Policy Statement

Laparoscopic and percutaneous techniques of myolysis as a treatment of uterine fibroids are considered investigational.

Policy Guidelines

The following codes might be used for a laparoscopic procedure:
- 58578: Unlisted laparoscopy procedure, uterus
- 58674: Laparoscopy, surgical, ablation of uterine fibroid(s) including intraoperative ultrasound guidance and monitoring, radiofrequency
- 58999: Unlisted procedure, female genital system (nonobstetrical)

For percutaneous procedures, the following code would likely be used to describe the magnetic resonance imaging component of the procedure:
- 77022: Magnetic resonance guidance for, and monitoring of, parenchymal tissue ablation

For ultrasound guidance, one of the following codes might be used:
- 76940: Ultrasound guidance for and monitoring of, parenchymal tissue ablation
- 76998: Ultrasonic guidance, intraoperative

In November 2014, the U.S. Food and Drug Administration published a safety communication on laparoscopic power morcellators used for myomectomy and hysterectomy in most women. (Morcellators are not otherwise addressed herein). The Administration recommended that manufacturers of these devices include in their product labels a boxed safety warning and wording on contraindications (see https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM424123.pdf).

Description

Various minimally invasive treatments for uterine fibroids have been proposed as alternatives to surgery. Among these approaches are laparoscopic and percutaneous techniques to induce myolysis, which includes radiofrequency volumetric thermal ablation (RFVTA), laser and bipolar needles, cryomyolysis, and magnetic resonance imaging-guided laser ablation.

Related Policies

- Magnetic Resonance-Guided Focused Ultrasound
- Occlusion of Uterine Arteries Using Transcatheter Embolization

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.
Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

**Regulatory Status**

In 2012, the Acessa™ System (Acessa Health, formerly Halt Medical) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for percutaneous laparoscopic coagulation and ablation of soft tissue and treatment of symptomatic uterine fibroids under laparoscopic ultrasound guidance (K121858). The technology was previously approved in 2010, at which time it was called the Halt 2000GI™ Electrosurgical Radiofrequency Ablation System. In 2014, the ultrasound guidance system received marketing clearance from the FDA (K132744). FDA product code: GEI. In 2018, the third-generation Acessa™ ProVu System® was cleared for marketing by the FDA through the 510(k) process for use in percutaneous, laparoscopic coagulation and ablation of soft tissue, including treatment of symptomatic uterine fibroids under laparoscopic ultrasound guidance. (K181124). FDA product code: HFG.

Cryoablation is a surgical procedure that uses previously approved and available cryoablation systems; and as a surgical procedure, it is not subject to regulation by the FDA. Other products addressed in this review (e.g., Nd:YAG lasers, bipolar electrodes) have long-standing FDA approval, and there are no products specifically approved for the treatment of uterine fibroids.

**Rationale**

**Background**

**Uterine Fibroids**

Uterine fibroids, also known as leiomyomas, are among the most common conditions affecting women in their reproductive years; symptoms include menorrhagia, pelvic pressure, or pain.

**Treatment**

Surgery, including hysterectomy and various myomectomy procedures, is considered the criterion standard for symptom resolution. However, there is the potential for surgical complications and, in the case of a hysterectomy, the uterus is not preserved. In addition, multiple myomectomies may be associated with longer operating time, postoperative febrile morbidity, and development of pelvic adhesions. There has been long-standing research interest in developing minimally invasive alternatives for treating uterine fibroids, including procedures that retain the uterus and permit future childbearing. Treatment options include uterine artery embolization (see Blue Shield of California Medical Policy: Occlusion of Uterine Arteries Using Transcatheter Embolization) and the transcatheter magnetic resonance imaging-guided focused ultrasound therapy (see Blue Shield of California Medical Policy: Magnetic Resonance-Guided Focused Ultrasound). Various techniques to induce myolysis have also been studied including Nd:YAG lasers, bipolar electrodes, cryomyolysis, and radiofrequency ablation.

With these techniques, an energy source is used to create areas of necrosis within uterine fibroids, reducing their volume and thus relieving symptoms. Early methods involved multiple insertions of probes into the fibroid, performed without imaging guidance. There were concerns about serosal injury and abdominopelvic adhesions with these techniques, possibly due to the multiple passes through the serosa needed to treat a single fibroid.1 Newer systems using radiofrequency energy do not require repetitive insertions of needle electrodes.

Ultrasonography is used laparoscopically to determine the size and location of fibroids, to guide the probe, and to ensure the probe is in the correct location so that optimal energy is applied to
the fibroid. Percutaneous approaches using magnetic resonance imaging guidance have also been reported.

