Occlusion of Uterine Arteries Using Transcatheter Embolization or Laparoscopic Occlusion to Treat Uterine Fibroids

Policy #  00130
Original Effective Date:  03/25/2002
Current Effective Date:  02/15/2017

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.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Initial Procedure
Based on review of available data, the Company may consider transcatheter embolization of uterine arteries as a treatment of uterine fibroids or as a treatment of postpartum uterine hemorrhage to be eligible for coverage.

Patient Selection Criteria
The use of transcatheter embolization of uterine arteries as a treatment of uterine fibroids or as a treatment of postpartum uterine hemorrhage may be considered for coverage when ONE of the following criteria is met:

- Asymptomatic fibroid of such size that they are palpable abdominally and are a concern to the patient; OR
- Excessive uterine bleeding as evidenced by either profuse bleeding lasting more than eight days, or anemia due to acute or chronic blood loss; OR
- Pelvic discomfort caused by myomata, either acute severe pain, chronic lower abdominal pain or low back pressure or bladder pressure with urinary frequency not due to urinary tract infection.

Repeat Procedure
Based on review of available data, the Company may consider one repeat transcatheter embolization of uterine arteries to treat persistent symptoms of uterine fibroids after an initial uterine artery embolization (UAE) to be eligible for coverage.

Note: One repeat UAE may be performed when there is documentation of continued symptoms such as bleeding or pain. Repeat procedures may be most appropriate when there are persistent symptoms in combination with findings on imaging of an incomplete initial procedure, as evidenced by continued blood flow to the treated regions. Limited data from case series suggest a high rate of success following repeat procedures for this purpose, with the majority of patients reporting relief of symptoms.
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When Services Are 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 the use of transcatheter embolization of uterine arteries as a treatment of uterine fibroids when patient selection criteria are not met to be investigational.*

Based on review of available data, the Company considers transcatheter embolization for the management of all other indications, including cervical ectopic pregnancy, uterine arteriovenous malformation, and adenomyosis to be investigational.*

Based on review of available data, the Company considers laparoscopic occlusion of the uterine arteries using bipolar coagulation to be investigational.*

Background/Overview
Transcatheter Embolization
Transcatheter UAE is a minimally invasive technique that involves the injection of small particles into the uterine arteries to block the blood supply to the uterus and uterine fibroids. It potentially serves as an alternative to hysterectomy. Uterine artery embolization has also been used to treat other conditions including postpartum hemorrhage (PPH) cervical ectopic pregnancy, uterine arteriovenous malformations, and adenomyosis.

Uterine leiomyomata (i.e., fibroids) are extremely common benign tumors that can be located primarily within the uterine cavity (submucosal fibroids) or on the serosal surface of the uterus. Treatment for uterine fibroids is usually sought when they are associated with menorrhagia, pelvic pain, urinary symptoms (i.e., frequency), or are suspected to be the cause of infertility. Treatment options include medical therapy with gonadotropin agonists or gestagen suppression or various types of surgical therapy. Hysterectomy is considered the definitive surgical treatment for those who no longer wish to maintain fertility. Various types of myomectomy, which describes removal of the fibroid with retention of the uterus, have also been described. Hysteroscopic myomectomy involves removal of submucosal fibroids using either a resectoscope or a laser. Subserosal fibroids can be removed via an open abdominal or laparoscopic approach.

Laparoscopic laser coagulation of uterine fibroids is a unique approach in that the fibroid is not physically removed, but instead multiple (up to 75) laparoscopic laser punctures of the uterine fibroids are performed in an effort to devascularize the fibroid and induce atrophy.

