Laparoscopic and Percutaneous Techniques for the Myolysis of Uterine Fibroids

Policy #  00445
Original Effective Date:  09/17/2014
Current Effective Date:  09/21/2016

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

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

Based on review of available data, the Company considers laparoscopic and percutaneous techniques of myolysis as a treatment of uterine fibroids are considered to be investigational.*

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

Uterine fibroids are one of the most common conditions affecting women in the reproductive years; symptoms include menorrhagia, pelvic pressure, or pain. Surgery, including hysterectomy and various myomectomy procedures, is considered the criterion standard treatment for symptom resolution. However, there is the potential for surgical complications and, in the case of hysterectomy, the uterus is not preserved. In addition, in the case of multiple uterine fibroids, myomectomy can be a time-consuming procedure.

There has been longstanding research interest in developing minimally invasive alternatives for treating uterine fibroids, including procedures that retain the uterus and allow for future childbearing. Treatment options include uterine artery embolization and the transcutaneous procedure magnetic resonance imaging (MRI)-guided focused ultrasound therapy (MRgFUS). Various techniques to induce myolysis have also been studied including Nd:YAG lasers, bipolar electrodes, cryomyolysis, and radiofrequency ablation. An energy source is used to create areas of necrosis within uterine fibroids, reducing their volume and thus relieving symptoms. Early methods involved the insertion of probes multiple times into the fibroid and were 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. 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 MRI guidance have also been reported.

FDA or Other Governmental Regulatory Approval
U.S. Food and Drug Administration (FDA)
Laparoscopic and Percutaneous Techniques for the Myolysis of Uterine Fibroids

Policy # 00445
Original Effective Date: 09/17/2014
Current Effective Date: 09/21/2016

In November 2012, the Acessa™ System (Halt Medical, Brentwood, CA) was cleared for marketing by the U.S. FDA for percutaneous laparoscopic coagulation and ablation of soft tissue and treatment of symptomatic uterine fibroids under laparoscopic ultrasound guidance. The technology was previously approved in 2010, at which time it was called the Halt 2000GI™ Electrosurgical Radiofrequency Ablation System (Halt Medical, Brentwood, CA). The intended use of the Halt 2000GI system was for percutaneous laparoscopic coagulation and ablation of soft tissue. Unlike FDA clearance of the Acessa™ System, the intended use statement for the Halt 2000GI system does not specifically mention treatment of uterine fibroids. FDA Product Code: GEI.

Rationale/Source
The most recent literature review for this policy was done through July 8, 2016.

Laparoscopic Procedures
Radiofrequency Volumetric Thermal Ablation
In 2014, Brucker et al in Germany published an industry-sponsored randomized controlled trial (RCT) comparing radiofrequency volumetric thermal ablation (RFVTA) with the Acessa system (Halt Medical) to laparoscopic myomectomy. The study included 51 premenopausal women at least 18 years old with symptomatic uterine fibroids less than 10 cm in any diameter and a uterine size of less than 17 weeks of gestation. Pregnancy and lactation were exclusion criteria. Prior to randomization, all participants underwent laparoscopic ultrasound mapping. Data on 50 of the 51 women were analyzed. The primary study outcome, mean time to hospital discharge (SD), was 10.0 (5.5) hours in the RFVTA group and 29.9 (14.2) hours in the myomectomy group. The criterion for noninferiority (no more than 10% longer hospital stay with RFVTA than laparoscopic myomectomy) was met at a significance level of p less than 0.001. 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 Acessa group, there was 1 unplanned hospitalization due to unexplained vertigo and 4 hospitalizations as standard procedure because the patients underwent adhesiolysis.