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

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

**Radiofrequency Ablation**

**Clinical Context and Therapy Purpose**
The purpose of radiofrequency ablation (RFA) in women who have uterine fibroids is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in women with uterine fibroids?

The following PICO was used to select literature to inform this review.

**Patients**
The relevant population of interest is women with symptomatic uterine fibroids.

**Interventions**
The therapy being considered is laparoscopic or transcervical RFA of fibroids under ultrasonic guidance.

**Comparators**
The following therapies are currently being used to manage symptomatic uterine fibroids: medical management, uterine artery embolization (UAE), myomectomy, and hysterectomy. Surgery, including hysterectomy and myomectomy are considered the criterion standard for symptom resolution. However, there is the need to recover from surgery, and in the case of a hysterectomy, the uterus is not preserved. UAE is associated with poor pregnancy outcomes and is not advised in patients who desire to become pregnant.

A retrospective cohort from claims data of over 35,000 women found that of the less invasive procedures, myomectomy had the lowest 12-month reintervention rate (4.2%), followed by UAE (7.0%), and endometrial ablation (12.4%).

**Outcomes**
The outcomes of interest are, complications, postoperative pain and recovery time, symptom resolution, fibroid recurrence and need for reintervention at 3 to 5 years, and health-related
quality of life. The symptom severity score (SSS) is a 0 to 100 scale where higher SSSs indicate more severe symptoms. The EuroQol 5-Dimension (EQ-5D) is a 0 to 100 scale where lower scores indicate worse quality of life.

**Review of Evidence**

**Systematic Reviews**

A systematic review and meta-analysis by Sandberg et al (2018) evaluated the risk of reintervention for hysterectomy and quality of life after uterine-sparing interventions for fibroids (see Tables 1 and 2). Risk of reintervention at 12 months was 0.3% for RFA compared with 3.6% for UAE and 1.1% for myomectomy. Symptom severity and quality of life scores were similar for the 3 treatments. Only 1 RFA study was identified on reintervention risk at 36 months; none was identified on reintervention risk at 60 months. A systematic review by Havryliuk et al (2017) that did not separate outcomes by the length of follow-up found a reintervention rate of 5.2% after RFA (4 studies, 12 to 36 mo follow-up) compared to 4.2% after myomectomy (6 studies, 12 to 52 mo follow-up). There was no significant difference in complication rates between RFA (6.3%) and myomectomy (7.9%). The length of stay after myomectomy was 2 days (range 0.5 to 6.0). No data were provided on length of stay after RFA.

Lin et al (2018) conducted a meta-analysis of improvement in symptom severity, quality of life, and reintervention after RFA. The review included 1 RCT and 7 non-comparative trials. The recurrence risk at a weighted mean follow-up of 24.65 months (range, 3 to 36 months) was 4.4%. Improvements in symptoms and quality of life were maintained out to 24 months in 3 studies and out to 36 months in 1 study. No studies were identified that had follow-up longer than 36 months. Bradley et al (2019) conducted a systematic review of 32 prospective studies on laparoscopic, transvaginal, or transcervical RFA. Most were conducted outside of the U.S. with devices that are not cleared or approved by the U.S. Food and Drug Administration. The overall reintervention risk was 4.2% at 12 months, 8.2% at 24 months, and 11.5% at 36 months. Reintervention rates at 12 months did not differ significantly for the laparoscopic, transvaginal, or transcervical RFA procedures. Because many of the devices are not available in the U.S., relevance for the current review is limited.

**Table 1. Characteristics of Systematic Reviews on RFA**

<table>
<thead>
<tr>
<th>Study</th>
<th>Dates</th>
<th>Trials</th>
<th>Participants</th>
<th>N</th>
<th>Design</th>
<th>Duration, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sandberg et al (2018)</td>
<td>2006-2016</td>
<td>45</td>
<td>Women with symptomatic uterine fibroids undergoing myomectomy, UAE, or RFA</td>
<td>17,789</td>
<td>Studies evaluating reintervention for hysterectomy and quality of life with consecutive enrollment and follow-up of ≥12 mo</td>
<td>11.2-34.7</td>
</tr>
<tr>
<td>Bradley et al (2019)</td>
<td>32</td>
<td></td>
<td>Women with symptomatic uterine fibroids undergoing laparoscopic, transvaginal, or transcervical RFA</td>
<td>1283</td>
<td>Prospective studies for treatment of uterine fibroids with RFA (variety of devices)</td>
<td>12-36 mo</td>
</tr>
</tbody>
</table>

RFA: radiofrequency ablation; UAE: uterine artery embolization.

