DYSFUNCTIONAL UTERINE BLEEDING AND UTERINE FIBROIDS

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CONDITIONS OF COVERAGE

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Note: This policy describes minimally invasive treatments used to treat uterine fibroids and reduce excessive blood loss in women with abnormal uterine bleeding.
DESCRIPTION OF SERVICE/BACKGROUND INFORMATION

Abnormal uterine bleeding in women of childbearing age is defined as any change in menstrual period frequency or duration, a change in amount of flow, or any bleeding between cycles. In postmenopausal women, abnormal uterine bleeding includes vaginal bleeding 12 months or more after the cessation of menstruation, or unpredictable bleeding in patients who have been receiving hormone therapy for 12 months or more. Abnormal uterine bleeding terms include oligomenorrhea (bleeding occurs at intervals of more than 35 days), polymenorrhea (bleeding occurs at intervals of less than 21 days), menorrhagia (bleeding occurs at normal intervals but with heavy flow or duration of more than 7 days), menometrorrhagia (bleeding occurs at irregular, noncyclic intervals and with heavy flow or duration more than 7 days), and metrorrhagia (irregular bleeding occurs between ovulatory cycles) (Milliman Care Guidelines). Menorrhagia can be idiopathic or can be associated with underlying uterine lesions such as fibroids or polyps, pelvic pathology, anatomical abnormalities, systemic illness, hormonal imbalance or certain medications. Idiopathic menorrhagia that is not related to a specific underlying condition is called dysfunctional uterine bleeding (DUB). All these conditions associated with menorrhagia can be referred to as dysfunctional uterine bleeding, although it is also possible to have some conditions such as fibroids or an anatomical abnormality with normal menses. The focus in this policy is on treatment options when the bleeding pattern is abnormal.

Conservative management of DUB includes watchful waiting and pharmacological therapy. Another treatment option is dilation and curettage. Hysterectomy is available when symptoms cannot be controlled by conservative treatment. Conservative management of symptomatic fibroids includes watchful waiting and hormonal therapy. Hormone therapy causes the fibroids to shrink; however they will quickly return to their original mass once therapy has been discontinued. Hysterectomy has been the primary treatment for symptomatic or rapidly enlarging fibroids. Hysteroscopic removal of fibroids has been the procedure of choice for those women who want to maintain their fertility, but this is a demanding and lengthy procedure and sometimes more difficult to perform than a hysterectomy and does not prevent the recurrence of fibroids. The resulting endometrial cavity may be problematic for fertility.

Alternate minimally invasive techniques have emerged. An advantage of these procedures over hysterectomy is that they do not involve surgical removal of the uterus; therefore, the operative and recovery times are shorter and the complication rates seem to be lower. Some may be performed as outpatient procedures, avoiding the hospital stay required after hysterectomy.

Uterine fibroids (also known as leiomyomata) are benign tumors of the uterus. They have a rich blood supply and may cause excessive uterine bleeding, uterine enlargement and mass or bulk related symptoms such as pelvic pain and pressure, urinary frequency and abdominal distension.

**Endometrial Cryoablation (ECA):** In this procedure, a cryoprobe introduced through the vagina under ultrasound guidance delivers extreme cold (below -15° C to -20° C) in freeze-thaw cycles to the endometrium.

**Thermal Balloon Endometrial Ablation (TBEA):** In this procedure, heat is delivered to the endometrial lining of the uterus via a latex balloon is filled with a small volume of sterile dextrose and water. The temperature of the fluid is raised by a heating element to 87 degrees C resulting in thermal coagulation of 3 to 5 mm of endometrium. A variation of this technique, hydrothermal endometrial ablation (HTEA), involves direct exposure of the uterine lining to saline heated to 90 degrees C.

**Radiofrequency Endometrial Ablation (RFA):** This procedure uses a radiofrequency signal generator, a controller and a probe to generate heat in the uterus in an attempt to destroy the endometrial lining.

**Microwave Endometrial Ablation (MEA):** This procedure uses microwave energy to ablate the endometrium.
Manual Endometrial Ablation: This includes procedures that use a resectoscope to surgically remove, electrically desiccate or vaporize the endometrium, as well as laser destruction of the endometrium.