Secondary outcomes of the RCT were reported in a 2015 publication by Hahn et al (12-month outcomes) and a 2016 publication by Kramer et al (24-month outcomes). Analysis was per protocol and 43 (84%) of 51 randomized participants were available for both the 12- and 24-month analyses. Each publication reported on 12 symptoms: heavy menstrual bleeding, increased abdominal gait, dyspareunia, pelvic discomfort/pain, dysmenorrhea, urinary frequency, urinary retention, sleep disturbance, backache, localized pain, and “other symptoms” (not specified). At 12 months, no participants reported 4 of the symptoms (dyspareunia, urinary retention, sleep disturbance, uterine pain) and there were no statistically significant between-group differences in the frequency of any of the remaining 8 symptoms (at the p<0.05 level). The most commonly reported symptom at 12 months (heavy menstrual bleeding) occurred in 7 (33%) of women in the RFVTA group and 2 (9%) of women in the laparoscopic myomectomy group (p=0.069) after controlling for baseline bleeding. At 24 months, no participants reported urinary retention or “other” symptoms, and there were no statistically significant between-group differences in any of the 10 reported symptoms. The most commonly reported symptom at 24 months (dysmenorrhea) occurred in 8 (38%) in the RFVTA group and in 78 (32%) in the laparoscopic myomectomy group (p=0.67). Patients were also assessed using several validated questionnaires (eg, the Uterine Fibroid Symptom and Quality of Life). There were no statistically significant
Laparoscopic and Percutaneous Techniques for the Myolysis of Uterine Fibroids

Policy # 00445
Original Effective Date: 09/17/2014
Current Effective Date: 09/21/2016

between-group differences at 12 or 24 months on these validated questionnaires. In addition, the authors described pregnancy outcomes. Three patients in the RFVTA group conceived and all delivered a healthy neonate; the number of women who desired to become pregnant was not reported. Limitations of the 12- and 24-month analyses included lack of intention-to-treat analysis and failure to describe secondary study hypotheses and statistical analyses clearly. The RCT was relatively small in size and thus may have been underpowered to detect clinically meaningful differences in secondary outcomes, so these results do not rule out potential differences between treatments.

In addition to the RCT, several uncontrolled case series were identified. In 2013, Chudnoff et al published a prospective industry-funded multicenter study. The study included 135 premenopausal women at least 25 years-old with symptomatic uterine fibroids, a uterine size of 14 weeks of gestation or less, and 6 or fewer treatable fibroids, with no single fibroid larger than 7 cm. In addition, women desired to preserve their uteri but not to have children in the future. Radiofrequency thermal ablation was conducted using the Acessa system. According to the study protocol, most fibroids less than 1 cm in diameter were not treated. The primary efficacy outcomes were change in the volume of menstrual bleeding and the surgical reintervention rate after 12 months. A total of 127 of 135 women (94%) completed the study. From baseline to 12 months, 53 of 127 women (42%; 95% confidence interval, 32% to 49%) experienced at least a 50% reduction in the volume of menstrual bleeding. Most women (104/127 [82%]) experienced a decrease in menstrual bleeding at 12 months. Only 1 woman underwent a surgical reintervention during 12 months (this woman had been lost to follow-up and was not included in the other efficacy analyses). Three-year outcomes were reported by Berman et al in 2014. A total of 104 of the 135 women who participated in the study (77%) were evaluable at 3 years. Fourteen women underwent reintervention over the 3 years to treat uterine fibroid symptoms. Eleven women had hysterectomies, 2 had myomectomies, and 1 had uterine artery embolization. Bleeding outcomes were not reported for the cohort at 3 years, but the authors stated that quality-of-life variables improved from baseline to 36 months and that most of the improvement in quality of life occurred in the 3 months following the procedure.

A large retrospective case series was published by Yin et al in 2015. The study was conducted in China and used Chinese gynecologic RFA devices. It included 1216 consecutive patients treated at a single hospital over a 10-year period. All fibroids were less than 6 cm in size and mean diameter was 4.5 cm (range, 3.1-6.0 cm). Mean follow-up time was 36.5 months. Among the 476 premenopausal women, the mean reduction in myoma diameter was 2.7 cm at 6 months, 2.4 cm at 12 months, and 2.2 cm at 24 months. Among the 740 peri- or postmenopausal women, mean reduction was 3.3 cm at 6 months, 2.3 cm at 12 months, and 2.3 cm at 24 months. Myoma diameter was significantly lower at each of these time points posttreatment compared with pretreatment. In the premenopausal subgroup, the proportion of women with dysmenorrhea decreased from 43.7% at baseline to 7.6% at 12 months and to 6.7% at 24 months; rates were significantly lower after treatment.