**Table 2. Results of Systematic Reviews on RFA**

<table>
<thead>
<tr>
<th>Study</th>
<th>Reintervention Risk (95% CI), %</th>
<th>Symptom Severity Score (95% CI)</th>
<th>QOL (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At 12 Months</td>
<td>At 36 Months</td>
<td>At 60 Months</td>
</tr>
<tr>
<td>Sandberg et al (2018)</td>
<td>40</td>
<td>8</td>
<td>27</td>
</tr>
<tr>
<td>Total studies</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reproduction without authorization from Blue Shield of California is prohibited.
Myomectomy & 1.1 (0.0 to 3.7) & 1.2 (0.0 to 5.2) & 12.2 (5.2 to 21.2) & -37.6 (-43.8 to -31.4) & 39.9 (33.0 to 46.8) \\
UAE & 3.6 (2.4 to 4.9) & 7.4 (0.9 to 10.7) & 14.4 (9.8 to 19.6) & -35.8 (-40.6 to -30.9) & 38.9 (35.8 to 41.9) \\
RFA & 0.3 (0.0 to 1.6) & 10.4 (1 study) & Unknown & -37.0 (-44.6 to -29.4) & 35.1 (28.7 to 41.6) \\
Lin et al (2019) & Range, 3 to 36 mo & \\
Total Studies & 7 & 6 & 3 & 1 & 3 & 1 \\
RFA & 4.39 (1.60–8.45) & -39.37 (-34.70 to -22.24 to -44.40) & -32.60 (-27.75 to -37.45) & 29.21 (12.44 to 45.98) & 38.60 (35.8 to 41.9) & p<0.001 & p<0.001 & p<0.001 \\
P Value & \\
Bradley et al (2019) & \\
Total Studies & 4.2 & 11.5 & 40 & +39 & <0.001 & <0.001 & <0.001 \\
RFA & \\
CI: confidence interval; QOL: quality of life; RFA: radiofrequency volumetric thermal ablation; UAE: uterine artery embolization.

Randomized Controlled Trials

One RCT evaluating RFA was included in the Sandberg et al (2018) systematic review, with Tables 3 and 4 describe trial characteristics and results.

Table 3. Summary of Key Randomized Controlled Trial Characteristics for RFA

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Menstruating</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Symptomatic uterine fibroids &lt;10 cm</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Uterine size ≤16 gestational wk</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Desire uterine conservation</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Not pregnant or lactating</td>
<td></td>
</tr>
<tr>
<td>Lin et al (2019)</td>
<td></td>
<td></td>
<td></td>
<td>Range, 3 to 36 mo</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LM: laparoscopic myomectomy; RFA: radiofrequency volumetric thermal ablation.

Table 4. Summary of Key Randomized Controlled Trial Outcomes for RFA

<table>
<thead>
<tr>
<th>Study</th>
<th>Primary Outcome</th>
<th>Secondary Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hospital LOS (SD), h</td>
<td>Mean SSS</td>
</tr>
<tr>
<td>Laparoscopic RFA</td>
<td></td>
<td>43</td>
</tr>
<tr>
<td>Laparoscopic myomectomy</td>
<td></td>
<td>10.0 (5.5)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
</tbody>
</table>

HRQOL: health-related quality of life; LOS: length of stay; NS: not significant; RFA: radiofrequency volumetric thermal ablation; SSS: Symptom Severity Score.

a Analyses at 12 and 24 months were per protocol and included 84% of randomized participants.
b Met criteria for noninferiority: hospital LOS after RFA no more than 10% longer than after laparoscopic myomectomy.
c Exact between-group p values were not reported.
In the Brucker et al (2014) trial, all patients in the myomectomy group were hospitalized overnight; although not explicitly stated, this appeared to be the standard procedure at the study hospital. In the RFA (Acessa) group, there was an unplanned hospitalization due to unexplained vertigo and 4 hospitalizations as a standard procedure because the patients also underwent adhesiolysis.

Secondary outcomes of the RCT were reported by Hahn et al (2015)\(^8\) (12-month outcomes) and by Kramer et al (2016)\(^9\) (12-month and 24-month outcomes). In addition to summary symptom and quality of life measures, the publications reported on 11 symptoms: heavy menstrual bleeding, increased abdominal girth, dyspareunia, pelvic discomfort/pain, dysmenorrhea, urinary frequency, urinary retention, sleep disturbance, backache, localized pain, and "other symptoms" (not specified).