There is interest in techniques to directly devascularize the uterine fibroid by interrupting the uterine arteries. One technique, UAE involves selective catheterization of the uterine arteries with injection of embolization material. Uterine artery embolization has also been used to control bleeding in other situations such as severe postpartum hemorrhage, cervical ectopic pregnancy, bleeding uterine arteriovenous malformation, and adenomyosis.
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FDA or Other Governmental Regulatory Approval
U.S. Food and Drug Administration (FDA)
In April 2000, Embosphere® Microspheres (Biosphere Medical) were cleared for marketing by the U.S. FDA through the 510(k) process for hypervascularized tumors and arteriovenous malformations (AVMs). In November 2002, this product was cleared for marketing specifically for use in uterine fibroid embolization. Since that time, several other devices have been cleared for marketing. In 2003, Contour® Emboli PVA (Boston Scientific) was cleared for the embolization of peripheral hypervascular tumors and peripheral AVMs. In March 2004, the Contour SE™ (Boston Scientific) was cleared by the FDA for treatment of uterine fibroids. In December 2008, Cook Incorporated Polyvinyl Alcohol Foam Embolization Particles received FDA marketing clearance for use in uterine fibroid embolization.

No devices have specific clearance/approval from the FDA for laparoscopic bipolar occlusion of the uterine vessels.

Rationale/Source
Transcatheter Embolization
The policy is based in part on a 2002 Technology Evaluation Center (TEC) Assessment and was updated regularly with literature searches. Following is a summary of the key literature to date on UAE therapy.

Uterine Artery Embolization for Treatment of Uterine Fibroids
A number of randomized controlled trials (RCTs) evaluating UAE for treatment of uterine fibroids and several systematic reviews of these RCTs have been published. A 2014 Cochrane review included 7 RCTs comparing UAE with other surgical interventions in women with symptomatic uterine fibroids. Four of the RCTs excluded women who desired pregnancy in the future. The comparison intervention was hysterectomy in 3 trials, hysterectomy or myomectomy in 2 trials, and myomectomy in 2 trials. The review’s primary outcomes were patient satisfaction and live birth rates (the latter analysis limited to studies where the comparison intervention was a uterine-sparing procedure). Pooled analyses did not find statistically significant differences in patient satisfaction with UAE or other interventions after 2 years (6 trials; odds ratio [OR], 0.94; 95% confidence interval [CI], 0.59 to 1.48) or 5 years (2 trials; OR=0.90; 95% CI, 0.45 to 1.80). Only 1 study reported live birth rates so meta-analysis was not possible. UAE was associated with a higher rate of minor complications at 1 year (6 trials; OR=1.99; 95% CI, 1.41 to 2.81), and there was no statistically significant difference between groups in the rate of major complications. Moreover, the UAE group was significantly less likely to require a blood transfusion than the surgery group (2 trials; OR=0.07; 95% CI, 0.01 to 0.52). The rates of further surgical interventions within 2 years was significantly increased in the UAE group (6 trials; OR=3.72; 95% CI, 2.28 to 6.04).

Systematic Reviews
In 2011, van der Kooij and colleagues published a meta-analysis of RCTs comparing UAE and surgery for treating symptomatic uterine fibroids and presented up to 5-year follow-up data. The investigators identified 11 articles reporting on 5 RCTs. The overall intra-procedural and early post-procedural complication rates were similar with the 2 procedures. However, length of hospital stay need for blood transfusion, and febrile morbidity were significantly lower in the UAE group compared to the surgery group. At 12 months, a pooled
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A 2013 systematic review by Martin and colleagues focused on complication and reintervention rates following UAE for symptomatic uterine fibroids. Eight RCTs comparing UAE to another intervention were included. Among the 350 UAE cases in the RCTs, the most common complications were discharge and fever (4%), post-embolization syndrome (2.9%), pain (2.9%) and groin complications (2.9%). Six trials also provided data on 346 cases of surgery for uterine fibroids. The most common complications following surgery were urinary stress incontinence (3.8%), pressure symptoms (2.9%) and menorrhagia (2.6%). Three trials presented reintervention data and, in a meta-analysis of these studies, there was a significantly higher risk of reintervention after UAE compared to surgery, but a wide CI indicating imprecision of the risk estimate (OR: 6.04, 95% CI: 2.0 to 18.1).