Levonorgestrel-Releasing Intrauterine Device (LNG-IUD): The local administration of the progestin levonorgestrel is delivered via an intrauterine device (IUD). The MIRENA® device consists of a T-shaped polyethylene frame with a steroid reservoir around the vertical stem. The reservoir contains 52 mg of levonorgestrel, which is released at a dose of 20 ug per day. The local delivery of this hormone causes the endometrium to become insensitive to ovarian estradiol leading to atrophy of the endometrial glands, inactivation of the endometrial epithelium and suppression of endometrial growth and activity. The effects of this IUD last for approximately 5 years and are reversible upon removal of the IUD.

Magnetic Resonance Imaging (MRI)-Guided Cryoablation: This procedure is also known as interventional MRI (I-MRI) cryoablation. It uses a specially designed, i-MRI scanner to locate the fibroids and guide their cryosurgical destruction through a transabdominal percutaneous approach.

Magnetic Resonance Imaging (MRI)-Guided Focused Ultrasound (FUA): This procedure combines real-time MRI-guidance with high-intensity focused ultrasound for the noninvasive thermal ablation of uterine fibroids. Tumor ablation is performed by focusing a collection of ultrasonic beams to increase sonic beam intensity at a point deep within the tissue to cause thermal coagulation while sparing normal tissues. The procedure is also referred to as MRgFUS.

Uterine Artery Embolization (UAE): This procedure attempts to block the blood supply to uterine fibroid tumors thus promoting shrinkage through blood deprivation. For UAE to be effective, the arteries and their vascular beds must be completely occluded. The resultant ischemia can result in postembolization pain, but the abundant collateral blood supply in the pelvis protects against ischemic necrosis.

CLINICAL EVIDENCE

Endometrial Ablation
A 2009 Cochrane systematic review by Lethaby et al. compared the efficacy, safety and acceptability of methods used to destroy the endometrium to reduce heavy menstrual bleeding (HMB) in premenopausal women. The evidence base included 21 RCTs comparing different endometrial ablation techniques in women (n = 3395, mostly within the age range 30 to 55 years) with HMB. The outcomes included reduction of HMB, improvement in quality of life (QOL), operative outcomes, satisfaction with the outcome, complications and need for further surgery or hysterectomy. Duration of surgery was an average of 15 minutes less, local anesthesia was more likely to be used and equipment malfunction was more likely with second-generation ablation. In addition, women who underwent more recent ablative procedures compared to those who underwent the more traditional type of ablation and resection were less likely to have complications such as fluid overload, uterine perforation, cervical lacerations and hematometra. The authors concluded that endometrial ablation techniques offer a less invasive surgical alternative to hysterectomy.

Cryoablation
A National Institute for Health and Clinical Excellence (NICE) guidance document states that limited short-term evidence on the safety and efficacy of endometrial cryotherapy for menorrhagia appears adequate to support the use of this procedure in carefully selected patients provided that normal arrangements are in place for consent, audit and clinical governance (NICE, 2006).

Zupi et al. (2005) reported on cryomyolysis with the HerOption Cryoablation Unit for treatment of symptomatic uterine myomas in 20 menstruating women. At one year follow-up, all patients reported no bleeding and no myoma-related symptoms, comparable with patients who underwent
hysterectomy. Mean reduction of myoma volume was 60% one year after surgery. No intraoperative or postoperative complications occurred.

**Thermal Balloon Endometrial Ablation (TBEA) and Hydrothermal Endometrial Ablation (HTEA)**

Barrington et al. (2003) reported no significant differences between TBEA and the levonorgestrel-intrauterine system (LNG-IUS), an intrauterine device that continuously releases a hormone. In this study, 50 women were randomized to menorrhagia treatment with TBEA or the LNG-IUS and at 6 months follow-up, the two treatments had essentially equal efficacy. After TBEA, menstrual blood loss ended for 9% of patients and menstrual blood loss decreased for another 70%.

A randomized controlled trial by Hawe et al. (2003) enrolled 71 patients and compared TBEA with endometrial ablation using a surgical laser. Again, the two minimally invasive techniques for endometrial ablation had essentially equal efficacy and 1 year after TBEA, 29% of women had no menstrual blood loss, 44% had loss that was less than normal menstrual blood loss, and 12% had normal levels of blood loss.

Three case series studies of women with menorrhagia (total n = 205) treated by thermal balloon ablation with a follow-up ranging from 6 months to 3 years had overall improvement rates ranging from 65 to 85% with only minor complications (Clark, 2004; Gallinat, 2004; Shaamash, 2004).