Limitations of the 12- and 24-month analyses, shown in Tables 5 and 6, included lack of intention-to-treat analysis and failure to describe secondary study hypotheses and statistical analyses clearly. The RCT had a small sample size and thus might have been underpowered to detect clinically meaningful differences in secondary outcomes, so these results do not rule out potential differences between treatments.

**Table 5. Study Relevance Limitations**

<table>
<thead>
<tr>
<th>Study</th>
<th>Population(^a)</th>
<th>Intervention(^b)</th>
<th>Comparator(^c)</th>
<th>Outcomes(^d)</th>
<th>Follow-Up(^e)</th>
</tr>
</thead>
</table>

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

\(^a\) Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

\(^b\) Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

\(^c\) Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

\(^d\) Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

\(^e\) Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

**Table 6. Study Design and Conduct Limitations**

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocation(^a)</th>
<th>Blinding(^b)</th>
<th>Selective Reporting(^c)</th>
<th>Data Completeness(^d)</th>
<th>Power(^e)</th>
<th>Statistical(^f)</th>
</tr>
</thead>
</table>

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.


\(^b\) Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

\(^c\) Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

\(^d\) Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

\(^e\) Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

\(^f\) Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event;
2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

**Prospective Single Arm Studies**

Prospective single-arm studies are described in Tables 7 and 8. The pivotal study for the SONATA transcervical RFA system was a prospective single-arm study with 147 premenopausal women who had symptomatic uterine fibroids with heavy menstrual bleeding. Patients were excluded if they desired to become pregnant. There were 2 (1.4%) procedure-related adverse events during the first year of follow-up and no additional device-related adverse events between the 1- and 2-year follow-up. At the 24 month follow-up, patients reported significantly improved symptom severity scores, HRQL, and EQ-5D. The cumulative rate of surgical intervention for heavy menstrual bleeding was 5.2% (95% confidence interval [CI] 2.5% to 10.6%). Follow-up is continuing through 3 years.

The Fibroid Ablation Study EU (FAST-EU) was a prospective single-arm trial with the previously named VizAblate transcervical RFA. Fifty women who had heavy menstrual bleeding were included in the study. Patients were excluded if they desired to become pregnant. The primary outcome measure, that at least 50% of patients with >30% reduction in perfused fibroid volume, was achieved at the 3 month follow-up. Twelve-month follow-up was not in the original study design, and only 28 (58.3%) of participants agreed to return for an MRI at this time point. The Symptom Severity Score was obtained in all patients except for 1 patient due to pregnancy. A clinically significant minimum 10 point reduction in the Symptom Severity Score was obtained in 82% of patients at 3 months, 86% at 6 months, and 78% at 12 months. There were 34 adverse events deemed possibly, probably, or definitely related to the procedure. Four patients (8%) underwent surgical reintervention between 6 and 12 months post-ablation.

**Table 7. Summary of Single Arm Study Characteristics**

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Location</th>
<th>Participants</th>
<th>Treatment Delivery</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brolmann et al (2016)</td>
<td>7 community or academic gynecologists in EU and Mexico</td>
<td>50 women ≥ 28 years of age with heavy menstrual bleeding for at least 3 months and no desire to become pregnant</td>
<td>VizAblate(TM) transcervical RFA</td>
<td>12 mo</td>
</tr>
<tr>
<td>Miller et al (2020)</td>
<td>Community or academic gynecologists in the US and Mexico</td>
<td>147 premenopausal women 25-50 years of age with symptomatic uterine fibroids with heavy menstrual bleeding and no desire to become pregnant</td>
<td>Sonata transcervical RFA</td>
<td>2 years</td>
</tr>
</tbody>
</table>

RFA: radiofrequency ablation

**Table 8. Case Series Results**

<table>
<thead>
<tr>
<th>Study</th>
<th>Baseline</th>
<th>3 mo</th>
<th>12 mo</th>
<th>24 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brolmann et al (2016)</td>
<td></td>
<td>50</td>
<td>50</td>
<td>48</td>
</tr>
<tr>
<td>n (%)</td>
<td></td>
<td>18.3 (20.6)</td>
<td>5.8 (9.6)</td>
<td>6.6 (11.3)</td>
</tr>
<tr>
<td>Percentage change in perfused fibroid volume (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptom Severity Score (SD)</td>
<td></td>
<td>61.7 (16.9)</td>
<td>31.7 (20.1)</td>
<td>26.6 (24.0)</td>
</tr>
<tr>
<td>HRQL (SD)</td>
<td></td>
<td>34.3 (19.0)</td>
<td>76.4 (22.2)</td>
<td>80.7 (24.7)</td>
</tr>
<tr>
<td>Surgical reintervention</td>
<td></td>
<td>4 (8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miller et al (2020)</td>
<td>147</td>
<td>125 (85%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td></td>
<td>55 (19)</td>
<td>24 (18) P&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Symptom Severity Score (SD)</td>
<td></td>
<td>40 (21)</td>
<td>83 (19) P&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>HRQL (SD)</td>
<td></td>
<td>0.72 (0.21)</td>
<td>0.89 (0.14) P&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Surgical reintervention</td>
<td></td>
<td>5.5%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

