncancerous growths that develop from the smooth muscular tissue of the uterus (also known as myometrium) usually during childbearing years. The size and growth pattern of uterine fibroids varies and may be found as subserosal, intramural, submucosal or pedunculated masses. They may also be located in the cervix or broad ligament. Although the cause is unknown, hormones seem to be a related factor.
Uterine fibroids represent the most common gynecological tumor in women of reproductive age and are responsible for over 200,000 hysterectomies per year. Most fibroids, even large ones, do not produce symptoms. However, they can cause a variety of symptoms including menometrorrhagia, dysmenorrhea, pelvic pain, reproductive failure, and compression of adjacent pelvic viscera, or be totally asymptomatic. A large array of treatment options exist for this disorder. Surgical treatments include hysterectomy, abdominal myomectomy, laparoscopic myomectomy, myolysis, and more recently magnetic resonance imaging (MRI)-guided ultrasound ablation. Non-surgical treatments include medical therapy (e.g., gonadotropin-releasing hormone agonist) and uterine artery embolization (UAE).

Uterine Artery Embolization:

For the last 20 years, therapeutic embolization has been successfully performed on various parts of the body. In more recent years, this technology has been applied to uterine fibroids in an effort to eliminate the nagging symptoms associated with uterine fibroids and offer women an alternative to hysterectomy and myomectomy. This outpatient procedure, which may require an over-night admission for pain control, uses angiographic techniques and fluoroscopic guidance to embolize the uterine arteries, similar to the methods used to control post-operative and post-partum hemorrhage. The embolization, consisting of tiny particles of polyvinyl alcohol (500 to 700 micron size), occludes the blood supply to the fibroids, which results in their ischemic infarction and subsequent degeneration over a period of weeks and months. Average fibroid volume reduction is approximately 50 % in 3 months and 65 % at 1 year. Uterine volume decreases by approximately 40 % in 3 months. The reduction in the fibroid's size leads to a decrease or resolution in the symptoms they cause. The procedure takes approximately 1 to 2 hours and it is anticipated that most women can return to work 7 days after the procedure.

The initial studies that have been published to date suggest that both menorrhagia and symptoms caused by the bulk of these fibroids will be significantly improved or will resolve in 80 to 90 % of patients on short-term follow-up. The patients in these series have tolerated the procedure well and patient satisfaction is high, but they all require careful post-procedural pain management. While severe ischemic injury to the uterus has been feared, the literature suggests that this occurs in only 1 to 2 % of patients. Unlike myomectomy, all fibroids can be treated simultaneously, regardless of their location or size in the uterus. Unlike Lupron, the literature indicates that premature menopause is rarely
induced. It has been shown that if the procedure is not successful and surgery is needed, this surgery is rendered easier, with a likelihood of less bleeding.

However, long-term follow-up on a larger number of cases will be required before any definitive statement can be made about the ultimate role of embolization in the treatment of uterine fibroids as compared to the other available therapies. The long-term outcome is not known, in that recanalization of the arteries could occur or collateral vessels could be recruited which might allow re-growth of the fibroids. Post-procedure fertility and the ability to carry a pregnancy to term are not presently known since most patients in published series have not sought to become pregnant. The effect on ovarian function has been a question, given the sporadic reports of amenorrhea after treatment. It is not known whether ovarian infarction occasionally occurs to affect function or whether merely decreasing uterine flow is sufficient to affect ovarian function. Further, it is not clear whether ovarian function is affected in only a few patients or whether it is more common and just not apparent clinically.

In a review on percutaneous UAE for the treatment of symptomatic fibroids, Lupattelli et al (2005) stated that although randomized trials are still underway, UAE appears a good option for those patients who wish to conserve their fertility or when surgery is contra-indicated. However, to assess the long-term effects of UAE longer follow-up is needed. This is in agreement with the observation of Bachmann (2006) who noted that treatment options for women with symptomatic uterine leiomyomas have been expanded to include radiological interventions with UAE and focused ultrasound surgery despite the lack of long-term efficacy data.

Despite the unknowns, it is clear that the initial experience with UAE suggests that this procedure is effective and safe in the short term and represents a promising new therapy for this very common medical condition.

A report by the American College of Obstetricians and Gynecologists (2004) stated that "UAE for the treatment of symptomatic fibroids, when performed by experienced physicians, appears to provide good short-term relief among appropriate candidates." ACOG strongly recommends that women who wish to undergo UAE have a thorough evaluation with an obstetrician/gynecologist to help facilitate optimal collaboration with interventional radiologists and ensure that the procedure is appropriate. There is insufficient data at this time to ensure that UAE is safe for women who may wish to become pregnant in the future, the report
notes. Moreover, few studies have assessed the effect of embolization on pregnancy-related outcomes. For these reasons, ACOG considers the procedure investigational or relatively contraindicated in such women. Also, the report warns that UAE is rarely, if ever, indicated in post-menopausal women.

Uterine artery embolization is contraindicated in women with any of the following conditions:

- Post-menopausal women with fibroid growth or rapid growth at any time (may indicate development of sarcoma); or
- Women who have evidence of current genito-urinary infection and/or malignancy; or
- Women who may wish to become pregnant in the future; or
- Women with a history of prior pelvic X-ray treatments, pelvic malignancy, chronic infections or severe endometriosis.

A report on the management of uterine fibroids prepared for the Agency for Healthcare Research and Quality (Viswanathan et al, 2007) stated that women who undergo UAE have shorter recoveries and spend less time in the hospital than women who have hysterectomies.

MRI-Guided Focused Ultrasound:

High intensity focused ultrasound with the imaging guidance of magnetic resonance imaging (MRI) known as magnetic resonance guided focused ultrasound sonication (MRgFUS) is now available. Currently, there is very little information regarding the effectiveness of MRI-guided ultrasound ablation for the treatment of uterine leiomyomata. In a review on the surgical and non-surgical management of uterine leiomyomata, Myers et al (2002) concluded that available evidence on the management of uterine leiomyomata is of poor quality. This is in agreement with the observation of Olive (2000) who stated that existing studies are generally small and of poor quality. There is a strong need for appropriately designed and analyzed randomized clinical trials, and surgical trials should preferably be multi-center/multi-surgeon.

Studies by Tempany et al (2003) as well as Stewart et al (2003) suggested that MRI-guided focused ultrasound surgery appeared to be safe and effective for the treatment of uterine leiomyomas. However, both studies were authored by the same group of investigators and addressed only the safety and feasibility of this approach in treating uterine fibroids. These studies had small number of patients -- 9 in the study by Tempany et al (2003), and 55 in the study by Stewart et al
They only demonstrated the safety and feasibility of MRI-guided focused ultrasound ablation for the treatment of uterine fibroids; however, its clinical value has not been established.

The first FDA-approved MRI-guided focused ultrasound system for the treatment of women with symptomatic uterine fibroids is the ExAblate 2000 System (InSightec, Ltd.). The U.S. pivotal trial included 192 women who had symptomatic uterine fibroids and were randomized to a hysterectomy \( n = 83 \) or the ExAblate procedure \( n = 109 \). At 6 months, 70.6\% of the ExAblate patients experienced a greater than 10-point reduction in the Uterine Fibroid Symptoms and Quality of Life Questionnaire score. The mean reduction in fibroid volume at 6 months was 13.5\%, but non-enhancing volume remained within the treated fibroid at 6 months. The hysterectomy patients performed better at 6 months than the ExAblate patients on several quality-of-life measurements, including role physical, body pain, general health, vitality, and mental health. The hysterectomy patients had a much higher rate of having at least 1 significant complication than the ExAblate patients (46% versus 12%). The ExAblate patients missed less work than the hysterectomy patients (1.2 versus 19.2 working days) during the first 30 days post-surgery (FDA Summary of Safety and Effectiveness Results).

The FDA required InSightec to conduct a 3-year post-market study to better assess the long-term safety and effectiveness of the ExAblate 2000 System. The study includes additional numbers of African-American women, because, as a group, these women have a greater incidence of uterine fibroids but were under-represented in the original study.

Further studies are needed to elucidate the exact role of MRI-guided focused ultrasound ablation in the management of uterine fibroids, especially studies that examine the correlation of treatment effect with changes in symptoms as well as comparisons of this new technology with other treatment methods such as UAE.