A 2014 systematic review and meta-analysis by Das et al identified 10 studies comparing the efficacy of 1 embolic agent used in UAE to another intervention or comparing 2 embolic agents. Five studies were RCTs and 5 were controlled trials that were not randomized. Embosphere microspheres were used in all of the RCTs. In a pooled analysis of data from 2 studies comparing Embosphere with spherical polyvinyl alcohol for treatment of uterine fibroids, there was no statistically significantly between-group difference in outcomes (uterine volume reduction and dominant fibroid volume reduction). Data from other studies were not pooled, but a qualitative analysis of study findings did not suggest that any agent was clearly superior or inferior to any other agent.

Randomized Controlled Trials

The Randomized Trial of Embolization versus Surgical Treatment for Fibroids (REST) multicenter trial assigned patients in a 2:1 ratio to undergo UAE (n = 106) or surgery (43 hysterectomies and 8 myomectomies). The embolization group had lower postoperative pain (3.0 vs. 4.6, respectively) and faster recovery (e.g., 1- vs. 5-day median hospitalization, respectively). Of 7 identified pregnancies in the UAE group, 2 resulted in successful live births. Five-year follow-up data from the REST trial were published in 2011. A total of 144 of 157 (92%) randomized patients were included in the 5-year analysis. Quality-of-life and symptom scores were similar in the 2 groups at 5 years. For example, the mean symptom score was 4.5 in the UAE group and 4.8 in the surgery group (scores ranged from 15, markedly worse to 5, markedly better). By the 5-year follow-up, 27 of 106 (25%) in the UAE group and 2 of 51 (4%) in the surgery group had received an additional intervention for continued or recurrent symptoms. The total rate of further intervention for symptoms or adverse events over the 5-year period was 32% in the UAE group and 4% after surgery. In the UAE group, there were 3 technical failures of the procedure, 8 repeat UAEs, and 18 hysterectomies. Note that one woman had both a repeat UAE and a hysterectomy, and 2 women were not embolized after randomization and subsequently underwent surgery.
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The Embolization versus hysterectomy (EMMY) trial from the Netherlands included 177 women with uterine fibroids and heavy menstrual bleeding who were scheduled to undergo hysterectomy. They were randomized to receive UAE (n = 88) or hysterectomy (n = 89). By the 2-year follow-up, 19 of the 81 (23%) women who actually received UAE had undergone a hysterectomy. An analysis of health-related quality of life (HRQOL) outcomes at 2 years found similar improvement in both groups overall. The defecation distress inventory (DDI) score improved significantly in only the UAE group starting at 6 months. A report of 5-year outcome data from the EMMY trial was published in 2010. A total of 70 of the 89 (79%) patients originally randomized to the hysterectomy group and 75 of 88 (85%) in the UAE group completed questionnaires at 60 months. In an intention-to-treat (ITT) analysis, 23 of 81 (28.4%) women who had received UAE underwent hysterectomy during the 5 years. Including the hysterectomies, 58 of 81 (71.6%) women in the UAE group no longer had menorrhagia. There were no significant differences between groups in HRQOL at 5 years, as assessed by mental and physical components of the Short Form-36 (SF-36). Ten-year outcomes were reported by de Bruijn et al in 2016.11 Completed questionnaires were available for 131 (75%) of 177 randomized patients at 10 years. An additional 5 hysterectomies were performed between the 5- and 10-year follow-ups, for a total of 28 (35%) hysterectomies in the UAE group. At 10 years, there were no statistically significant differences between groups in HRQOL or in urinary and defecation function.

In 2012, findings of the Fibroids of the Uterus: Myomectomy versus Embolization (FUME) trial from the U.K. were published. The investigators randomized women with symptomatic fibroids to UAE (n = 82) or myomectomy (n = 81). Mean hospital stay was significantly shorter after UAE than surgery (2 vs. 4 days, respectively; p < 0.0001). There were no significant differences in minor or major complications. A total of 120 of 163 (74%) were available for the analysis of quality of life, the primary outcome measure. There were no significant differences between groups in change in quality-of-life scores from baseline to 1 year. Nine patients (11%) in the UAE group required additional intervention, and 3 patients (4%) in the myomectomy group later underwent hysterectomy.