EQ-5D Euroqol 5-dimension; HRQL: Health-related quality of life; SD: standard deviation
Pregnancy Outcomes After Radiofrequency Ablation

Keltz et al (2017) published a systematic review of published literature on pregnancy outcomes after thermal ablation of uterine fibroids. For RFA, reviewers identified 20 pregnancies reported in 4 case series; the denominator (i.e., the number of patients treated in these series) was not reported. Of the 20 pregnancies, 7 were undesired and were electively terminated. For the remaining 13 pregnancies, there was 1 spontaneous abortion and 12 full-term births. Nine of the 12 live births were delivered by cesarean section.

Section Summary: Radiofrequency Ablation

Prospective case series, systematic reviews, and an RCT comparing RFA with laparoscopic myomectomy have been published. The meta-analyses found low rates of reintervention with RFA and quality of life outcomes that were similar to myomectomy and UAE at 12 months. Data on reintervention rates at 36 months was limited to a single study and no studies reported reintervention rates at 60 months. The RCT found that RFA was noninferior to laparoscopic myomectomy on the primary outcome (length of hospitalization). A number of secondary outcomes of the RCT were reported at 12 and 24 months, including symptoms and quality of life outcomes; none differed significantly between groups. The RCT only had 43 patients in subgroup analyses at 12 and 24 months, and may have had insufficient power for the secondary outcomes. The procedure is associated with a reduction in symptoms and improvement in quality of life in the short-term. The reintervention rate at longer follow-up is unknown. Because most trials excluded women who desired to become pregnant, the impact of RFA on pregnancy outcomes is also uncertain. Additional well-designed comparative trials with longer follow-up are needed to determine the effect of RFA on health outcomes compared with other treatment options, including myomectomy.

Laser or Bipolar Needles

Clinical Context and Therapy Purpose

The purpose of therapy with laser or bipolar needles in patients who have uterine fibroids is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of laser or bipolar needles improve the net health outcome in women with uterine fibroids?

The following PICO was used to select literature to inform this review.

Patients
The relevant population of interest is women with symptomatic uterine fibroids.

Interventions
The therapy being considered is laser or bipolar needles.

Comparators
The following therapies are currently being used to manage symptomatic uterine fibroids: medical management, uterine artery embolization (UAE), myomectomy, and hysterectomy. Surgery, including hysterectomy and myomectomy are considered the criterion standard for symptom resolution. However, there is the need to recover from surgery, and in the case of a hysterectomy, the uterus is not preserved. UAE is associated with poor pregnancy outcomes and is not advised in patients who desire to become pregnant.

A retrospective cohort from claims data of over 35,000 women found that of the less invasive procedures, myomectomy had the lowest 12-month reintervention rate (4.2%), followed by UAE (7.0%), and endometrial ablation (12.4%).

Outcomes
The outcomes of interest are, complications, postoperative pain and recovery time, symptom resolution, need for reintervention, and health-related quality of life. The immediate follow-up
would be a week for postoperative pain and recovery, and 3 to 5 years of follow-up would be
needed to monitor for fibroid recurrence and retreatment.

Review of Evidence

Case Series
Several case series were identified, most published in the 1990s. For example, Goldfarb (1995)
reported on outcomes for 300 women with symptomatic fibroids no larger than 10 cm who
underwent myolysis using either Nd:YAG or bipolar needles.13 The author reported that the
coagulating effect of the bipolar needle devascularized the fibroids, and the resulting shrinkage
was comparable to that produced by Nd:YAG laser. An earlier study by Goldfarb (1992),
included 75 patients who presented with symptomatic fibroids 5 to 10 cm in diameter.14, Symptons included pelvic pain, pressure, dyspareunia, and recurrent menorrhagia. The Nd:YAG
laser was inserted into the fibroid multiple times (eg, 75 to 100 punctures to coagulate a 5-cm
fibroid). Based on an assessment by endovaginal ultrasound, the fibroids regressed in size and,
after 6 to 14 months of follow-up, the size remained stable. No patient experienced significant
instead of myomectomy if they had completed childbearing.15 The authors reported that
maximal decrease in fibroid size had occurred by 6 months, however, as reported, it is unclear
among the 28 of 48 patients with more than 2 fibroids whether all fibroids were treated in each
patient, and, if not, how treated fibroids were selected. Additionally, no associated patient
symptoms were reported.
Several authors have reported pelvic adhesions as a complication of the Nd:YAG laser
procedure, presumably due to thermal damage to the serosal surface. In addition, the Nd:YAG
laser produces a significant amount of smoke, which can obscure visibility.16,17