Cooley et al. (2005) determined the medium-term (1-3 years) and long-term (3-5 years) outcome for 44 women who underwent ablation by uterine balloon technique and 40 women who had ablation by VESTA (radiofrequency) technique. Outcome measures were the amenorrhea rate and patient satisfaction and were determined by chart review and questionnaire. Combined medium-term follow-up had a success rate of 90%; long-term follow-up had a success rate of 80% and a patient satisfaction rate of 73%.

Two cohort studies evaluated HTEA for the management of menorrhagia in women with myomata. One year after treatment, Glasser and Zimmerman (2003) evaluated twenty-two women with myomata up to 4 cm. in diameter who were treated for menorrhagia with HTEA. Twelve patients reported complete amenorrhea (7 of these women were premenopausal and 5 were postmenopausal), five women reported oligomenorrhea and 3 reported eumenorrhea. There were 2 failures which resulted in one woman having a repeat HTEA for menorrhagia and another electing to have a vaginal hysterectomy.

Rosenbaum et al. (2005) evaluated HTEA in 47 premenopausal women with abnormal uterine bleeding; 20 of these women had normal endometrial cavities and 27 had had intracavitary pathology, most often leiomyomas. Follow-up ranged from 5 to 25 months with a mean of 12.7 months. Baseline and follow-up scores were similar for both groups.

**Radiofrequency Endometrial Ablation (RFA)**

Kleijn et al. (2008) previously reported that NovaSure was more effective than balloon ablation at 12 months follow up in the treatment of menorrhagia. In this follow-up study, the same authors report 5-year outcomes. The objective was to evaluate amenorrhea rates, hysterectomy rate and quality of life associated with the bipolar impedance-controlled endometrial ablation technique (NovaSure) in comparison with balloon ablation technique (ThermaChoice) at 5 years after administration. A total of 126 premenopausal women with menorrhagia were randomly allocated to bipolar radio-frequency ablation and balloon ablation in a 2:1 ratio. At 5 years of follow up, amenorrhea was reported in the bipolar group by 48% of women and in the balloon arm by 32%. There were eight women in the bipolar group (9.8%) and five in the balloon group (12.9%) who had undergone a hysterectomy. Furthermore, there was a significant equal improvement of health-related QoL over time in both groups. The authors concluded that, at 5 years follow up, bipolar thermal ablation was superior over balloon ablation in the treatment of menorrhagia.

Bongers et al. (2004) compared the effectiveness of two second-generation ablation techniques, bipolar radio-frequency impedance-controlled endometrial ablation (NovaSure) and balloon ablation (ThermaChoice), in the treatment of menorrhagia. One hundred twenty-six women with
menorrhagia, without intracavitary abnormalities, were randomly allocated to bipolar radio-frequency ablation (bipolar group) (n=83) and balloon ablation (balloon group) (n=43) in a 2:1 ratio. At follow up, both women and observers were unaware of the type of treatment that had been performed. The main outcome measure was amenorrhea at 3, 6 and 12 months after randomization. At the one-year follow up stage, amenorrhea rates were 43% (34/83) in the bipolar group and 8% (3/43) in the balloon group. At this stage, 90% of the patients in the bipolar group were satisfied with the result of the treatment against 79% in the balloon group.

Thermal balloon ablation was compared with RFA in 1 randomized, 2-arm clinical trial and in 1 nonrandomized, multi-center, 2-arm trial (Abbott, 2003; Laberge, 2003). In these studies, treatment time was significantly shorter for RFA (3 to 4 minutes) compared with thermal balloon ablation (12 to 23 minutes). At 12 months follow-up, RFA was effective in 96% of patients; 43% of patients developed amenorrhea, 27% hypomenorrhea, and 16% eumenorrhea (Abbott, 2003). Thermal balloon ablation was effective in 100% of patients; 12% of patients developed amenorrhea, 59% hypomenorrhea, and 29% eumenorrhea. RFA caused less intra- and postoperative pain compared with thermal balloon ablation (Laberge, 2003). The Abbott study had the statistical power to detect a 20% difference in efficacy based on the PBAC scores. The results therefore suggest that the efficacy of RFA compares to that of thermal balloon ablation.

A National Institute for Health and Clinical Excellence (NICE) guidance document states that while information is lacking about the long-term results of the procedure, current evidence on the safety and efficacy of impedance-controlled bipolar radiofrequency ablation for menorrhagia appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance (NICE, 2004).