An assessment by the Canadian Coordinating Office of Health Technology Assessment on MRI-guided focused ultrasound for the treatment of uterine fibroids (Chen, 2005) concluded that "[l]ong-term studies of larger patient groups are needed to provide further reliable evidence on the safety of this procedure, as well as its clinical and cost-effectiveness".
An assessment by the BlueCross BlueShield Association Technology Evaluation Center (BCBSA, 2005) concluded that MRI-guided focused ultrasound for uterine fibroids did not meet the TEC criteria: "The evidence is insufficient to determine whether the use of MR-guided, focused ultrasound improves net health outcome or whether it is as beneficial as any established alternatives." The TEC assessment stated that limitations in quality of the existing evidence include significant loss to follow-up at longer follow-up intervals, lack of adequate well-controlled comparison studies, and lack of comparability between treatment groups in the available nonrandomized comparisons. The TEC assessment considered both published evidence on MRI-guided focused ultrasound and unpublished evidence from the InSightec study that was submitted to the FDA to support a PMA. The TEC assessment noted that the few available comparisons suggest that MRI-guided focused ultrasound may not be as effective as available alternatives. The TEC assessment reported that patient satisfaction from the procedure is higher with hysterectomy, as is the degree of symptom relief. The TEC assessment found no direct comparisons of MRI-guided ultrasound to either UAE or myomectomy available in the literature, but that this did not preclude TEC to reach some general and preliminary comparisons. The TEC assessment noted that durability of MRI-guided ultrasound is a major concern; a substantially greater proportion of women undergo other (or repeat) procedures after MRI-guided ultrasound compared to either UAE or myomectomy. The TEC assessment also found that available data suggest that fibroid volume reduction with MRI-guided ultrasound is much lower than with comparison procedures. Uterine artery embolization appears to produce a more profound improvement in symptom severity scores than MRI-guided ultrasound. For fertility preservation, myomectomy is the treatment of choice (TEC, 2005). The TEC assessment stated that neither UAE nor MRI-guided ultrasound is recommended if the woman desires to preserve fertility. The TEC assessment concluded that further study of the procedure and its durability, especially in light of other available treatments, is needed.

The National Institute for Health and Clinical Excellence (NICE, 2007) released interventional procedures guidance that concluded that "[c]urrent evidence on the safety and efficacy of magnetic resonance image (MRI)-guided focused ultrasound for uterine fibroids does not appear adequate" and that "further research on the procedure and publication of long-term outcomes would be useful." NICE reviewed the evidence on the safety and efficacy of the procedure, which comes from three uncontrolled case series. Most of the papers excluded from the analysis were earlier reports on some of the same women. The NICE assessment noted that a majority of published data have been reported
by one study group. The NICE advisors observed that the primary endpoint in these case series was change in symptom severity rather than fibroid shrinkage, and that there is limited reduction in fibroid volume following the procedure (NICE, 2007). The assessment stated that there is no evidence on the effects of this procedure on fertility.

A related NICE interventional procedure consultation document (NICE, 2006) stated that the maximum follow-up reported across all the studies was 19.5 months, and that most of the studies report on outcomes at 6 months. A significant proportion of women included in these studies were lost to follow-up. In addition, a significant proportion of women sought alternative treatments following the procedure, such as hysterectomy. The NICE assessment listed skin burns as a potential complication from the procedure, occurring in 5% of subjects in 1 case series (NICE, 2007). Another potential complication was reversible neural damage; 2 studies reported on cases of pain in the distribution of the sciatic nerve which resolved in both cases within 1 year of the procedure. The NICE advisors also commented that thermal damage to adjoining structures was a theoretical concern.

The Agency for Healthcare Research and Quality's report on management of uterine fibroids (Viswanathan et al, 2007) concluded that research is lacking for the long-term symptom relief of MRI-guided-ultrasound ablation.

An assessment of the evidence on treatment of uterine fibroids by BMJ Clinical Evidence concluded that the effectiveness of MRI-guided focused ultrasound is unknown (Lethaby and Vollenhoven, 2006).

The American College of Radiology's clinical guideline on “Radiologic management of uterine leiomyomas” (Burke et al, 2012) rendered MRI-guided high-frequency focused ultrasound ablation a “2” rating for a woman with multiple uterine fibroids resulting in a 20-week-sized uterus on physical examination and menorrhagia; a “3” rating for a woman with multiple submucosal and intramural fibroids presenting with menorrhagia and pelvic pain; a “4” rating for a woman with menometrorrhagia who presents with 3 dominant leiomyomas, ranging in size from 6 to 8 cm and intramural in location; a “3” rating for a woman with menorrhagia with a single 3 cm intramural fibroid and diffuse adenomyosis; a “3” rating for a woman with pelvic discomfort and 8 cm pedunculated subserosal fibroid; and a “3” rating for a woman with constipation and a 12 cm subserosal leiomyoma compressing the rectum (Rating scale: 1, 2, 3 denotes usually
not appropriate; 4,5,6 denotes may be appropriate). Furthermore, the guideline stated that “To date, there is little long-term information on the efficacy of this technology”.

An UpToDate review on “Overview of treatment of uterine leiomyomas (fibroids)” (Stewart, 2013) states that “Magnetic resonance guided focused ultrasound surgery (MRgFUS) (e.g., ExAblate 2000) is a more recent option for the treatment of uterine leiomyomas in premenopausal women who have completed childbearing. This noninvasive thermoablative technique converges multiple waves of ultrasound energy on a small volume of tissue, which leads to its thermal destruction, and can be performed as an outpatient procedure. The maximum size of a leiomyoma for this procedure is uncertain. It is not typically size alone that limits treatment, but size, vascularity, access and other factors. This system is not indicated for leiomyomas which are resectable with a hysteroscope, heavily calcified, or when intervening bowel of bladder could be damaged by treatment. While desire for future pregnancy was originally a contraindication for this therapy, labeling for the device now allows treatment in women considering future pregnancy following counseling …. Studies are needed to determine long-term outcome and optimal candidates for this procedure; comparative studies are also needed”.

The Australasian CREI Consensus Expert Panel on Trial evidence (ACCEPT) group’s consensus statement on “Fibroids in infertility” (Kroon et al, 2011) stated that “Newer treatments such as uterine artery embolisation, radiofrequency ablation, bilateral uterine artery ligation, magnetic resonance-guided focussed ultrasound surgery and fibroid myolysis require further investigation prior to their establishment in the routine management of fibroid-associated infertility”. Furthermore, the updated French College of Gynecology and Obstetrics' guideline on “Therapeutic management of uterine fibroid tumors” (Marret et al, 2012) stated that “Myolysis is under assessment, and research on its use is recommended”.

In a multi-center, clinical study, Stewart et al (2006) evaluated outcomes at 6 and 12 months after magnetic resonance-guided focused ultrasound surgery (MRgFUS) for symptomatic uterine leiomyomas. Premenopausal women with symptomatic uterine leiomyomas and no plans for future pregnancy (n = 109 at 6 months and n = 82 at 12 months) received a single treatment session of MRgFUS for uterine fibroids. Main outcome measures were reduction in fibroid symptoms as measured by the symptom severity score (SSS) of the Uterine Fibroid Quality-of-Life Instrument (UFS-QOL), the only validated measure of
leiomyoma symptomatology. A 10-point reduction in the SSS was selected as the targeted improvement. A total of 71% of women undergoing MRgFUS reached the targeted symptom reduction at 6 months, and 51% reached this at 12 months. The magnitude of improvement in SSS was greater than predicted, with subjects having a mean decrease of 39% and 36% at 6 and 12 months, respectively. This paralleled the improvement seen using the short form-36 instrument. A modest volume reduction similar in magnitude to the treated volume was seen. The incidence of adverse events was low. These researchers concluded that MRgFUS treatment results in short-term symptom reduction for women with symptomatic uterine leiomyomas with an excellent safety profile.

Sharp (2006) stated that new technologies for the treatment of uterine leiomyomata include UAE, MRI-guided focused ultrasonography, laparoscopic uterine artery occlusion, and cryomyolysis. There is sound evidence for shorter hospital stay, quicker return to work, and a similar major complication rate compared with hysterectomy. Uterine artery embolization appears to be effective for up to 5 years in reducing bulk symptoms and menorrhagia associated with leiomyomata. The chance of re-operation for leiomyoma-related symptoms within 5 years is 20 to 29%. Women who wish to become pregnant should be cautioned about potential complications during pregnancy. There is insufficient evidence to recommend UAE in post-menopausal women. With regard to MRI-guided focused ultrasonography, fibroid cryomyolysis (freezing), and laparoscopic uterine artery occlusion, Sharp (2006) commented that although the initial symptom reduction outcomes have been reported as favorable, more data are needed to better understand the durability of these results.

In a review of treatment of uterine fibroids, Van Voorhis (2009) stated that although early outcomes of up to 1 year are encouraging, long-term effectiveness and comparative studies are needed before focused ultrasound can be recommended for the treatment of uterine fibroids.

Mindjuk et al (2015) reported on the 12-month technical and clinical results of MRgFUS treatment and factors affecting clinical treatment success. A total of 252 women (mean age, 42.1 ± 6.9 years) with uterine fibroids underwent MRgFUS. All patients underwent MRI before treatment. Results were evaluated with respect to post-treatment nonperfused volume (NPV), symptom severity score (SSS), reintervention rate, pregnancy and safety data. NPV ratio was significantly higher in fibroids characterized by low signal intensity in contrast-enhanced T1-weighted fat saturated MR images and in fibroids
distant from the spine (>3 cm). NPV ratio was lower in fibroids with septations, with subserosal component and in skin-distant fibroids (p < 0.001). NPV ratio was highly correlated with clinical success: NPV of more than 80% resulted in clinical success in more than 80% of patients. Reintervention rate was 12.7% (mean follow-up time, 19.4 ± 8 months; range, 3-38). Expulsion of fibroids (21%) was significantly correlated with a high clinical success rate. No severe adverse events were reported.