Section Summary: Radiofrequency Volumetric Thermal Ablation

One RCT comparing RFVTA and laparoscopic myomectomy has been published. The trial found that RFVTA was noninferior to laparoscopic myomectomy on the primary outcome, length of hospitalization. A number of secondary outcomes were reported at 12 and 24 months, none of which were significantly different between groups. There were methodologic limitations, such as per protocol analyses and
substantial missing data at 12 and 24 months, and the trial may not have been adequately powered to detect differences in clinical outcomes. Additional well-designed RCTs are needed to determine the effect of RFVTA on long-term health outcomes.

**Laser and Bipolar Needles**

Several case series were identified and most of these were published in the 1990s. For example, in 1995 Goldfarb et al reported the outcomes of 300 women with symptomatic fibroids no larger than 10 cm who underwent myolysis using either Nd:YAG or bipolar needles. The author reported that the coagulating effect of the bipolar needle devascularized the fibroids, and the resulting shrinkage was comparable with that produced by Nd:YAG laser. Another study by Goldfarb et al, published in 1992, included 75 patients who presented with symptomatic fibroids 5 to 10 cm in diameter. Symptoms included pelvic pain, pressure, dyspareunia, and recurrent menorrhagia. The Nd:YAG laser was inserted into the fibroid multiple times; for example, 75 to 100 punctures were used to coagulate a 5-cm fibroid. Based on 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 complications. In 1993, Nisolle et al reported on a case series of 48 women who were apparently offered myolysis instead of myomectomy if they had completed childbearing. Although the report states that 28 of the 48 had more than 2 fibroids, it is not clear if all fibroids were treated in each patient, and if not, how the treated fibroids were selected. The authors reported that maximal decrease in fibroid size had occurred by 6 months. However, there is no report of associated patient symptoms.

Several authors have reported pelvic adhesions as a complication, 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.

**Section Summary: Laser and Bipolar Needles**

Only case series were available and most were published in the 1990s. RCTs comparing laser and bipolar needles to alternative treatments for uterine fibroids and reporting health outcomes are needed.

**Cryomyolysis**

Cryomyolysis is a technique in which a cryoprobe is inserted into the center of a fibroid. Freezing temperatures of -180°C create an “iceball” within the fibroid. Several freeze/thaw cycles are typically used. In 1998, Zreik et al published a prospective pilot study with 14 patients, and in in 2004, Zupi et al presented their experience with 20 patients. In both of these small case series, the authors reported that patients had symptom resolution. In the Zreik study, patients were given a gonadotropin-releasing hormone (GnRH) agonist before the procedure to reduce the size of the fibroid. Cryomyolysis maintained or slightly reduced the post-GnRH uterine size. In contrast, in the Zupi study, GnRH was not used, and cryomyolysis was associated with a 25% reduction in fibroid size. In 2005, Zupi et al reported 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%. Patients reported absence of symptoms. Interpretation of these studies is limited due to their small size and lack of a comparison group.
Laparoscopic and Percutaneous Techniques for the Myolysis of Uterine Fibroids

Policy # 00445
Original Effective Date: 09/17/2014
Current Effective Date: 09/21/2016

Section Summary: Cryomyolysis
Only several small case series are available. RCTs comparing cryomyolysis to alternative treatments for uterine fibroids and reporting health outcomes are needed.