**Microwave Endometrial Ablation (MEA)**

In a systematic review, Garside et al. (2005) compared the effectiveness of microwave and thermal balloon endometrial ablation with first generation techniques of endometrial ablation to treat heavy menstrual bleeding in women. Two randomized controlled trials of microwave endometrial ablation and eight trials (six randomized controlled trials) of thermal balloon endometrial ablation were included in the review. No significant differences were found between first and second generation techniques in terms of amenorrhea, bleeding patterns, pre-menstrual symptoms, patient satisfaction or quality of life. Microwave endometrial ablation and thermal balloon endometrial ablation had significantly shorter operating times than first generation techniques. Adverse effects were few with all techniques, but there were fewer peri-operative adverse effects with second generation techniques.

Cooper et al. (2004) compared the effectiveness, safety and acceptability of microwave endometrial ablation (MEA) with those of rollerball electroablation (REA) for the treatment of menorrhagia. Three hundred twenty-two women with documented menorrhagia due to benign causes were randomized to either MEA or REA in a 2:1 allocation scheme. Of the 215 patients in the MEA group, 209 were treated, with 194 available for evaluation at 1 year. Of the 107 patients in the REA group, 106 were treated, with 96 available for evaluation at 1 year. The success rate of MEA at 12 months did not differ significantly from that of REA. The amenorrhea rate in evaluable patients after MEA was 61.3% and 51% after REA. Patient satisfaction with results of treatment was high (98.5% of the MEA and 99.0% of the REA group). The authors concluded that MEA is an efficacious and safe procedure for the treatment of menorrhagia and is suitable for women with myomas and irregular uterine cavities.

Cooper, et al. (1999) conducted a randomized controlled trial, comparing microwave endometrial ablation (MEA) with transcervical resection of the endometrium (TCRE), for women with heavy menstrual loss. Two hundred sixty three women were randomly assigned to MEA (n=129) or TCRE (n=134). Questionnaires were completed at recruitment and at 12 months' follow-up. The primary outcome measures were patients' satisfaction with and the acceptability of treatment. At 1 year of follow-up, 116 of the 129 women in the MEA group and 124 or the 134 women in the TCRE group were available for evaluation. At 1 year, 89 (77%) women in the MEA group and 93 (75%) in the TCRE group were totally or generally satisfied with their treatment and 109 (94%) versus 112 (90%) found it acceptable. Mean operating times were shorter for MEA than for TCRE.
(11.4 vs 15.0 min) and the postoperative stay slightly but not significantly shorter. Of eight health-related quality of life dimensions, all were improved after MEA (six significantly) and seven were improved after TCRE (all significantly). Both techniques achieved high rates of satisfaction and acceptability and both improved quality of life after 1 year. Follow-up after 2, 5 and 10 years reported similar results (Bain, 2002; Cooper, 2005; Sambrook, 2009).

**Magnetic Resonance Imaging (MRI)-Guided Cryoablation**

Two feasibility studies representing an ongoing, manufacturer-sponsored clinical trial on this specific technique that were conducted at the same study center were identified in the peer-reviewed literature. The first study consisted of 2 patients who were included in the second study. The second published study is a prospective case series that evaluated the efficacy and safety of MRI-guided cryoablation of uterine fibroids in 9 symptomatic women whose disease was confirmed by clinical examination and MRI. The outcomes assessed included surgical time, postoperative fibroid volume, postoperative hemoglobin level, overall reduction in fibroid size, and complications. Postoperative MRI findings were available for the patients for a period of 48 to 334 days after surgery (Sewell, 2001; Cowan, 2002).

While the preliminary data from a manufacturer-sponsored pilot study show that MRI-guided cryoablation of uterine fibroids can reduce the volume of uterine fibroids by an average of 65% as determined by serial MRI and improve patient-reported symptoms over the short term, the procedure has been evaluated in very few patients, and the long-term outcomes and overall health benefits remain unknown. During this short-term study, none of the fibroids disappeared completely, and it remains unclear whether this would eventually occur. In the clinical trial, 3 of 9 (33%) patients experienced what the researchers described as important procedure-related complications. One patient developed persistent bleeding following laceration of a tumor blood vessel. The patient required emergent laparotomy and myomectomy. She recovered without complications but was ineligible for follow-up of the cryoablation procedure since her fibroids were removed. Another patient sustained a mild peroneal nerve injury that resulted in a mild footdrop, which resolved at 4 months postoperatively. A third patient was observed for 24 hours due to nausea. No other serious complications were reported during follow-up.