Gorny et al (2014) assessed the mid-term outcomes of magnetic resonance (MR)-guided focused ultrasound (US) treatments of uterine fibroids. Investigators conducted a retrospective follow-up of 138 patients treated at a single institution between March 2005 and November 2011. The patients were not part of a clinical study and were followed through retrospective review of their medical records and telephone interviews to assess additional treatments for fibroid-related symptoms. Survival methods, including Cox proportional hazards models, were used to assess the association between incidence of additional treatments and patient data obtained during screening before treatment. The average length of follow-up was 2.8 years (range, 1-7.2 y). The cumulative incidence of additional treatments at 36 months and 48 months after MR-guided focused US was 19% and 23%, respectively. Women who did not need additional treatment were older than women who did (46.3 y ± 5.6 vs 43.0 y ± 5.8; P = .006; hazard ratio, 0.855; 95% confidence interval, 0.789-0.925). Additionally, women with heterogeneous or bright fibroids on T2-weighted MR imaging were more likely to require additional treatment compared with women with homogeneous dark fibroids (hazard ratio, 5.185 or 5.937, respectively; 95% confidence interval, 1.845-14.569 or 1.401-25.166, respectively). Physician predictions of treatment success, recorded during the screening process, had significant predictive value (P = .018). An accompanying editorial (Matsumoto, 2014) noted that this study was limited by lack of symptom and quality-of-life assessments, a skewed patient population (90% white), absence of imaging follow-up, and the need to treat approximately 48% of patients (66 of 138) twice with MR-guided focused US. The mean non-perfused volume (NPV) of fibroids reported by Gorny, et al. was only 45.5%. After uterine artery embolization (UAE) for fibroids, the NPV is typically 490% and often 100%, with a positive correlation noted between the percent of fibroid infarction and long-term clinical outcomes. The editorialist noted that, given the limitations of the technology, only 20% of patients who present with symptoms related to fibroids are likely to be good candidates for MR-guided focused US therapy. In the German experience, only 16% of the patients screened were candidates (citing Mindjik, et al.). The editorialist stated that the
hope is that the FIRSTT (Fibroid Interventions: Reducing Symptoms Today and Tomorrow) trial, which will compare focused US versus UAE therapy for uterine fibroids, will demonstrate that outcomes with MR-guided focused US are at least equivalent to UAE so that we can incorporate “Sound” technology into reimbursable therapies for women in the United States with uterine fibroids.

Dobotwir et al (2012) described and evaluated treatment of uterine fibroids using MRgFUS during its first 24 months of use at The Royal Women's Hospital Melbourne. The investigators reported that 100 Victorian women were treated with MRgFUS using the ExAblate 2000 system. Treatment outcomes based on fibroid volume shrinkage measured at 4 and 12 months post-treatment and symptom severity score assessment (Symptom Severity Score Quality of Life - SSS-QOL) pre- and post- (4-6 weeks, 4, 6 and 12 months) treatment. Mean non-perfused volume of the treated fibroids were 67% ± 25% (n =100) immediately post-treatment. At 4 months post-treatment, the treated fibroids demonstrated an average volume reduction of 29% ± 32% (n = 74) and at 12 months 38% ± 45% (n = 32). Mean symptom severity scores (SSS-QOL) improved by 51% from 59 ± 21 (n = 97) at baseline to 29 ± 17 (n = 36) by 12 months.

Desai et al (2012) reported on the results of MRgFUS treatment carried out on Indian patients in one hospital. The investigators treated 50 Indian women (mean age = 36.2 ± 8.3 years) for fibroids as outpatients using the ExAblate MRgFUS system (InSightec). Non-perfused volumes (NPVs) were measured immediately after treatment to calculate the treatment outcomes. A validated symptom-specific questionnaire to record their symptoms prior to treatment and six months following treatment was completed by patients. The size of the fibroids was measured on the day of the treatment and during the 6-month checkup to calculate shrinkage. Adverse events during and following treatment were recorded and monitored. The average NPV ratio measured after the treatment was 88% ± 6%, indicative of high ablated fibroid tissue. Prior to treatment, the mean Symptoms Severity Score was 56.9 ± 4.8 (n = 50), which is indicative of highly symptomatic patients. Six months following treatment, there was an average fibroid shrinkage of 30% ± 11%, and a significant decrease in the mean score to 28.6 ± 6.0 (n = 50) (P < 0.001). There were no reports of serious or unexpected adverse events at any point during treatment or during the follow-up period from any of the 50 women treated in the current study.
Himabidu et al (2014) reported on a prospective study of 32 consecutive Indian women with clinically symptomatic uterine fibroids who were treated with MRgFUS from February 2011 to October 2011. Pre and post treatment symptom severity scores (SSS) were assessed at the time of enrolment and at one, three and six months follow up using a validated uterine fibroid symptom - quality of life questionnaire (UFS-QOL). Pre and post treatment fibroid volumes were compared immediately after treatment and at six months follow up using contrast enhanced MRI scan. Non-perfused volume (NPV) ratios were calculated and correlated with fibroid volume reductions immediately after the treatment and at the end of six months follow up. The investigators reported that the procedure was well tolerated by the patients and procedure related adverse effects were non-significant. Significant reductions in SSS were seen at one, three and six month intervals after the treatment (P<0.01). Significant reductions were noticed in fibroid volumes at six months follow up compared to pretreatment fibroid volumes (P<0.01). Significant positive correlations were observed between NPV ratios and reduction in fibroid volumes at six months follow-up (r=0.659, P<0.01).

Clark et al (2014) stated that the role of MRgFUS in the treatment of fibroids has been evolving since its introduction in 2004. Several new devices and techniques including location-specific treatment, volumetric therapy, and vessel-targeted therapy have been introduced over the last few years. Several case series reported uncomplicated pregnancy following MRgFUS; however, results of the ongoing studies will further elucidate the utility of MRgFUS in patients planning future fertility. These investigators performed a systematic review of the literature and studies that reported quality of life at baseline and after 6 months were included in a meta-analysis. The authors concluded that MRgFUS represents a minimally invasive treatment for uterine fibroids that is able to improve the quality of life and fibroid size with durability. They stated that it is possible that MRgFUS could be the treatment of choice for patients desiring future fertility; however, further investigation is needed.

Pron (2015) evaluated patients' eligibility for magnetic resonance imaging-guided high-intensity focused ultrasound (MRgHIFU) treatment of symptomatic uterine fibroids and the technical success, safety, effectiveness, and durability of this treatment. This review also compared the safety and effectiveness of MRgHIFU with other minimally invasive uterine-preserving treatments and surgeries for uterine fibroids. A literature search was performed on March 27, 2014, using Ovid Medline, Ovid Medline In-Process and Other Non-Indexed Citations, Ovid Embase, Ebsco Cumulative Index to Nursing & Allied Health Literature (CINAHL), and EBM Reviews, for studies published from
January 1, 2000 to March 27, 2014. The evidence review identified 2 systematic reviews, 2 RCTs, 45 cohort study reports, and 19 case reports involving HIFU treatment of symptomatic uterine fibroids. Eligibility for MRgHIFU treatment was variable, ranging from 14% to 74%. In clinical cohort studies involving 1,594 patients, 26 major complications (1.6%) were reported. Magnetic resonance-guided HIFU resulted in statistically and clinically significant reductions in fibroid-related symptoms in studies conducted in 10 countries, although few involved follow-up longer than 1 year. Re-treatment rates following MRgHIFU were higher in early clinical studies involving regulated restrictions in the extent of fibroid ablation than in later reports involving near-complete ablation. Emergent interventions, however, were rare. Although a desire for fertility was an exclusion criterion for treatment, spontaneous term pregnancies did occur following HIFU. There were no randomized trials comparing MRgHIFU and other guidance methods, other minimally invasive treatments, or surgeries for symptomatic uterine fibroids. Limitations with MRgHIFU included restricted eligibility, requirement for a dedicated MR device to guide the treatment, lengthy procedure time, and loss of MR opportunity time. The authors concluded that for women failing medical therapy and seeking alternatives to hysterectomy for symptomatic uterine fibroids, MRgHIFU provided a safe and effective, non-invasive, uterine-preserving treatment from which they rapidly recover. The treatment advantages of MRgHIFU are potentially offset by restrictive eligibility, lengthy procedure time, and dependence on availability of an MR device. They stated that the lack of comparative evidence between MRgHIFU and other, more established uterine-preserving treatments limits informed decision-making among therapeutic options.