An RCT by Hald and colleagues in Norway evaluated clinical outcomes in 66 premenopausal women (mean age: 43 years) with symptomatic uterine fibroids who were randomized to treatment with either laparoscopic occlusion of uterine arteries or UAE. Women who wanted to bear children in the future, had a large uterus, had undergone multiple previous open abdominal surgeries, and who had bleeding disorders were excluded. The primary outcome was reduction in blood loss at 6 months' post-intervention, as measured by a pictorial blood loss assessment chart. Fifty-eight women underwent treatment, 29 with UAE and 29 with laparoscopic occlusion. The proportion of women who had a reduction in blood loss after 6 months did not differ between the treatment groups (52% after UAE and 53% after laparoscopy, respectively; p = 0.96). An additional publication reported on follow-up data at a median of 48 months after treatment (range: 8-73 months). The cumulative clinical failure and recurrence rate was significantly lower for patients in the UAE group (17%, n = 5) compared to the laparoscopy group (48%, n = 17), p = 0.02. Moreover, fewer patients in the UAE group (7%, n = 2) had a hysterectomy than in the laparoscopy group (28%, n = 8), p = 0.41. The authors concluded that UAE is superior to laparoscopic UAO for treatment of uterine fibroids.
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Section Summary Initial UAE for Uterine Fibroids
A number of RCTs and systematic reviews have compared UAE and surgery (hysterectomy or myomectomy) for treating uterine fibroids. A Cochrane review found similar levels of patient satisfaction after UAE and surgery. There were a lower blood transfusion rates and higher reintervention rates after UAE. Other meta-analyses have found lower complication rates and higher reintervention rates after UAE than after surgery; however, some women were able to avoid surgery and maintain their uteruses. The available evidence from RCTs does not suggest that any one embolization agent is clearly superior to another.

Repeat UAE Procedures for Recurrent or Persistent Uterine Fibroid Symptoms
No RCTs focusing on repeat UAE were identified; there are published case series. In 2009, McLucas and Reed published a study in which the charts of 1058 women who had undergone initial bilateral UAE at several U.S. centers were reviewed. Forty-two (4%) patients had documented persistent symptoms, and they were offered a second bilateral UAE. Thirty-nine patients had repeat procedures, and 34 (87%) of them completed a follow-up questionnaire at least 6 months postembolization. Before the second UAE procedure, 27 (79%) of the 34 women reported severe bleeding, with only 2 (6%) women reported severe bleeding postprocedure. Similarly, the number of women with severe pain decreased from 20 (59%) to 2 (6%), and with severe pressure decreased from 18 (53%) to 2 (6%). Four women experienced severe levels of 1 or more symptoms after the second UAE.

In 2006, Yousefi and colleagues reported on 24 patients who underwent repeat embolization for recurrent or persistent symptoms 6-66 months after the initial procedure. The most common symptoms were pressure and/or bulk symptoms (n = 15), recurrent heavy bleeding, (n = 12) and pelvic pain or cramping (n = 7). Follow-up data were available on 21 of 24 (87.5%) after the second UAE; 19 (90%) reported symptom control.

Section Summary Repeat UAE Procedures for Recurrent or Persistent Uterine Fibroid Symptoms
There is a lack of RCTs on repeat UAE for treatment of symptoms associated with uterine fibroids. However, there are data from case series showing a high rate of success after a second UAE for recurrent or persistent symptoms. Moreover, evidence from RCTs on the safety and efficacy of an initial UAE for treating uterine fibroids can be extrapolated to the repeat UAE situation.