Dohi et al. (2004) published a study evaluating MRI-guided transvaginal cryotherapy to treat 8 uterine fibroids. They assessed the ratio of pre-treatment to post-treatment volume of the uterine fibroids as well as symptoms of anemia, abdominal pain and dysfunctional uterine bleeding. The mean ratio of reduction in uterine fibroid volume was 31.0% at 9-12 months (0-75.0%). Symptoms caused by uterine fibroids improved in seven cases. There were no complications requiring surgical intervention.

**Magnetic Resonance Imaging (MRI)-Guided Focused Ultrasound Ablation (FUA)**

Taran et al. (2009) compared women undergoing magnetic resonance-guided focused ultrasound (MRgFUS) to a group of contemporaneously recruited women undergoing total abdominal hysterectomy. Patient demographics, safety parameters, quality of life outcomes and disability measures are reported. One hundred and nine women were recruited in seven centers for MRgFUS treatment and 83 women who underwent abdominal hysterectomy were recruited in seven separate centers to provide contemporaneous assessment of safety. Overall, the number of significant clinical complications and adverse events was lower in women in the MRgFUS group compared to women undergoing hysterectomy. MRgFUS was associated with significantly faster recovery, including resumption of usual activities. At 6 months of follow-up, there were four (4%) treatment failures in the MRgFUS arm. There was improvement in all quality of life scales for both treatment groups at 6 months. However, scores were significantly better in the hysterectomy group than in the MRgFUS group. Women undergoing MRgFUS had steady improvement in all parameters throughout the 6-month follow-up period, despite the fact that they continued to have symptomatic myomatous uteri and menstruation. The authors concluded that MRgFUS treatment of uterine leiomyomas leads to clinical improvement with fewer significant clinical complications and adverse events compared to hysterectomy at 6 months' follow-up. Longer follow-up from randomized trials is needed to confirm these results.
Identified studies reported data from the manufacturer sponsored PMA trial (Stewart, 2006; Hindley, 2004). The PMA trial considered quality of life and recovery of non-randomized patients who received either MRI-guided focused ultrasound (FUA) \( n=109 \) or hysterectomy \( n=83 \) to treat uterine fibroids. FUA treated patients were followed for 12 months and hysterectomy treated patients were followed for 6 months. At 12-month follow-up, 42 of 82 FUA treated patients maintained a 10 point score improvement.

The Uterine Fibroid Symptoms and Quality of Life (UFS-QOL) questionnaire was used to assess uterine fibroid symptoms. Stewart et al. reported the mean symptom severity scores for the FUA patients at 12-months compared to baseline were 38.8 versus 61.1, respectively. By 12-month follow-up, 23 of 82 evaluable FUA patients had sought alternative treatment for fibroids (Stewart, 2006).

Limitations of these studies include short follow-up, no comparison of FUA to other minimally invasive technologies intended to treat uterine fibroids and preserve uterine structure and function, the subjective nature, measurement, and interpretation of principal outcomes, small sample size and the incomplete reporting of results.

According to an evidence report prepared for the Agency for Healthcare Research and Quality (AHRQ), the strength of evidence for MRI-guided ultrasound ablation of fibroids is weak (AHRQ, 2007).

A National Institute for Health and Clinical Excellence (NICE) guidance document states that current evidence on the safety and efficacy of magnetic resonance image guided focused ultrasound ablation for uterine fibroids is such that this procedure should only be used with special arrangements for consent and for audit or research. The guidance also indicates that patients should be told about the uncertainties of the procedure’s safety and efficacy and that future research should look at long-term outcomes (NICE, 2007).

**Levonorgestrel-Releasing Intrauterine Device (LNG-IUD)**

Kaunitz et al. (2010) compared the efficacy and safety of the levonorgestrel-releasing intrauterine system and oral medroxyprogesterone acetate in the treatment of idiopathic heavy menstrual bleeding. In this multicenter, randomized, controlled study, women aged 18 years or older with heavy menstrual bleeding (menstrual blood loss 80 mL or more per cycle) were randomly assigned to six cycles of treatment with either levonorgestrel-releasing intrauterine system or oral medroxyprogesterone acetate. Of 807 women screened, 165 were randomly assigned to treatment (levonorgestrel-releasing intrauterine system \( n=82 \), oral medroxyprogesterone acetate \( n=83 \)). At the end of the study, the absolute reduction in median menstrual blood loss was significantly greater in the levonorgestrel-releasing intrauterine system group than in the medroxyprogesterone acetate arm, and the proportion of women with successful treatment was significantly higher for the levonorgestrel-releasing intrauterine system (84.8%) than for medroxyprogesterone acetate (22.2%).