Section Summary: Laser or Bipolar Needles
The evidence base on the use of lasers or bipolar needles only includes case series, small in size,
and published in the 1990s. RCTs comparing laser and bipolar needles with alternative
treatments for uterine fibroids and reporting health outcomes are needed.

Cryomyolysis

Clinical Context and Therapy Purpose
The purpose of cryomyolysis in patients who have uterine fibroids is to provide a treatment
option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does cryomyolysis improve the net health
outcome in women with uterine fibroids?

The following PICO was used to select literature to inform this review.

Patients
The relevant population of interest is women with symptomatic uterine fibroids.

Interventions
The therapy being considered is cryomyolysis. Cryomyolysis entails inserting a -180°C cryoprobe
into the center of a fibroid, which creates an "iceball" within the fibroid. Several freeze-thaw
cycles are typically used, and the process may not be standardized.

Comparators
The following therapies are currently being used to manage symptomatic uterine fibroids:
medical management, uterine artery embolization (UAE), myomectomy, and hysterectomy.
Surgery, including hysterectomy and myomectomy are considered the criterion standard for
symptom resolution. However, there is the need to recover from surgery, and in the case of a
hysterectomy, the uterus is not preserved. UAE is associated with poor pregnancy outcomes and
is not advised in patients who desire to become pregnant.
A retrospective cohort from claims data of over 35,000 women found that of the less invasive procedures, myomectomy had the lowest 12-month reintervention rate (4.2%), followed by UAE (7.0%), and endometrial ablation (12.4%).

**Outcomes**
The outcomes of interest are, complications, postoperative pain and recovery time, symptom resolution, need for reintervention, and health-related quality of life. The immediate follow-up would be a week for postoperative pain and recovery, and 3 to 5 years of follow-up would be needed to monitor for fibroid recurrence and retreatment.

**Review of Evidence**

**Case Series**
No controlled studies evaluating cryomyolysis were identified. Two case series have been identified. Zeik et al (1998) published a prospective pilot study with 14 patients, and Zupi et al (2004) presented their experience with 20 patients. In both case series, the authors reported that patients had symptom resolution. In the Zeik et al (1998) series, cryomyolysis maintained or slightly reduced the myoma volume by 6%. In the Zupi et al (2004) study, cryomyolysis was associated with a 25% reduction in fibroid size. Zupi et al (2005) reported on the 1-year follow-up of these patients. Mean shrinkage in fibroid size continued until 9 months after surgery, to a mean volume reduction of 60%. In the Sandberg et al (2018) systematic review (discussed above), the risk of reintervention was 15%. Interpretation of these studies is limited due to their small sample sizes and lack of comparison groups.

**Section Summary: Cryomyolysis**
The literature on cryomyolysis includes small case series, with no literature identified in the last decade. Controlled studies comparing cryomyolysis with alternative treatments for uterine fibroids and differentiating between outcomes related to fibroid treatment and outcomes related to the treatment of abnormal bleeding are needed.

**Magnetic Resonance Imaging-Guided Laser Ablation**

**Clinical Context and Therapy Purpose**
The purpose of MRI-guided laser ablation in patients who have uterine fibroids is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does MRI-guided laser ablation improve the net health outcome in women with uterine fibroids?

The following PICO was used to select literature to inform this review.

**Patients**
The relevant population of interest is women with symptomatic uterine fibroids.

**Interventions**
The therapy being considered is MRI-guided laser ablation.

**Comparators**
The following therapies are currently being used to manage symptomatic uterine fibroids: medical management, uterine artery embolization (UAE), myomectomy, and hysterectomy. Surgery, including hysterectomy and myomectomy are considered the criterion standard for symptom resolution. However, there is the need to recover from surgery, and in the case of a hysterectomy, the uterus is not preserved. UAE is associated with poor pregnancy outcomes and is not advised in patients who desire to become pregnant.