In a pilot, randomized, placebo-controlled trial, Jacoby et al (2016) evaluated the feasibility of a full-scale placebo-controlled trial of MRgFUS and obtained estimates of safety and effectiveness. Premenopausal women with symptomatic uterine fibroids were randomized in a 2:1 ratio to receive MRgFUS or placebo procedure. Primary outcome was change in fibroid symptoms from baseline to 4 and 12 weeks after treatment assessed by the Uterine Fibroid Symptom Quality of Life Questionnaire (UFS-QOL); secondary outcome was incidence of surgery or procedures for recurrent symptoms at 12 and 24 months. A total of 20 women with a mean age of 44 years (± standard deviation 5.4 years) were enrolled, and 13 were randomly assigned to MRgFUS and 7 to placebo. Four weeks after treatment, all participants reported improvement in the UFS-QOL: a mean of 10 points in the MRgFUS group and 9 points in the placebo group (for difference in change between groups). By 12 weeks, the MRgFUS group had improved more
than the placebo group (mean of 31 points and 13 points, respectively). The mean fibroid volume decreased 18% in the MRgFUS group with no decrease in the placebo group at 12 weeks. Two years after MRgFUS, 4 of 12 women who had a follow-up evaluation (30%) had undergone another fibroid surgery or procedure. The authors concluded that women with fibroids were willing to enroll in a randomized, placebo-controlled trial of MRgFUS; and a placebo effect may explain some of the improvement in fibroid-related symptoms observed in the first 12 weeks after MRgFUS.

An UpToDate review on “Overview of treatment of uterine leiomyomas (fibroids)” (Stewart, 2016) states that “Magnetic resonance guided focused ultrasound surgery (MRgFUS) (e.g., ExAblate 2000) is a more recent option for the treatment of uterine leiomyomas in premenopausal women who have completed childbearing …. Studies are needed to determine long-term outcome and optimal candidates for this procedure; comparative studies are also needed”.

In a multi-center prospective, single-arm pilot study, Parsons and colleagues (2017) evaluated the safety and acute tissue ablation efficacy of a trans-abdominal HIFU prototype device that uses ultrasound imaging guidance for rapid non-invasive ablation of uterine fibroids. The secondary objective was to assess preliminary fibroid-related symptom improvement and fibroid volume reduction at 3 to 6 months post-treatment in subsets of patients. Women with a diagnosis of symptomatic uterine fibroids planning to undergo hysterectomy were considered for this pilot study; 73 subjects underwent trans-abdominal ultrasound-guided HIFU treatment using a volumetric ablation technique referred to as “shell ablation”, in which the HIFU energy was deposited in patterns that partially encapsulate the peripheral region of the targeted fibroid(s). Patients were divided into 2 sequential cohorts: (i) the Development Cohort (the first 37 patients treated), and (ii) the Validation Cohort (the final 36 patients treated). Development Cohort treatments were performed for dose-ranging purposes to identify the optimum HIFU treatment parameters, while the Validation Cohort treatments were performed to validate these final settings; 65 patients (89.0%) received only prophylactic oral, sublingual, or intra-muscular (IM) analgesia before treatment, sometimes with oral anxiolytics. The remaining 8 patients (11.0%) were anesthetized prior to treatment; 67 patients (91.8%) then had scheduled hysterectomies between 0 to 179 days after treatment completion. Adverse events (AEs) were monitored until study exit, which ranged from 10 to 191 days post-treatment. The primary efficacy end-point measured in all 73 patients was the non-perfused volume (NPV) of tissue produced, which was assessed
between 0 to 7 days post-treatment either by tissue sectioning following hysterectomy or by gadolinium-enhanced MRI. The following secondary efficacy end-points were also measured in subsets of patients who were prospectively scheduled for delayed hysterectomies: changes in menstrual blood loss (MBL), symptom severity (SS), and quality of life (QOL) scores were assessed using validated techniques at 3 months post-treatment in 10 patients, and changes in treated fibroid volume were assessed using MRI at 3 to 6 months post-treatment in 14 patients. In all 73 patients, there were no reports of any serious adverse device effects, including no damage to any extra-uterine collateral tissues or the abdominal skin. In the Development Cohort, a mean NPV of 17.9 ± 24.9 cm³ (range of 0 to 123.0) was produced in a mean total treatment time of 4.9 ± 2.4 minutes (range of 1.1 to 11.3 minutes). These metrics improved in the Validation Cohort, where a mean NPV of 44.9 ± 58.5 cm³ (range of 0 to 284.7) was produced in a mean total treatment time of 3.6 ± 2.1 minutes (range of 1.5 to 9.5). In the subsets of patients with data available, there was a significant improvement in QOL score (median of 16.5 point increase, p = 0.011), an improving trend in SS score (median of 13.5 point decrease, p = 0.254), and a significant improvement in treated fibroid volume (mean of 24.0 % decrease, p = 0.013). In 8 patients who had above-average MBL scores at baseline and regular menstrual cycle lengths during follow-up, there was also a significant improvement in MBL score (median of 40.8 % decrease, p = 0.035). The authors concluded that ultrasound-guided HIFU ablation with the prototype device demonstrated an excellent safety profile and produced clinically relevant NPVs in a mean total treatment time of under 4 minutes using the final validated treatment settings. They stated that short-term clinical efficacy metrics assessed in subsets of patients were encouraging, and larger studies should be conducted to confirm these results.

Laparoscopic Uterine Artery Occlusion

Hald et al (2007) compared clinical outcome 6 months after treatment with bilateral laparoscopic occlusion of the uterine artery versus uterine leiomyoma embolization. A total of 66 pre-menopausal women with symptomatic uterine leiomyomata were randomized to treatment with either laparoscopic occlusion of uterine arteries or uterine leiomyoma embolization. The primary outcome was reduction of blood loss from pre-treatment to 6 months post-operatively, measured by a Pictorial Bleeding Assessment Chart. Secondary outcomes included patients’ own assessment of symptom reduction, post-operative pain assessed using visual analog scales, ketobemidone used post-operatively, complications, secondary interventions, and failures. Fifty-eight women were included; 6-month follow-up data were available for 28 participants.
in each group. The percentage reduction in Pictorial Bleeding Assessment Chart scores did not differ between the treatment groups (52 % after uterine leiomyoma embolization and 53 % after laparoscopy, \( p = 0.96 \)). The study had 52 % power to detect a 20 % difference on the Pictorial Bleeding Assessment Chart. Fewer participants in the group treated with uterine leiomyoma embolization complained of heavy bleeding after 6 months (4 % compared with 21 %, \( p = 0.044 \)). The post-operative use of ketobemidone was higher after uterine leiomyoma embolization (46 mg compared with 12 mg, \( p < 0.001 \)). The authors concluded that both laparoscopic occlusion of uterine vessels and embolization of uterine leiomyoma improved clinical symptoms in the majority of patients. Participants with the laparoscopic procedure had less post-operative pain but heavier menstrual bleeding 6 months after treatment. They noted that a larger study and longer follow-up is necessary before a definite conclusion can be made regarding the most effective treatment.

In a pilot randomized clinical trial, Cunningham and colleagues (2008) compared peri-operative pain and institutional use for women undergoing transcatheter UAE and transcatheter uterine artery occlusion (UAO) for the treatment of heavy uterine bleeding associated with uterine leiomyomas. Pre-menopausal women with heavy uterine bleeding related to uterine leiomyomas were enrolled. Either a standard UAE with microspheres or UAO using vascular coils was used. The main outcome measures were analgesic use, institutional stay, and post-procedural numeric pain scales. A total of 16 women were enrolled and 14 underwent study procedures (UAE \( n = 8 \), UAO \( n = 6 \)). Baseline Aberdeen Menorrhagia Severity Scale scores, also known as the Ruta scores, were similar in each group (UAE = 54, UAO = 53). Median pre-procedural uterine volume was similar for each group (UAE = 557 ml, UAO = 612 ml). The median post-procedural pain scale was less for UAO than UAE (UAO 1, UAE 5; \( p < 0.05 \)). Six patients with UAE and no patients with UAO required parenteral narcotic analgesia in the recovery room (\( p < 0.05 \)). Patients with UAE used 6 hospital nights and patients with UAO used 1 hospital night (\( p = 0.09 \)). Three-month Aberdeen Menorrhagia Severity Scale scores were reduced to a similar degree in each group (UAE = 58 %, UAO = 63 %). The authors concluded that transcatheter UAO is a promising alternative transcatheter technique for the treatment of symptoms related to uterine leiomyomas, with less post-procedural pain, reduced requirements for analgesics, and shorter hospital stays than transcatheter UAE. They stated that although the results of the study are promising, larger-scale trials with longer follow-up are needed to both confirm these results and evaluate the long-term efficacy of transcatheter UAO.
In a review of treatment of fibroids by means of UAO, Brill (2009) discussed the putative mechanism of action and clinical application of Doppler-guided UAO; and noted that this approach is a new investigational treatment modality for uterine fibroids.