There is evidence from several randomized controlled trials and a few nonrandomized controlled trials and prospective case series that the LNG-IUD is a relatively safe and efficacious minimally invasive therapy for DUB in premenopausal women with confirmed menorrhagia that is refractory to oral medications or for whom surgery has been recommended, who have no benign or malignant pelvic pathology that requires another type of therapy, who do not want or are ineligible for surgery, who cannot tolerate the drug side effects and/or who wish to retain their childbearing capacity. Overall, treatment with the LNG-IUD for 3 to 12 months resulted in significant reductions in menstrual blood loss (MBL) (ranging from 67% to 96%), improvement in menstrual bleeding patterns in the majority of patients, increases in blood hemoglobin and iron levels, high levels of satisfaction and improved quality of life (QOL). Surgery was cancelled or postponed in approximately 70% of patients on surgical waiting lists whose menstrual bleeding improved during LNG-IUD therapy. The rates of treatment discontinuation or failure varied from 3% to 52% (Hurskainen, 2001; Lahteenmaki, 1998; Istre, 2001; Crosignani, 1997; Barrington, 1997; Fedele, 1997; and Romer, 2000).
The evidence from the randomized controlled trials comparing the LNG-IUD with drug therapy (the progestin norethisterone, an NSAID and an antifibrinolytic) showed that the IUD reduced MBL by over 90% and induced amenorrhea in 32% to 44% of patients. While patients were more satisfied with the LNG-IUD than with oral norethisterone, and no serious side effects were reported, IUD use was associated with a higher incidence of spotting and intermenstrual bleeding at 3 months. While spotting and intermenstrual bleeding are initially common following insertion of the LNG-IUD, these symptoms tend to lessen or disappear. LNG-IUD was significantly more efficacious than the NSAID flurbiprofen and the antifibrinolytic tranexamic acid for reducing MBL and improving blood Hb and ferritin levels; however, the IUD was removed in 15% of patients due to side effects or persistent menorrhagia, and 5% of patients had a hysterectomy after device expulsion. No major side effects were associated with the LNG-IUD (Hurskainen, 2001; Lahteenmaki, 1998; Istre, 2001; Crosignani, 1997; Barrington, 1997; Fedele, 1997; and Romer, 2000).

Kaunitz et al. (2009) compared the effects of the levonorgestrel intrauterine system and endometrial ablation in reducing heavy menstrual bleeding. The systematic review and meta-analysis was restricted to randomized controlled trials in which menstrual blood loss was reported using pictorial blood loss assessment chart scores. Six randomized controlled trials that included 390 women (levonorgestrel intrauterine system, n=196; endometrial ablation, n=194) were reviewed. Three studies pertained to first-generation endometrial ablation (manual hysteroscopy) and three to second-generation endometrial ablation (thermal balloon). Both treatment modalities were associated with similar reductions in menstrual blood loss after 6 months, 12 months and 24 months. In addition, both treatments were generally associated with similar improvements in quality of life in five studies that reported this as an outcome. No major complications occurred with either treatment modality in these small trials. The authors concluded that the efficacy of the levonorgestrel intrauterine system in the management of heavy menstrual bleeding appears to have similar therapeutic effects to that of endometrial ablation up to 2 years after treatment.

Lethaby et al. (2005) conducted a metaanalysis of randomized controlled trials of women of reproductive age treated for heavy menstrual bleeding with progesterone or progestogen-releasing intrauterine devices. One trial compared LNG-IUD with medical therapy, two trials compared it with transcervical resection of the endometrium (TCRE), and three trials compared it with balloon ablation. There was a significantly greater mean reduction in menstrual bleeding in one trial in women who had balloon ablation, a lower score on the pictorial blood loss chart and higher rates of successful treatment in 3 trials including both balloon and TCRE. The LNG-IUD was compared to hysterectomy in one trial and the LNG-IUD treatment had lower costs than the hysterectomy at one- and at five-year follow-up.

Busfield et al. (2006) compared LNG-IUD (n=40) to thermal balloon ablation (n=39) in a prospective, randomized trial. Both treatments resulted in significant reductions in pictorial bleeding assessment chart (PBAC) scores. However at 12 and 24 months, median PBAC scores in women treated by LNG-IUD were significantly lower than those of women treated by thermal balloon (11.5 versus 60.0 and 12.0 versus 56.5, respectively) supporting LNG-IUD as more efficacious. Treatment failed in 11 (28%) women using the LNG-IUD and in 10 (26%) women treated with thermal balloon ablation.