A retrospective cohort from claims data of over 35,000 women found that of the less invasive procedures, myomectomy had the lowest 12-month reintervention rate (4.2%), followed by UAE (7.0%), and endometrial ablation (12.4%).
Outcomes

The outcomes of interest are, complications, postoperative pain and recovery time, resolution of symptoms, need for reintervention, and health-related quality of life. The immediate follow-up would be a week for postoperative pain and recovery, and 3 to 5 years of follow-up would be needed to monitor for fibroid recurrence and retreatment.

Review of Evidence

Nonrandomized Studies

No RCTs evaluating MRI-guided laser ablation were identified. A nonrandomized study by Hindley et al (2002) was identified (see Tables 9 and 10). Results from the women treated with MRI-guided laser ablation were compared with a historical control group of 43 women who underwent a hysterectomy. Compared with the historical control group, the total score on the Menorrhagia Outcomes Questionnaire was significantly lower (i.e., worse outcomes) in those undergoing percutaneous myolysis. The quality of life subscores did not differ statistically.

Table 9. Summary of Key Nonrandomized Trial Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Country</th>
<th>Participants</th>
<th>Treatment</th>
<th>Comparator</th>
<th>FU, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hindley et al (2002)</td>
<td>Cohort with historical controls</td>
<td>U.K.</td>
<td>109 women with symptomatic fibroids seeking to avoid surgery</td>
<td>66 to MRI-guided laser ablation</td>
<td>43 to hysterectomy</td>
<td>1</td>
</tr>
</tbody>
</table>

FU: follow-up; MRI: magnetic resonance imaging.

Table 10. Summary of Key Nonrandomized Trial Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean Fibroid Volume Reduction (Range), %</th>
<th>MOQ Total</th>
<th>MOQ QOL/Satisfaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At 3 Months</td>
<td>At 1 Year</td>
<td></td>
</tr>
<tr>
<td>MRI-guided laser ablation</td>
<td>47/66 (71)</td>
<td>24/66 (36)</td>
<td>34/66 33/66</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>0.02</td>
<td>0.06</td>
<td>48.7 49.0</td>
</tr>
</tbody>
</table>

MRI: magnetic resonance imaging; MOQ: Menorrhagia Outcomes Questionnaire; NR: not reported; QOL: Quality of Life.

The purpose of the limitations tables (see Tables 11 and 12) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of the evidence supporting the position statement.

Table 11. Study Relevance Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Outcomes</th>
<th>Follow-Up</th>
</tr>
</thead>
</table>

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

a Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

b Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

c Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

d Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.
Table 12. Study Design and Conduct Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocationa</th>
<th>Blindingb</th>
<th>Selective Reportingc</th>
<th>Data Completenessd</th>
<th>Powere</th>
<th>Statisticalf</th>
</tr>
</thead>
</table>

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

d Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
f Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Section Summary: MRI-Guided Laser Ablation

A single nonrandomized study with historical controls was identified. Data reporting was incomplete, and self-reported outcomes were worse compared with a historical control group of women undergoing a hysterectomy. RCTs comparing MRI-guided laser ablation with alternative treatments for uterine fibroids and reporting health outcomes are needed.

Summary of Evidence

For individuals who have symptomatic uterine fibroids who receive RFA, the evidence includes prospective cohorts, an RCT and systematic review. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. The meta-analysis found low rates of reintervention with RFA and quality of life outcomes that were similar to uterine artery embolization and myomectomy at 12 months. Data on reintervention rates at 36 months were limited to 1 study and no studies reported reintervention rates at 60 months. The single RCT with a follow-up longer than 3 months found that RFA was noninferior to laparoscopic myomectomy on the trial's primary outcome: length of hospitalization. A number of secondary outcomes were reported at 12 and 24 months, including symptoms and quality of life. None of the secondary outcomes demonstrated significant between-group differences in a subgroup analysis of 43 patients. The procedure has faster recovery than myomectomy, and provides a reduction in symptoms and improvement in quality of life in the short term. Recurrence and reintervention rates at longer follow-up are unknown. Well-designed comparative trials with longer follow-up are needed to determine the effect of RFA on health outcomes compared with other treatment options such as myomectomy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have symptomatic uterine fibroids who receive laser or bipolar needles, the evidence includes case series. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. The case series were published in the 1990s, and the procedures used then may not reflect current practice. RCTs comparing laser or bipolar needles with alternative treatments for uterine fibroids are needed to evaluate the safety and efficacy of this technology adequately. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have symptomatic uterine fibroids who receive cryomyolysis, the evidence includes case series. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. Among the few case series, sample sizes were small (≤20 patients). RCTs comparing cryomyolysis with alternative treatments for uterine fibroids are needed to evaluate the safety
and efficacy of this technology adequately. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have symptomatic uterine fibroids who receive magnetic resonance imaging-guided laser ablation, the evidence includes a study with historical controls. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. A single study with historical controls is not sufficiently robust to evaluate this technology. RCTs comparing magnetic resonance imaging-guided laser ablation with alternative treatments for uterine fibroids are needed to evaluate safety and efficacy adequately. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information
Practice Guidelines and Position Statements