Panagiotopoulou et al (2014) evaluated the effectiveness of uterine-sparing interventions for women with symptomatic uterine fibroids who wish to preserve their uterus. MEDLINE, EMBASE, CENTRAL, conference proceedings, trial registers and reference lists were searched up to October 2013 for RCTs. Outcome measures were patient satisfaction, re-intervention and complications rates, reproductive outcomes, and hospitalization and recovery times. A total of 5 trials, involving 436 women were included; 2 compared UAE with myomectomy and 3 compared UAE with laparoscopic UAO. Indirect treatment comparison showed that myomectomy and UAE resulted in higher rates of patient satisfaction (odds ratio [OR] 2.56, 95 % CI: 0.56 to 11.75 and 2.7, 95 % CI: 1.1 to 7.14, respectively) and lower rates of clinical failure (OR 0.29, 95 % CI: 0.06 to 1.46 and 0.37, 95 % CI: 0.13 to 0.93, respectively) than laparoscopic UAO. Myomectomy resulted in lower re-intervention rate than UAE (OR 0.08, 95 % CI: 0.02 to 0.27) and laparoscopic UAO (OR 0.08, 95 % CI: 0.01 to 0.37) even though the latter techniques had an advantage over myomectomy because of shorter hospitalization and quicker recovery. There was no evidence of difference between the three techniques in ovarian failure and complications rates. The evidence for reproductive outcomes is poor. The authors concluded that these findings suggested that laparoscopic UAO is less effective than UAE and myomectomy in treatment of symptomatic fibroids. The choice between UAE and myomectomy should be based on individuals' expectations and fully informed discussion.

Herbal Therapies:

In a Cochrane review, Liu and colleagues (2009) evaluated the risks and benefits of herbal preparations for uterine fibroids. These investigators searched following electronic databases: the Trials Registers of the Cochrane Menstrual Disorders and Subfertility Group and the Cochrane Complementary Medicine Field, the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2008, Issue 3), MEDLINE, EMBASE, the Chinese Biomedical Database, the Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS), AMED, and LILACS. The searches ended on 31st December 2008. Randomized controlled trials comparing herbal preparations with no intervention, placebo, medical treatment or surgical procedures in
women with uterine fibroids were selected. Trials of herbal preparations with or without conventional therapy were also included. Two review authors collected data independently. They assessed trial risk of bias according to their methodological criteria; and presented dichotomous data as risk ratios (RR) and continuous outcomes as mean difference (MD), both with 95% confidence intervals (CI). These investigators included 2 randomized trials (n = 150) with clear description of randomization methods. The methodological risk of bias of the trials varied. There were variations in the tested herbal preparations, and the treatment duration was 6 months. The outcomes available were not the primary outcomes selected for this review, such as symptom relief or the need for surgical treatment; trials mainly reported outcomes in terms of shrinkage of the fibroids. Compared with mifepristone, Huoxue Sanjie decoction showed no significant difference in the disappearance of uterine fibroids, number of patients with shrinking of uterine fibroids or average volume of uterine fibroids, but less effective than mifepristone on reducing average size of uterus (MD 23.23 cm³, 95% CI: 17.85 to 28.61). There was no significant difference between Nona Roguy herbal product and gonadotropin-releasing hormone agonist in average volume of uterine fibroids or size of uterus. No serious adverse effects from herbal preparations was reported. The authors concluded that current evidence does not support or refute the use of herbal preparations for treatment of uterine fibroids due to insufficient studies of large sample and high quality. They stated that further high quality trials evaluating clinically relevant outcomes are needed.

Acupuncture:

In a Cochrane review, Zhang and associates (2010) evaluated the benefits and harms of acupuncture in women with uterine fibroids. The following electronic databases were searched May 21, 2009: the Cochrane Central Register of Controlled Trials (CENTRAL); MEDLINE; EMBASE; AMED; the Menstrual Disorders and Subfertility Group's Specialised Register of Trials; Chinese Biomedical Literature Database (CBM); Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS); Chinese Medical Current Contents (CMCC) and China National Knowledge Infrastructure(CNKI). Citation lists, experts in the field and grey literature were also referred to. No restrictions such as language were applied. All randomized controlled trials (RCTs) comparing acupuncture management with placebo acupuncture, no management, Chinese medication, Western medication or other managements of uterine fibroids were considered for inclusion. Acupuncture management included either traditional acupuncture or contemporary acupuncture, regardless of the source of stimulation (e.g.,
body, electro, scalp, elongated, fire, hand, fine needle, moxibustion). Acupuncture management without needling was excluded. Two review authors assessed trial risk of bias according to our a priori criteria. No trials were included in this version of the review, therefore no data were collected. No randomized double-blind controlled trials met the inclusion criteria. The authors concluded that the effectiveness of acupuncture for the management of uterine fibroids remains uncertain. They stated that more evidence is needed to establish the safety and effectiveness of acupuncture for uterine fibroids. There is a continued need for well-designed RCTs with long-term follow-up.

Transversus Abdominis Plane (TAP) Block:

Young et al (2012) stated that the transversus abdominis plane (TAP) block is a relatively new regional anesthesia technique that provides analgesia to the parietal peritoneum as well as the skin and muscles of the anterior abdominal wall. It has a high margin of safety and is technically simple to perform, especially under ultrasound guidance. A growing body of evidence supports the use of TAP blocks for a variety of abdominal procedures, yet, widespread adoption of this therapeutic adjunct has been slow. In part, this may be related to the limited sources for anesthesiologists to develop an appreciation for its sound anatomical basis and the versatility of its clinical application.

Abdallah et al (2012) noted that ultrasound guidance has led a surge of interest in TAP block for post-operative analgesia following abdominal surgery. Despite or because of the numerous descriptive applications and techniques that have recently populated the literature, results of comparative studies for TAP block have been inconsistent. This systematic review pragmatically addressed many unanswered questions, specifically the following: what are the effects of surgical procedure, block dose, block technique, and block timing on TAP block analgesia? A total of 18 intermediate- to good-quality randomized trials that included diverse surgical procedures were identified. Improved analgesia was noted in patients undergoing laparotomy for colorectal surgery, laparoscopic cholecystectomy, and open and laparoscopic appendectomy. There was a trend toward superior analgesic outcomes when 15 ml of local anesthetic or more was used per side compared with lesser volumes. All 5 trials investigating TAP block performed in the triangle of Petit and 7 of 12 trials performed along the mid-axillary line demonstrated some analgesic advantages. Eight of 9 trials using pre-incisional TAP block and 4 of 9 with post-incisional block revealed better analgesic outcomes. Although the majority of trials reviewed suggested superior early pain control, these researchers were unable to definitively
identify the surgical procedures, dosing, techniques, and timing that provide optimal analgesia following TAP block. This review suggested that the understanding of the TAP block and its role in contemporary practice remains limited.

McDermott et al (2012) stated that any landmark-based regional anesthetic technique raises 2 important issues: (i) the accuracy of placement of the needle and thus the local anesthetic in a 'blind' technique, and (ii) the potential for damage to adjacent structures. These investigators designed a prospective, blinded study in an adult general surgical population to evaluate with ultrasound the placement of the needle tip and local anesthetic during TAP blocks using the landmark-based "double-pop" technique. After induction of general anesthesia, 36 adult patients had a TAP block performed bilaterally using the standard landmark-based technique. Ultrasonography was then used to record the actual needle position and local anesthetic spread. The anesthetist performing the block was blinded to the ultrasound images. A total of 36 adult patients were included in the study, which was terminated early due to what was considered an unacceptably high-level of peritoneal needle placements. The needle tip and local anesthetic spread were in the correct plane in only 17 (23.6 %) of the injections. In the remaining 55 (76.4 %), the needle was in the subcutaneous tissue 1 (1.38 %), external oblique muscle 1 (1.38 %), plane between the external and internal oblique muscles 5 (6.94 %), internal oblique muscle 26 (36.1 %), transversus abdominis muscle 9 (12.5 %), and peritoneum 13 (18 %). The authors concluded that the needle and local anesthetic placement using the standard landmark-based approach to the TAP block is inaccurate, and the incidence of peritoneal placement is unacceptably high. Furthermore, there is a lack of evidence regarding the safety and effectiveness of the TAP block in the management of patients with uterine fibroids.

**Laser Ablation:**

Law and associates (2000) reported that laser ablation of uterine fibroids using a percutaneous approach under local anesthetic in an open magnetic resonance scanner was performed in 12 symptomatic women awaiting hysterectomy. Accurate laser fiber placement was assisted by the use of a magnetic resonance needle tracking system, as well as laser heat dissipation monitored during treatment by a real-time imaging processor. This day case procedure was well-tolerated by all women, with 8 women subsequently declining their planned surgery. Follow-up measurements of treated fibroid volume by MRI demonstrated a mean
decrease of 37.5 % at 3 months. The authors concluded that this novel minimally invasive approach offers an alternative to surgery for women with fibroids, but longer follow-up is needed to ascertain maximal fibroid shrinkage and to compare outcome with traditional surgery.