Percutaneous Procedures
Magnetic resonance imaging-guided Laser Ablation
In 2002, Hindley et al reported on a case series of 66 patients with symptomatic fibroids who were treated with MRI–guided percutaneous Nd:YAG laser myolysis. Outcome measures included assessment of fibroid size and responses to a menorrhagia questionnaire. The mean reduction in fibroid size was 31%. Compared with a historical control group of women undergoing hysterectomy, the total outcome score was less in those undergoing percutaneous myolysis, but the quality-of-life score was similar. Although not entirely clear, it appears that treatment was targeted to only the largest fibroid in each patient. The study did not provide details on the number and location of fibroids.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this policy are listed in Table 1.

Table 1. Summary of Key Trials

<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>NCT01840124</td>
<td>Uterine Leiomyoma Treatment With Radiofrequency Ablation</td>
<td>100</td>
<td>Jun 2017</td>
</tr>
<tr>
<td>NCT01563783*</td>
<td>The Trust (Treatment Results of Uterine Sparing Technologies) Study</td>
<td>260</td>
<td>Dec 2021</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.
* Denotes industry-sponsored or cosponsored trial.

Summary
For individuals who have uterine fibroids who receive RFVTA, the evidence includes 1 RCT. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. The RCT found that RFVTA 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, none of which demonstrated significant between-group differences. The trial had methodologic limitations (eg, lack of intention-to-treat analysis) and the statistical hypotheses and analyses were not well-described. As a result, the validity of the reported results is decreased and no definitive conclusions about outcomes can be made. Additional high-quality RCTs are needed to determine the effect of RFVTA on long-term health outcomes. Moreover, future studies should focus more on fertility outcomes following RFVTA. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have 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 may not reflect current practice. RCTs comparing laser or bipolar needles to alternative treatments for uterine fibroids are needed to adequately evaluate the
Laparoscopic and Percutaneous Techniques for the Myolysis of Uterine Fibroids

Policy #  00445
Original Effective Date:  09/17/2014
Current Effective Date:  09/21/2016

safety and efficacy of this technology. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have 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 to alternative treatments for uterine fibroids are needed to adequately evaluate the safety and efficacy of this technology. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have uterine fibroids who receive MRI-guided laser ablation, the evidence includes 1 case series. Relevant outcomes are symptoms, quality of life, and treatment-related morbidity. A single case series (N=66) is insufficient for evaluating the technology. RCTs comparing MRI-guided laser ablation to alternative treatments for uterine fibroids are needed to adequately evaluate the safety and efficacy of this technology. The evidence is insufficient to determine the effects of the technology on health outcomes.

References
Laparoscopic and Percutaneous Techniques for the Myolysis of Uterine Fibroids

Policy # 00445
Original Effective Date: 09/17/2014
Current Effective Date: 09/21/2016


Policy History
Original Effective Date: 09/17/2014
Current Effective Date: 09/21/2016
09/04/2014 Medical Policy Committee review
08/03/2015 Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
09/03/2015 Medical Policy Committee review
09/23/2015 Medical Policy Implementation Committee approval. No change to coverage.
01/01/2016 Coding update
09/08/2016 Medical Policy Committee review
09/21/2016 Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes and CPT coding update
Next Scheduled Review Date: 09/2017

Coding
The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®), copyright 2015 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

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

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>0404T, 58578, 58999, 77022, 76940, 76998</td>
</tr>
<tr>
<td></td>
<td>Code deleted eff 1/1/17: 0336T</td>
</tr>
<tr>
<td></td>
<td>New code 1/1/17: 58674</td>
</tr>
<tr>
<td>HCPCS</td>
<td>No codes</td>
</tr>
<tr>
<td>ICD-10 Diagnosis</td>
<td>D25.0-D25.9</td>
</tr>
</tbody>
</table>

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

©2016 Blue Cross and Blue Shield of Louisiana
An independent licensee of the Blue Cross and Blue Shield Association
No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.
Laparoscopic and Percutaneous Techniques for the Myolysis of Uterine Fibroids

Policy # 00445
Original Effective Date: 09/17/2014
Current Effective Date: 09/21/2016

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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