American College of Obstetricians and Gynecologists
In 2019, the American College of Obstetricians and Gynecologists reaffirmed its 2008 position on alternatives to hysterectomy in the management of leiomyomas.22 Recommendations based on good and consistent scientific evidence were that abdominal myomectomy is a safe and effective treatment for women with symptomatic leiomyomas and that uterine artery embolization is a safe and effective option for appropriately selected women who want to retain their uteri. The bulletin contained no recommendations on myolysis using laparoscopic or percutaneous techniques.

U.S. Preventive Services Task Force Recommendations
Not applicable.

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

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this evidence review are listed in Table 13.

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02260752</td>
<td>Patient-Centered Results for Uterine Fibroids (COMPARE-UF)</td>
<td>3,094</td>
<td>Sep 2020</td>
</tr>
<tr>
<td>NCT01563783</td>
<td>The Trust (Treatment Results of Uterine Sparing Technologies) Study</td>
<td>260</td>
<td>Jun 2022</td>
</tr>
<tr>
<td>NCT03219385</td>
<td>Directed Ablation of Uterine Fibroids Using a Noninvasive Approach (DIANA)</td>
<td>180</td>
<td>Sep 2022</td>
</tr>
<tr>
<td>NCT03118037</td>
<td>Transcervical Radiofrequency Ablation of Uterine Fibroids Global Registry (SAGE)</td>
<td>100</td>
<td>Dec 2023</td>
</tr>
<tr>
<td>NCT02163525</td>
<td>Post Market TRUST - U.S.A. Study</td>
<td>114</td>
<td>Jun 2024</td>
</tr>
<tr>
<td>NCT021000904</td>
<td>Uterine Leiomyoma Treatment With Radiofrequency Ablation (ULTRA) Registry (ULTRA Registry)</td>
<td>400</td>
<td>Jan 2025</td>
</tr>
<tr>
<td>Unpublished</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01750008</td>
<td>The LUSTOR (Laparoscopic Uterine Sparing Techniques Outcomes and Reinterventions)Trial</td>
<td>51</td>
<td>Jun 2018</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.
References


**Documentation for Clinical Review**

- No records required

**Coding**

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT®</td>
<td>58578</td>
<td>Unlisted laparoscopy procedure, uterus</td>
</tr>
<tr>
<td></td>
<td>58674</td>
<td>Laparoscopy, surgical, ablation of uterine fibroid(s) including intraoperative ultrasound guidance and monitoring, radiofrequency</td>
</tr>
<tr>
<td></td>
<td>58999</td>
<td>Unlisted procedure, female genital system (nonobstetrical)</td>
</tr>
<tr>
<td></td>
<td>76940</td>
<td>Ultrasound guidance for, and monitoring of, parenchymal tissue ablation</td>
</tr>
<tr>
<td></td>
<td>76998</td>
<td>Ultrasonic guidance, intraoperative</td>
</tr>
<tr>
<td></td>
<td>77022</td>
<td>Magnetic resonance guidance for, and monitoring of, parenchymal tissue ablation</td>
</tr>
</tbody>
</table>

| HCPCS  | None |

**Policy History**

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>08/29/2014</td>
<td>BCBSA Medical Policy adoption</td>
</tr>
<tr>
<td>10/01/2016</td>
<td>Policy revision without position change</td>
</tr>
<tr>
<td>02/01/2017</td>
<td>Coding update</td>
</tr>
<tr>
<td>10/01/2017</td>
<td>Policy revision without position change</td>
</tr>
<tr>
<td>10/01/2018</td>
<td>Policy revision without position change</td>
</tr>
<tr>
<td>12/16/2019</td>
<td>Policy revision without position change</td>
</tr>
<tr>
<td>04/01/2020</td>
<td>Annual review. No change to policy statement. Literature review updated.</td>
</tr>
<tr>
<td>11/01/2020</td>
<td>No change to policy statement. Literature review updated.</td>
</tr>
</tbody>
</table>

**Definitions of Decision Determinations**

**Medically Necessary:** Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis;
(c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member’s illness, injury, or disease.

**Investigational/Experimental**: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation**: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

### Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member’s health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

**Disclaimer**: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.