Cryoablation:

Cowan et al (2002) developed a trans-abdominal interventional MRI-guided cryoablation procedure for the treatment of uterine fibroid tumors and reported this novel approach. This study represented the preliminary and first report of a prospective Institutional Review Board-approved protocol to study interventional MRI-guided cryoablation of uterine fibroid tumors. Women were selected on the basis of symptoms that were related to uterine fibroid tumors (bleeding, uterine pain, pelvic congestion, compression symptoms) and the absence of any desire for child bearing. A physical examination confirmed the presence of fibroid tumors, and MRI was performed before the procedure to measure the size and number of fibroid tumors. Patients returned to the interventional MRI and underwent placement of 3 to 5 probes (2 to 3 mm) under MRI-directed guidance. Follow-up MRI determined the size reduction of the lesion, and a clinical evaluation determined the change in symptoms. A total of 9 patients were treated and had substantial reduction in the uterine size (average, 66 % volume reduction), and their primary symptoms have either improved or resolved. The authors concluded that this was the first reported review of interventional MRI-directed cryotherapy of uterine fibroid tumors. These preliminary findings need to be confirmed by well-designed studies.

Sakuhara et al (2006) evaluated the feasibility and effectiveness of MRI-guided percutaneous cryoablation for uterine fibroids as a minimally invasive treatment alternative. From August 2001 to June 2002, MRI-guided percutaneous cryoablation was performed on 7 uterine fibroids in 6 patients who displayed clinical symptoms related to tumors. Using a horizontal-type open MR system, cryoablation probes were percutaneously placed in fibroids. Fibroids were ablated, and the site and size of ice balls were monitored on MR I. Post-operatively, patients completed a questionnaire to assess changes in presenting clinical symptoms, and MR images were obtained for all patients at follow-up. Changes in clinical symptoms and tumor volume were evaluated in each patient. All treated patients showed reductions in tumor size. Mean volume reduction rate was 40.3 % at 6 weeks post-operatively, and 79.4 % at 9 to 12 months. All patients reported fever after treatment. Surgical drainage was required for abscess in the probe channel in 1 patient, and transient liver damage occurred in another. Subjective symptoms
improved in all patients except 1 who had multiple tumors, and no patient complained of new symptoms after cryoablation during follow-up. The authors concluded that MRI-guided percutaneous cryoablation represents a feasible and effective treatment for uterine fibroids. These findings need to be confirmed by well-designed studies with more patients and longer-term follow-up.

In a multi-center, pilot case-series study, Pansky and colleagues (2009) evaluated cryoablation of uterine fibroids using laparoscopically assisted placement of 17-gauge cryoablation needles. Patient satisfaction was documented with a validated Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire. Procedural efficacy was evaluated by assessing fibroid shrinkage. Treatment was followed by assessments at 3, 6, and 12 months. Median fibroid volume reduction was 43.3 % (19 patients) and 66.4 % (15 patients) at 6 and 12 months, respectively. Median UFS-QOL score improvement was 61.9 % and 66.7 % at 6 and 12 months, respectively. Additionally, patients experienced marked improvement of bleeding and fibroid bulk symptoms. The median Symptom Severity Score at baseline was 50, 25.0 (-59 %) at 6 months, and 12.5 (-66.7 %) at 12 months. The authors concluded that these pilot data indicated that uterine fibroid cryoablation is a safe and effective minimally invasive alternative to treat symptomatic uterine fibroids. These preliminary findings need to be validated by well-designed studies.

Radiofrequency Ablation:

Bergamin et al (2005) evaluated the feasibility and effectiveness of laparoscopic radiofrequency ablation (RFA) of uterine fibroids. A total of 18 women with symptomatic intramural uterine myomas underwent RFA under laparoscopic guidance. Post-operative sonographic evaluations of the fibroids size were scheduled at 1, 3, 6, 9, and 12 months. The impact of myoma-related symptoms on quality of life (QOL) was assessed using a validated questionnaire. The median number of myomas treated per patient was 1 (1 to 3). The median baseline volume of the dominant myoma was 67.2 cm³ (14.8 to 332.8). No intra-operative or post-operative complications occurred. The median reductions in myomas volume were 41.5 %, 59 %, and 77 % at 1, 3, and 6-months, follow-up evaluation, respectively. No further change in fibroid size was observed at 9 months and 1 year. A significant improvement in the symptoms score and QOL score was observed at 3 and 6 months, follow-up. The authors concluded that in this pilot study, laparoscopic RFA successfully reduced fibroid symptoms and fibroid volume in short-term follow-up. Moreover, they stated that additional studies are needed before its safety and effectiveness can be confirmed.
Milic et al (2006) reported the findings of 4 patients (with symptomatic uterine fibroids measuring less than 6 cm) who underwent laparoscopic ultrasound-guided RFA using multi-probe array electrodes. Follow-up of the treated fibroids was performed with gadolinium-enhanced MRI and patients’ symptoms were assessed by telephone interviews. The procedure was initially technically successful in 3 of the 4 patients and MRI studies at 1 month demonstrated complete fibroid ablation.

Symptom improvement, including a decrease in menstrual bleeding and pain, was achieved in 2 patients at 3 months. At 7 months, 1 of these 2 patients experienced symptom worsening that correlated with recurrent fibroid on MRI. The third, initially technically successfully treated patient did not experience any symptom relief after the procedure and was ultimately diagnosed with adenomyosis. The authors concluded that these preliminary findings suggested that RFA is a technically feasible treatment for symptomatic uterine fibroids in appropriately selected patients.

Guido et al (2013) stated that although most myomas are asymptomatic, quality of life is compromised for many women with uterine fibroid disease. Twelve-month outcomes from the Halt Trial have been reported in the literature. These researchers analyzed the clinical success of radiofrequency volumetric thermal ablation (RFVTA) of symptomatic uterine fibroids at 2 years of follow-up. A prospective, multi-center, outpatient interventional clinical trial of fibroid treatment by RFVTA in 124 premenopausal women (mean age of 42.4 ± 4.4 years) with symptomatic uterine fibroids and objectively confirmed heavy menstrual bleeding (greater than or equal to 160 to less than or equal to 500 ml). Outcome measures included: subject responses to validated questionnaires, treatment-emergent adverse events, and surgical re-intervention for fibroids at 24 months post-procedure. Continuous and categorical variables were summarized using descriptive statistics and means and percentages. Comparisons between visits were based on t-tests using repeated measures models. P-values < 0.05, adjusted for multiplicity, were statistically significant. A total of 112 subjects were followed through 24 months. Change in symptom severity from baseline was -35.7 (95% confidence interval [CI]: -40.1 to -31.4; p < 0.001). Change in health-related quality of life (HRQL) was 40.9 (95% CI: 36.2 to 45.6; p < 0.001). HRQL sub-scores also improved significantly from baseline to 24 months in all categories (concern, activities, energy/mood, control, self-consciousness, and sexual function) [p < 0.001]. Six patients underwent surgical re-intervention for fibroid-related bleeding between 12 and 24 months providing a re-intervention rate of 4.8 % (6/124). The
authors concluded that radiofrequency volumetric thermal ablation of myomas significantly reduces symptom severity and improves quality of life with low surgical re-intervention through 24 months of follow-up.

Robles et al (2013) confirmed the results of an earlier study assessing the safety and effectiveness of a laparoscopic RFVTA system among women with symptomatic myomas. In a prospective study at the Hospital of Francisco Marroquin University, Guatemala City, consecutive pre-menopausal women with symptomatic myomas seeking uterine-sparing treatment were enrolled between August 2008 and July 2011. The women were treated by RFVTA. Uterine fibroid symptom and health-related quality-of-life (UFS-QOL) questionnaires were completed at 0, 3, 6, and 12 months. Among 114 women screened, 36 were enrolled (ages 33 to 51 years), and 35 were followed for 12 months. Symptom severity scores reduced significantly (p < 0.05): baseline (63.3), 3 months (23.1), 6 months (15.4), 12 months (9.6). Health-related quality-of-life scores improved significantly (p < 0.05): baseline (37.3), 3 months (79.9), 6 months (85.1), and 12 months (87.7). The mean ± SD difference in uterine volume from baseline (215.2 ± 117.9 cm3) to 12 months (167.0 ± 120.8 cm3) was 48.2 cm3 (95 % CI: -22.8 to 119.2; p = 0.192). Nine adverse events among 8 individuals were minor and unrelated to the procedure. The authors concluded that RFVTA of fibroids resulted in significantly improved symptom severity and quality-of-life scores and provides an outpatient uterine-sparing option for treatment of myomas.