Uterine Artery Embolization for treatment of Postpartum Uterine Hemorrhage (PPH)
Systematic Reviews
No RCTs or other comparative studies evaluating UAE for treating postpartum hemorrhage were identified. Several systematic reviews of the literature on treatments for postpartum hemorrhage have been published. In 2016, Sathe et al reported that rates of successful bleeding control with UAE in uncontrolled studies ranged from 58% to 98%, with a total of 1251 (87%) of 1435 patients in 15 studies achieving successful control of bleeding.17 Previously, In 2012, Rath et al published a systematic review of literature on second-line treatment of postpartum hemorrhage.18 Success rates of UAE for postpartum hemorrhage reported in uncontrolled studies ranged from 70% to 100%, and from 60% to 83% in placenta accreta.
Case Series

Representative larger case series are described below:

In 2013, Kim et al evaluated data on 60 women who underwent UAE for treatment of postpartum hemorrhage at a single center in Korea. The clinical success rate (which was not explicitly defined) was reported as 96%. Eleven patients treated with UAE experienced transient fever after the procedure, and there was 1 case of ovarian failure. During the time of data collection for this study, another 61 patients at the same center underwent cesarean hysterectomy for treatment of postpartum hemorrhage; the success rate associated with that procedure was 93%.

In 2011, Ganguli and colleagues published data on 66 women who underwent UAE for the treatment of postpartum hemorrhage. The clinical success rate, defined as obviation of hysterectomy, was 95%. Three of 66 (5%) women had a subsequent hysterectomy. In addition to the 3 clinical failures, there were 3 (5%) major complications after UAE: one case of lower-extremity deep vein thrombosis, one case of postprocedural pancreatitis, and one admission for intravenous antibiotic treatment for presumed endometritis. Nine pregnancies after UAE were identified; there were 2 spontaneous abortions and 7 viable gestations.

In 2009, Kirby and colleagues published a retrospective analysis of data from 43 women who underwent UAE for primary PPH. In this study, clinical success was defined as cessation of bleeding without need for repeat embolization, laparotomy or hysterectomy and without mortality. Eight of 43 (19%) of women had a hysterectomy prior to UAE. Of the remaining 35 women, clinical success was achieved in 29 women (83%). Considering the sample as a whole, the clinical success rate was 29 of 43 (67%). Complications among women who had a UAE without a previous hysterectomy included one case of a groin hematoma, one inadvertent perforation of the left obturator artery during UAE, one bleeding necrotic fibroid tumor, and one case of symptoms consistent with endometritis.

Section Summary UAE for Postpartum Uterine Hemorrhage

There is a lack of RCTs or other controlled studies on repeat UAE for treatment of postpartum hemorrhage. Case series involving nearly 1500 patients have shown a high rate of successfully stopping bleeding. Without treatment, there is a high likelihood of significant ongoing hemorrhage and maternal mortality. Given that this is an emergent, often clinically complex situation that can result in maternal mortality, it may not be practical to conduct RCTs and positive case series data may suffice.

Fertility and Pregnancy Outcomes after UAE for Uterine Fibroids or Postpartum Hemorrhage

Several systematic reviews on fertility and pregnancy outcomes after UAE have been published. In 2014, Doumouchtsis et al identified 17 studies (total N=675 participants) reporting on fertility outcomes after UAE for postpartum hemorrhage. To be selected, studies had to report on a minimum of 5 cases. None identified was an RCT. A total of 168 (25%) of the 675 patients wanted a pregnancy following UAE, and 126 (75%) of the 168 women who desired pregnancy conceived. There were 136 term live births and 30 cases of pregnancy loss (ectopic pregnancy, miscarriage, elective abortion). Previously, in 2013, Mohan et al identified 21 studies reporting pregnancy outcomes and/or pregnancy complications after UAE for treatment of uterine fibroids or postpartum hemorrhage. The authors reported that the cumulative pregnancy and
miscarriage rates among women trying to conceive following UAE for uterine fibroids were 59% and 28%, respectively, and the cumulative live birth rate was 65%. The term delivery rate was 61%. In the studies on UAE for postpartum hemorrhage, the cumulative pregnancy rate, based on a small number of pregnancies, was 87.2%. Rates of miscarriage and live births were not reported following UAE for postpartum hemorrhage. Most studies included in the systematic review were observational and had no or inadequate controls. There was 1 RCT. This 2008 study, by Mara et al in Czech Republic, randomized 121 women with uterine fibroids who desired future pregnancies to UAE or myomectomy. Participants were followed for a mean of 25 months; they were advised to wait for at least 6 months postprocedure before attempting to conceive. At final follow-up, 13 (50%) of 26 women in the UAE group who tried to conceive became pregnant compared with 31 (76%) of 40 in the myomectomy group; the difference between groups was not statistically significant. Among women in the UAE group who became pregnant, the abortion rate was 64% and the delivery rate was 19%. In the myomectomy group, the abortion rate was 23%, and the delivery rate was 48%.