**Uterine Artery Embolization (UAE)**

A National Institute for Health and Clinical Excellence (NICE) guidance document states that current evidence on uterine artery embolization (UAE) for fibroids shows that the procedure is efficacious for symptom relief in the short and medium term for a substantial proportion of patients. There are no major safety concerns. Therefore, this procedure may be used provided that normal arrangements are in place for clinical governance and audit (NICE, 2010).

van der Kooij et al. (2010) compared clinical outcomes and health related quality of life (HRQOL) 5 years after uterine artery embolization (UAE) or hysterectomy in the treatment of menorrhagia caused by uterine fibroids. Patients with symptomatic uterine fibroids who were eligible for hysterectomy were assigned randomly 1:1 to hysterectomy (n=89) or UAE (n=88). Endpoints after 5 years were reintervention rates, menorrhagia and HRQOL measures that were assessed.
by validated questionnaires. Five years after treatment 23 of 81 UAE patients (28.4%) had undergone a hysterectomy because of insufficient improvement of complaints (24.7% after successful UAE). HRQOL measures improved significantly and remained stable until the 5-year follow-up evaluation, with no differences between the groups. UAE had a positive effect both on urinary and defecation function.

Goodwin et al. (2008) assessed the long-term clinical outcomes of uterine artery embolization across a wide variety of practice settings in 2112 patients with symptomatic leiomyomata. At 36 months after treatment, 1,916 patients remained in the study, and of these, 1,278 patients completed the survey. The primary measures of outcome were the symptom and health-related quality-of-life scores from the Uterine Fibroid Symptom and Quality of Life questionnaire. Mean symptom scores improved 41.41 points (P<.001), and the quality of life scores improved 41.47 points (P<.001), both moving into the normal range for this questionnaire. The improvements were independent of practice setting. During the 3 years of the study, Kaplan-Meier estimates of hysterectomy, myomectomy, or repeat uterine artery embolization were 9.79%, 2.82%, and 1.83% of the patients, respectively. The investigators concluded that uterine artery embolization results in a durable improvement in quality of life.

Agdi et al. (2008) evaluated intraabdominal adhesions after uterine artery embolization (UAE) in a case-control study of patients who underwent hysterectomy after UAE. The control group consisted of patients who underwent hysterectomy for uterine myoma in the same week. The study included 30 patients in the UAE group and 72 in the control group. In the UAE group, the diameter of the dominant myoma in patients with adhesions (11.3 ± 1.9 cm) was larger than in those without adhesions (5.6 ± 0.6 cm; P = .003; confidence interval, 1.9-8.5). The prevalence of adhesion in the UAE group (20%) was higher than in the control group (1.4%; P = .002; odds ratio, 17.2). The investigators concluded that UAE is associated with intraabdominal adhesion formation and that large myoma predisposes to adhesion formation.

Goodwin et al. (2006) compared results of UAE (n=149) with myomectomy (n=60) 6 months after procedure. Both groups experienced statistically significant improvements in menstrual bleeding and uterine volume as compared to menstrual bleeding and uterine volume pretreatment. When the two groups were compared to each other, there were no significant differences in bleeding improvement and uterine volume reduction. Patients who received UAE required fewer days off work, fewer hospital days and experienced fewer adverse events.

Mara et al. (2006) compared UAE to myomectomy in 63 women and followed-up for a mean of 17 months. Both methods were clinically successful in the majority of cases and were without a significant number of serious complications.

Siskin et al. (2006) compared UAE to hysterectomy in 146 women for treatment of fibroids. UAE was associated with greater sustained improvements in symptom severity and quality of life scores and with fewer complications than myomectomy. MRI at 6-month follow-up demonstrated significant reductions in uterine and tumor volumes (Siskin, 2006).

Spies et al. (2005) reported a 5-year follow-up in 182 patients treated with UAE for leiomyomata. 73% continued to experience symptom control. 13.7% (25) had undergone hysterectomies, 4.4% (8) had undergone myomectomies, and 1.6% (3) had repeat embolizations.

Joffre et al. (2004) concluded that UAE using large microspheres provided good symptom control with low post procedural pain and complications. A total of 9% of the study patients required a follow up hysterectomy but 72% had a reduction in fibroid size.