Chudnoff et al (2013) examined the safety and effectiveness of laparoscopic ultrasound-guided RFVTA of uterine myomas in symptomatic women. A cohort of 135 pre-menopausal symptomatic women with uterine myomas, uteri 14 weeks of gestation-sized or less with no single myoma exceeding 7 cm, and objectively confirmed heavy menstrual bleeding participated in this prospective, international trial of outpatient laparoscopic ultrasound-guided RFVTA. Bleeding outcomes were measured by alkaline hematin analysis at baseline and again at 3, 6, and 12 months post-treatment. Validated QOL and patient satisfaction scales and objective measurements of uterine and myoma volume were conducted at 3, 6, and 12 months. The mean baseline menstrual blood loss of women in the full analysis set (n=127) was 272.7 ± 82.3 ml. At 3-, 6-, and 12-month follow-ups, mean alkaline hematin and associated menstrual blood loss decreased from baseline levels by 31.8 %, 40.7 %, and 38.3 %, respectively (p < 0.001, paired t test). Symptom severity decreased from a baseline mean transformed score of 61.1 to 26.6 at 12 months post-procedure (p < 0.001, paired t-test). Health-related QOL improved from a mean transformed score of 37.3 at baseline to 79.5 at
12 months (p < 0.001, paired t-test). At 12 months post-procedure, total mean myoma volume decreased from baseline by 45.1% (measured by magnetic resonance imaging). There was 1 serious adverse event (1 of 135 [0.7%]) requiring re-admission 5 weeks post-procedure and 1 surgical re-intervention for persistent bleeding; 94% of the women reported satisfaction with the treatment. The authors concluded that RFVTA of myomas is well-tolerated and results in rapid recovery, high patient satisfaction, improved quality of life, and effective symptom relief.

Berman and colleagues (2014) found that radiofrequency volumetric thermal ablation of uterine fibroids resulted in sustained relief from fibroid symptoms and continued improvement in health-related quality of life through 36 months postablation. A total of 135 pre-menopausal women (mean age of 42.5 ± 4.6 years; mean BMI of 30.5 ± 6.1) with symptomatic uterine fibroids and objectively confirmed heavy menstrual bleeding (greater than or equal to 160 to less than or equal to 500 ml) were enrolled in the study of radiofrequency ablation of uterine fibroids. A total of 104 participants were followed prospectively through 36 months after fibroid treatment by RFVTA. For 104 evaluable subjects with 36-month data, change in symptom severity from baseline (60.2 ± 18.8) to 36 months was -32.6 (95% CI: -37.5 to -27.8; p < 0.001). Health-related quality of life also improved from the baseline value of 39.2 ± 19.2 to 36 months by a change of 38.6 (95% CI: 33.3 to 43.9; p < 0.001). Patient-reported UFS-QOL subscores showed statistically significant improvement from baseline to 36 months in all categories (concern, activities, energy/mood, control, self-consciousness, and sexual function) [p < 0.001]. For the 104 subjects with 36-month data, mean health state scores (EQ-5D) improved from a baseline value of 71.0 ± 19.3 to 86.2 ± 11.7 at 36 months. The cumulative re-intervention rate of 10.4% (14/135) at 36 months was well below the possible 25% maximum expected at the beginning of the trial. The investigators concluded that the low re-intervention data through 36 months is a positive outcome for patient well-being.

Brucker et al. (2014) reported that radiofrequency volumetric thermal ablation resulted in the treatment of more fibroids, a significantly shorter hospital stay, and less intraoperative blood loss than laparoscopic myomectomy. The investigators reported on a prospective, randomized, single-center study of the outcomes of RFVTA versus laparoscopic myomectomy (LM) for symptomatic uterine fibroids in women who desired uterine conservation. The surgeons were blinded to the treatment until all fibroids had been mapped by laparoscopic ultrasound. The mean hospitalization times were 10.0 ± 5.5 (median of 7.8 [range of 4.2 to 25.5]) hours for the RFVTA group and 29.9 ± 14.2 (median of 22.6
Intra-operative blood loss was 16 ± 9 (median of 20 [range of 0 to 30]) ml for the RFVTA procedures and 51 ± 57 (median of 35 [range of 10 to 300]) ml for the LM procedures. The percentage of fibroids imaged by laparoscopic ultrasound that were treated/excised was 98.6 % for RFVTA and 80.3 % for LM. Two complications were reported: vertigo (n = 1; RFVTA) and port site hematoma (n = 1; LM).

This study had 2 drawbacks. The racial makeup of the participants was homogeneous (100 % white); a more heterogeneous population might have resulted in decreased bias. However, all participants had symptomatic fibroids and their surgeons had extensive experience in LM but no experience with RFVTA prior to training for the study. The lack of long-term data, including pregnancy outcomes. The participants will be followed for 5 years and pregnancy outcomes, symptom improvement, and overall treatment satisfaction will be evaluated on the basis of the participants’ responses to validated questionnaires. It should also be noted that the study was sponsored by Halt Medical.

The Society of Obstetricians and Gynaecologists of Canada (SOGC)’s guideline on “Abnormal uterine bleeding in pre-menopausal women” (Singh et al, 2013) states that “Several non-hysteroscopic ablation techniques are currently available. Balloon, microwave, and radiofrequency ablation devices have a large reported clinical experience. One of the main advantages of these techniques is their successful implementation in a surgical suite or clinic setting, which avoids the use of operating room resources and general anaesthetic”.

Power Morcellation:

Laparoscopic power morcellators are medical devices used during different types of minimally invasive surgeries (FDA, 2014). These can include certain procedures to treat uterine fibroids (e.g., hysterectomy and myomectomy). Morcellation refers to the division of tissue into smaller pieces or fragments and is often used during laparoscopic surgeries to facilitate the removal of tissue through small incision sites. Recent clinical information suggested that laparoscopic power morcellation poses a risk of spreading unsuspected cancerous tissue (e.g., uterine sarcomas) to travel beyond the uterus (FDA, 2014).

In April 2014, the U.S. Food and Drug Administration (FDA, 2014)) issued a warning about laparoscopic power morcellators because of this risk of spreading cancer. The FDA estimates that 1 in 350 women undergoing hysterectomy or myomectomy for the treatment of fibroids is
found to have an unsuspected uterine sarcoma. The FDA discouraged
the use of laparoscopic power morcellation of uterine fibroids since no
reliable method exists to predict whether a woman’s uterine fibroid may
have sarcoma and with the risk of spreading possible cancerous tissue
within the abdomen and pelvis.

In July 2014, a morcellation device manufacturer (Ethicon, Inc.) instituted
a recall on all its morcellation devices (including generators and
disposables product codes MX0100, MX0200, MX0100R, MX0200R,
DV0015, DV0025, MD0100, MD0200, MD0140, MD0120), citing
uncertainty in the risk-benefit assessment associated with the use of
power morcellators.

In November 2014, the FDA issued an updated warning on the use of
laparoscopic power morcellators (FDA, 2014). The FDA warned against
using laparoscopic power morcellators in the majority of women
undergoing hysterectomy or myomectomy for uterine fibroids. The FDA
stated: “Health care providers and patients should carefully consider
available alternative treatment options for the removal of symptomatic
uterine fibroids. Limiting the patients for whom laparoscopic morcellators
are indicated, the strong warning on the risk of spreading unsuspected
cancer, and the recommendation that doctors share this information
directly with their patients, are part of FDA guidance to manufacturers of
morcellators. The guidance strongly urges these manufacturers to
include this new information in their product labels”.

The FDA (2014) concluded that laparoscopic power morcellation is
contraindicated in women who are peri- or post-menopausal; women
who are candidates for alternative surgical procedures that would allow
en bloc tissue removal of uterine tissue such as through the vagina route
or through mini-laparotomy incision; and women with known or
suspected uterine malignancy. The FDA suggests that morcellation may
continue to be an acceptable therapeutic option for a small group of
women, which might include some younger women not yet peri-
menopausal who wish to keep their uterus and maintain their fertility after
being informed of therisks.

Some investigators have suggested that the use of an intraperitoneal bag
during morcellation may be helpful in reducing intraperitoneal tissue
dissemination. However, power morcellation within a bag is not well
studied and has several limitations that potentially increase the risk of the
procedure (ACOG, 2014).
An UpToDate review on “Differentiating uterine leiomyomas (fibroids) from uterine sarcomas” (Stewart, 2015) states: “Surgical techniques that disrupt the uterine specimen (scalpel or power morcellation, supracervical hysterectomy) should NOT be performed in women with known or suspected uterine or other gynecologic cancer. We recommend NOT using power morcellation of uterine tissue for women who have significant risk factors for uterine sarcoma (e.g., postmenopausal status, history of ≥2 years of tamoxifen therapy, history of pelvic irradiation, history of childhood retinoblastoma, or personal history of hereditary leiomyomatosis and renal cell carcinoma [HLRCC] syndrome). For premenopausal women with uterine fibroids and no significant uterine sarcoma risk factors, based upon appropriate counseling regarding risks and benefits of morcellation versus laparotomy, the patient can then make an informed choice regarding the surgical approach”.