Section Summary: Fertility and Pregnancy Outcomes after UAE for Uterine Fibroids or Postpartum Hemorrhage
Reviews of fertility and pregnancy outcomes after UAE have suggested that successful pregnancy is possible after UAE for treatment of uterine fibroids or postpartum hemorrhage. One review found higher rates of miscarriage and postpartum hemorrhage with UAE than with myomectomy. There are limited data on pregnancy outcomes in women who became pregnant following UAE for treatment of postpartum hemorrhage.

UAE for Cervical Ectopic Pregnancy
No RCTs or other comparative studies evaluating UAE for treating cervical ectopic pregnancy were identified. The published literature consisted of small case series. Sample sizes ranged from 2 to 20 patients, and most studies had fewer than 10 patients. The largest prospective series was conducted in China by Xiaolin et al. Patients received methotrexate injections before, during, and after the UAE procedure. Median follow-up was 12 months (range, 1-50 months). Two (10%) of 20 patients had recurrent vaginal bleeding; the other 18 had no significant bleeding after UAE. Five (25%) patients had an additional curettage procedure due to bleeding and/or high levels of β-human chorionic gonadotropin. The uterus was preserved in all patients, and normal menses resumed after 2 to 4 months. Eight (50%) of 16 women who attempted to conceive achieved a normal pregnancy within 1 year. There were 2 miscarriages and 6 live births at term.

Section Summary: UAE for Cervical Ectopic Pregnancy
There is a lack of RCTs or other controlled studies on repeat UAE for treatment of cervical ectopic pregnancy. Only a few case series are available, the largest of which included 20 patients. The limited noncomparative evidence is insufficient to determine the effect of UAE on health outcomes. Additional data, ideally controlled trials comparing UAE to alternative treatments (eg, medication, surgery) are needed to determine the safety and efficacy of UAE for treating cervical ectopic pregnancy.
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UAE for Uterine Arteriovenous Malformation
No RCTs or other comparative studies evaluating UAE for treating uterine arteriovenous malformations (AVMs) were identified. The published literature consists of case reports, small case series, and a systematic review. A 2016 systematic review of literature on acquired uterine AVMs identified 54 women treated with UAE in 40 studies, primarily case reports. There were 22 unilateral and 32 bilateral procedures. Thirty-three (61%) of 54 patients had symptoms controlled with the initial embolization procedure. No major complications were reported after UAE. The most recent and largest series, published in 2014 by Kim et al in Korea, retrospectively reviewed data from a single center on 19 patients who underwent UAE as first-line treatment of bleeding uterine AVMs. All patients presented with intermittent or progressive vaginal bleeding after gynecologic procedures or obstetric events. The UAE procedures were bilateral, and a variety of embolization agents were used. Seventeen (89.5%) of 19 patients had immediate clinical success following the UAE, defined as cessation of bleeding without symptom recurrence and resolution of the uterine AVMs on postoperative imaging studies.

Section Summary: UAE for Uterine Arteriovenous Malformation
The limited noncomparative evidence is insufficient to determine the effect of UAE on health outcomes in patients with bleeding associated with uterine AVMs. Additional data, ideally controlled trials comparing UAE to alternative treatments (eg, hysterectomy), are needed to determine the safety and efficacy of UAE for treating uterine AVMs.