Bogani and colleagues (2015) reviewed the current evidence on the effects of intra-abdominal morcellation on survival outcomes of patients affected by unexpected uterine leiomyosarcoma (ULMS) and estimated the risk of recurrence in those patients. PubMed (MEDLINE), Scopus, Embase, Web of Science databases as well as ClinicalTrials.gov, were searched for data evaluating the effects of intra-abdominal morcellation on survival outcomes of patients with undiagnosed ULMS. Studies were evaluated per the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) and the ACOG guidelines. A total of 60 manuscripts were screened, 11 (18 %) were selected and 4 (7 %) were included. Overall, 202 patients were included: 75 (37 %) patients had morcellation of ULMS, while 127 (63 %) patients had not. A meta-analysis of these studies showed that morcellation increased the overall (62 % versus 39 %; odds ratio [OR]: 3.16 (95% CI: 1.38 to 7.26)) and intra-abdominal (39 % versus 9 %; OR: 4.11 (95 % CI: 1.92 to 8.81)) recurrence rates as well as death rate (48 % versus 29 %; OR: 2.42 (95 % CI: 1.19 to 4.92)). No between-group difference in cumulative extra-abdominal recurrence (OR: 0.34 (95 % CI: 0.07 to 1.59)) rate was observed. The authors concluded that these findings support a significant correlation between uterine morcellation and an increased risk of intra-abdominal recurrence in patients affected by unexpected ULMS. However, they stated that the limited data on this issue and the absence of high level of evidence suggest the need of further studies designed to estimate the risk to benefit ratio of morcellation in patients with uterine fibroids and undiagnosed ULMS.
In December 2017, the FDA confirmed that power morcellation used for laparoscopic myomectomy or hysterectomy for uterine fibroids is associated with increased risk for spreading cancer. The review was the first undertaken since its 2014 safety communication warning of the risk. In an analysis of 23 recent studies, the prevalence of undiagnosed uterine sarcoma during myomectomy or hysterectomy for presumed fibroids was 1 in 225 to 1 in 580, and that of leiomyosarcoma was 1 in 495 to 1 in 1,100. These figures were similar to the FDA's 2014 estimates. The prevalence increases with age -- occult sarcoma prevalence reached 2 % to 3 % for women over age 60. In addition, overall survival (OS) and disease-free survival (DFS) were lower with morcellator use. The report concluded that "While minimally invasive surgery conveys several significant advantages over open surgery for women with fibroids, the use of laparoscopic power morcellators during these surgeries poses a risk due to the potential presence of unsuspected sarcoma in this population. FDA continues to caution against the use of LPMs in the majority of women undergoing myomectomy or hysterectomy for treatment of fibroids".

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT codes covered if selection criteria are met:</td>
<td></td>
</tr>
<tr>
<td>37243</td>
<td>Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction</td>
</tr>
<tr>
<td>58674</td>
<td>Laparoscopy, surgical, ablation of uterine fibroid(s) including intraoperative ultrasound guidance and monitoring, radiofrequency</td>
</tr>
</tbody>
</table>

CPT codes not covered for indications listed in the CPB:

There is no specific code for electrical ablation:

<p>| 0071T | Focused ultrasound ablation of uterine leiomyomata, including MR guidance; total leiomyomata volume less than 200 cc of tissue |</p>
<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0072T</td>
<td>Focused ultrasound ablation of uterine leiomyomata, including MR guidance; total leiomyomata volume greater or equal to 200 cc of tissue</td>
</tr>
<tr>
<td>0404T</td>
<td>Transcervical uterine fibroid(s) ablation with ultrasound guidance, radiofrequency</td>
</tr>
<tr>
<td>37617</td>
<td>Ligation, major artery (eg, post-traumatic, rupture); abdomen [laparoscopic uterine artery occlusion]</td>
</tr>
<tr>
<td>58353</td>
<td>Endometrial ablation, thermal, without hysteroscopic guidance [interstitial thermotherapy] [lasers]</td>
</tr>
<tr>
<td>58356</td>
<td>Endometrial cryoablation with ultrasonic guidance, including endometrial curettage, when performed [cryotherapy]</td>
</tr>
<tr>
<td>97810</td>
<td>Acupuncture</td>
</tr>
<tr>
<td>97814</td>
<td></td>
</tr>
</tbody>
</table>

ICD-10 codes covered if selection criteria are met:

- D25.0 - D25.9 Uterine leiomyoma

ICD-10 codes contraindicated for this CPB:

- C41.4 Malignant neoplasm of pelvic bones, sacrum and coccyx
- C51.0 - C68.9 Malignant neoplasm of genitourinary organs
- C76.3 Malignant neoplasm of pelvis
- N30.0 - N30.9 Cystitis [current]
- N39.0 Urinary tract infection, site not specified [current]
- N70.01 - N73.9 Inflammatory disease of female pelvic organs
- N95.0 - N95.9 Menopausal and other perimenopausal disorders
- N97.0 - N97.9 Female infertility [for women who may wish to become pregnant in the future]
- Z78.0 Asymptomatic menopausal state
- Z79.890 Hormone replacement therapy (postmenopausal)
<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z85.40</td>
<td>Personal history of malignant neoplasm of female genital organs [pelvic malignancy]</td>
</tr>
<tr>
<td>Z85.44</td>
<td></td>
</tr>
<tr>
<td>Z92.3</td>
<td>Personal history of irradiation [prior pelvic x-ray treatments]</td>
</tr>
</tbody>
</table>

**Power Morcellator:**

CPT codes not covered for indications listed in the CPB (not covered when performed using power morcellation):

- **58140** - **58146** Myomectomy
- **58150** - **58294** Hysterectomy
- **58541** - **58544** Laparoscopy, surgical, supracervical hysterectomy
- **58545** - **58546** Laparoscopy, surgical, myomectomy
- **58548** Laparoscopy, surgical, with radical hysterectomy
- **58550** - **58554** Laparoscopy, surgical, with vaginal hysterectomy
- **58570** - **58573** Laparoscopy, surgical, with total hysterectomy
- **58591** Resection of ovarian malignancy with bilateral salpingo-oophorectomy and omentectomy; with total abdominal hysterectomy, pelvic and limited para-aortic lymphadenectomy
- **58953** - **58954** Bilateral salpingo-oophorectomy with omentectomy, total abdominal hysterectomy and radical dissection for debulking
- **58956** Bilateral salpingo-oophorectomy with total omentectomy, total abdominal hysterectomy for malignancy

**HCPCS codes covered if selection criteria are met:**

- **C1782** Morcellator

**ICD-10 codes covered if selection criteria are met:**

- **E66.01** Morbid (severe) obesity due to excess calories

**ICD-10 codes contraindicated for this CPB:**
<table>
<thead>
<tr>
<th>Code</th>
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</tr>
</thead>
<tbody>
<tr>
<td>C18.3</td>
<td>Malignant neoplasm of hepatic flexure [Lynch Syndrome]</td>
</tr>
<tr>
<td>C20</td>
<td>Malignant neoplasm of rectum [Lynch Syndrome]</td>
</tr>
<tr>
<td>C54.0 - C54.9</td>
<td>Malignant neoplasm of corpus uteri</td>
</tr>
<tr>
<td>C64.1 - C64.9</td>
<td>Malignant neoplasm of kidney, except pelvis</td>
</tr>
<tr>
<td>C69.20 - C69.22</td>
<td>Malignant neoplasm of retina [history of childhood retinoblastoma]</td>
</tr>
<tr>
<td>D48.1</td>
<td>Neoplasm of uncertain behavior of connective and other soft tissue [hereditary leiomyomatosis]</td>
</tr>
<tr>
<td>N95.0 - N95.9</td>
<td>Menopausal and other perimenopausal disorders</td>
</tr>
<tr>
<td>N97.0 - N97.9</td>
<td>Female infertility [for women who may wish to become pregnant in the future]</td>
</tr>
<tr>
<td>Z78.0</td>
<td>Asymptomatic menopausal state</td>
</tr>
<tr>
<td>Z79.890</td>
<td>Hormone replacement therapy</td>
</tr>
<tr>
<td>Z84.81</td>
<td>Family history of carrier of genetic disease [history of Lynch Syndrome]</td>
</tr>
<tr>
<td>Z85.3</td>
<td>Personal history of malignant neoplasm of breast [history of tamoxifen therapy]</td>
</tr>
<tr>
<td>Z85.40 - Z85.44</td>
<td>Personal history of malignant neoplasm of female genital organs [pelvic malignancy]</td>
</tr>
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<td>Personal history of irradiation [prior pelvic x-ray treatments]</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:


Laparoscopic Power Morcellation:

1. U.S. Food and Drug Administration (FDA). Laparoscopic uterine power morcellation in hysterectomy and myomectomy: FDA Safety Communication. Silver Spring, MD: FDA; April 17, 2014. Available at:


6. Stewart EA. Differentiating uterine leiomyomas (fibroids) from uterine sarcomas. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed February 2015.

AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number:
0304 Fibroid Treatment

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania  Updated 7/25/2018