UAE for Adenomyosis

Systematic Reviews
No RCTs or other comparative studies evaluating UAE for treating adenomyosis were identified. A 2011 systematic review by Popovic et al evaluated literature on UAE for patients with adenomyosis, alone or in conjunction with uterine fibroids. The reviewers identified 8 case series reporting short-term follow-up in patients with adenomyosis alone. After a median follow-up of 9.4 months (range, 3-12 months), 85 (83%) of 102 patients had marked or complete improvement in clinical symptoms. Six case series reported long-term follow-up (median, 40.6 months; range, 17-60 months). Marked or complete improvement occurred in 135 (65%) of 208 patients, suggesting recurrence of symptoms over time in some patients. No deaths or serious adverse events were reported.

Case Series
Additional case series have been published after the Popovic systematic review. In 2016, Wang et al prospectively reported on 117 premenopausal patients with adenomyosis who underwent UAE. A total of 115 (98%) of 117 patients who successfully underwent bilateral UAE were included in the analysis. At 12 months, patients were queried about change in dysmenorrhea symptoms. Thirteen (11.3%) patients reported slight symptom improvement, 64 (55.7%) reported moderate improvement, and 31 (27.0%) reported marked improvement. Seven (6%) patients reported no change. In 2015, Bae et al retrospectively reviewed outcomes in 50 women who underwent UAE for symptomatic adenomyosis and were followed for at least 18 months. At baseline, 41 (82%) of 50 women had both heavy menstrual bleeding and dysmenorrhea; the remainder reported only 1 of these 2 symptoms. The extent of necrosis of adenomyosis was significantly associated with the likelihood of experiencing symptoms at follow-up. In receiver operating
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characteristic curve analysis, a cutoff of 34.3% necrosis was the most predictive of symptom recurrence (area under the curve, 0.721; 95% CI, 0.577 to 0.839; p=0.004). Among 12 patients with less than 34.3% necrosis, 58% were symptom-free at 18 months; among 40 patients with greater than 34.3% necrosis, 94% were symptom-free at 18 months.

Section Summary: UAE for Adenomyosis
There is a lack of RCTs or other controlled studies on repeat UAE for treatment of cervical ectopic pregnancy. Several case series and a systematic review are available. The systematic review found short-term symptom improvement in 83% of patients and long-term improvement in 65% of patients. Additional data from controlled trials are needed, especially on long-term efficacy and recurrence rates.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review 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>
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<tr>
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<td>NCT00995878</td>
<td>The FIRSTT Study: Comparing Focused Ultrasound and Uterine Artery Embolization for Uterine Fibroids</td>
<td>180</td>
<td>Dec 2016</td>
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<tr>
<td>NCT01834703</td>
<td>Randomized Controlled Trial of Uterine Artery Embolization (UAE) Versus High-Intensity-Focused-Ultrasound (HIFU) for Treatment of Patients With Uterine Fibroids</td>
<td>200</td>
<td>May 2017</td>
</tr>
</tbody>
</table>

NA: not available; NCT: national clinical trial.

Summary of Evidence
For individuals who have uterine fibroids who receive transcatheter UAE, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, quality of life, resource utilization, and treatment-related morbidity. The studies have generally found similar levels of symptoms and quality of life after UAE versus surgery. There were more reinterventions in the UAE group, but some women avoided surgery and maintained their uteruses. Moreover, studies have found lower complication rates after UAE versus surgery. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have persistent uterine fibroids despite prior uterine artery embolization who receive repeat transcatheter UAE, the evidence includes case series. Relevant outcomes are symptoms, quality of life, resource utilization, and treatment-related morbidity. Case series have shown that a high degree of symptom relief is possible after a repeat UAE for uterine fibroids. Moreover, evidence from RCTs on the safety and efficacy of UAE for initial treatment of uterine fibroids can be extrapolated to repeat procedures for the same indication. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.
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For individuals who have postpartum uterine hemorrhage who receive transcatheter UAE, the evidence includes case series and a systematic review. Relevant outcomes are overall survival, symptoms, and treatment-related morbidity. The systematic review of case series with over 1400 women found a rate of success of stopping bleeding. Postpartum uterine hemorrhage is an emergency situation with serious potential consequences (i.e., maternal mortality). Conducting RCTs is particularly difficult in this setting and may be unnecessary when there are sufficient uncontrolled data. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have cervical ectopic pregnancy who receive transcatheter UAE, the evidence includes case series. Relevant outcomes are resource utilization and treatment-related morbidity. Only a few case series with a small number of patients have been published. Additional studies, especially controlled studies comparing UAE to medication or surgery, are needed to draw conclusions about the safety and efficacy of UAE in patients with cervical ectopic pregnancy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have uterine AVM who receive transcatheter UAE, the evidence includes case reports, case series, and a systematic review. Relevant outcomes are symptoms, resource utilization, and treatment-related morbidity. Only case reports and case series with a small number of patients have been published. A systematic review identified 54 women in 40 studies with uterine AVM treated using UAE. Additional studies, especially controlled studies comparing UAE to hysterectomy, are needed to draw conclusions about the safety and efficacy of UAE in patients with uterine AVM. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have adenomyosis who receive transcatheter UAE, the evidence includes case series and a systematic review. Relevant outcomes are symptoms, resource utilization, and treatment-related morbidity. A systematic review of case series data found short-term improvement in 83% of patients and long-term improvement in 65% of patients, suggesting possible recurrence of symptoms over time. All studies were case series and may have been subject to selection and/or observational biases. Controlled studies comparing UAE to medication or surgery and studies reporting long-term symptom recurrence rates are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

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04/15/2003 Medical Policy Committee review
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06/28/2004 Managed Care Advisory Council approval
06/07/2005 Medical Director review
06/21/2005 Medical Policy Committee review. Format revision. Patient selection criteria added. Clinical criteria revision to include laparoscopic closure of uterine arteries. Policy title changed from, "Transcatheter Uterine Artery Embolization" to "Oclusion of Uterine Arteries Using Transcatheter Embolization or Laparoscopic Occlusion to Treat Uterine Fibroids".
07/15/2005 Managed Care Advisory Council approval
07/07/2006 Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
09/06/2006 Medical Director review
09/20/2006 Medical Policy Committee approval. No change to policy guidelines.
11/07/2007 Medical Director review
11/15/2007 Medical Policy Committee approval. No change to policy guidelines.
11/05/2008 Medical Director review
11/18/2008 Medical Policy Committee approval. No change to coverage eligibility.
11/12/2009 Medical Policy Committee approval
11/18/2009 Medical Policy Implementation Committee approval. No change to coverage eligibility.
11/04/2010 Medical Policy Committee approval
11/16/2010 Medical Policy Implementation Committee approval. No change to coverage eligibility.
11/03/2011 Medical Policy Committee approval
11/16/2011 Medical Policy Implementation Committee approval. No change to coverage eligibility.
11/01/2012 Medical Policy Committee review
11/28/2012 Medical Policy Implementation Committee approval. Postpartum uterine hemorrhage added to eligible for coverage statement. Investigational statement added on UAE for management cervical ectopic pregnancy. Statement on repeat UAE changed to state that one repeat procedure may be considered eligible for coverage with a Note following the coverage statement.
11/07/2013 Medical Policy Committee review
02/05/2015 Medical Policy Committee review
02/18/2015 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/03/2015 Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
02/04/2016 Medical Policy Committee review.
02/17/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
02/02/2017 Medical Policy Committee review.
02/15/2017 Medical Policy Implementation Committee approval. Adenomyosis and uterine arteriovenous malformation added to investigational policy statement.

Next Scheduled Review Date: 02/2018
Occlusion of Uterine Arteries Using Transcatheter Embolization or Laparoscopic Occlusion to Treat Uterine Fibroids

Policy # 00130
Original Effective Date: 03/25/2002
Current Effective Date: 02/15/2017

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

<table>
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<th>Code Type</th>
<th>Code</th>
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<tr>
<td>CPT</td>
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*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:

A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the 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 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.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. in accordance with nationally accepted standards of medical practice;

B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
Occlusion of Uterine Arteries Using Transcatheter Embolization or Laparoscopic Occlusion to Treat Uterine Fibroids

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C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and 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 that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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