Spies et al. (2004) completed a randomized comparative study to evaluate the differences in response to PVA particles and tris-acryl gelatin microspheres used to complete the embolization. Recovery for all women was brief and “relatively mild”. There were no differences between the two methodologies. Complications occurred in 19 of the 100 study participants and included allergic reactions, pain with fibroid passage, urinary retention, hematoma, and one person had a pulmonary embolus.
Pinto et al. (2003) completed a randomized trial comparing UAE with hysterectomy. They concluded that UAE reduced abnormal bleeding in 86% of the patients and was associated with significantly shorter hospitalization and recovery time compared with hysterectomy. The total complication rate was higher for UAE than hysterectomy, although there were few major complications with UAE. Patient satisfaction was high for both procedures.

Pron et al. (2003) completed a multicenter case series involving 555 patients evaluating fibroid uterine volume reduction, symptom relief and patient satisfaction following UAE. Their findings indicate that UAE reduced symptoms in the majority of patients as menorrhagia (83%), dysmenorrhea (77%) and bulk related urinary complaints were decreased (86%). They also noted that complications occurred in 44 patients (8%) including increased pain (26), eight patients required a hysterectomy, two had post procedure infections, one had vaginal bleeding and one had a prolapsed fibroid. The procedure could not be completed in 3 patients due to variant anatomy. Patient satisfaction was 91% and nearly half of the patients remained amenorrheic three months after the procedure. Hospital stays were 1.3 days and recovery time was an average of 10 days.

Walker and Pelage (2002) concluded in their study of 400 patients that UAE reduced uterine volumes and improved symptoms, but 6% of the patients had treatment failure and required a hysterectomy. Other complications reported include permanent amenorrhea and chronic vaginal discharge.

Broder et al. (2002) completed a study of 97 women who had either a myomectomy or UAE. They concluded that women who had UAE were more likely than those who had myomectomy to require further invasive fibroid procedures 3-5 years post-surgery. Both procedures were effective in symptom control (92% for the UAE group and 90% for the myomectomy group). The satisfaction rate was higher in the UAE group.

Razavi also studied 111 patients who had an UAE or a myomectomy. They concluded that the UAE was less invasive and safer than myomectomy with a shorter hospitalization, recovery time and duration of pain medication. UAE was also superior for control of menorrhagia, whereas myomectomy was superior for correction of mass/bulk effect. Both procedures were equal with respect to pain control. Of the patients who had complications, 11% were in the UAE group but 25% of the myomectomy patients had complications that were more serious and included blood transfusions, wound infections, ileus and adhesions (Razavi, 2003).

According to an evidence report prepared for the Agency for Healthcare Research and Quality (AHRQ), studies comparing uterine artery embolization (UAE) with other procedures reported procedure time and length of stay favoring UAE. However, the absence of key information on longer-term outcomes suggests that the evidence base is inadequate to comment on the relative risks and benefits of UAE versus hysterectomy or myomectomy (AHRQ, 2007).

**Professional Societies**

**Endometrial Ablation**

**American College of Obstetricians and Gynecologists (ACOG)**

Endometrial ablation is indicated for the treatment of menorrhagia or patient-perceived heavy menstrual bleeding in premenopausal women with normal endometrial cavities who have no desire for future fertility. The various techniques appear to be equivalent with respect to successful reduction in menstrual flow and patient satisfaction at one year following index surgery (ACOG, 2007; reaffirmed 2009).

**American Society for Reproductive Medicine (ASRM)**

An ASRM practice bulletin states that endometrial ablation is an effective therapeutic option for the management of menorrhagia in premenopausal women. Hysteroscopic and nonhysteroscopic techniques offer similar rates of symptom relief and patient satisfaction. Endometrial ablation is
not indicated in postmenopausal women, in women with endometrial cancer or hyperplasia or in premenopausal women who wish to preserve their fertility (ASRM, 2008).

**Magnetic Resonance Imaging-Guided Focused Ultrasound Ablation**

**American College of Obstetricians and Gynecologists (ACOG)**

While short-term studies show safety and efficacy, long-term studies are needed to discern whether the minimally invasive advantage of MRI-guided focused ultrasound surgery will lead to durable results beyond 24 months (ACOG, 2008; reaffirmed 2010).

**Levonorgestrel-Releasing Intrauterine Device**

**American College of Obstetricians and Gynecologists (ACOG)**

An ACOG practice guideline on the use of noncontraceptive uses of hormonal contraceptives states the following:

- Combined oral contraceptives (OC) have been shown to regulate and reduce menstrual bleeding, treat dysmenorrhea, reduce premenstrual dysphoric disorder symptoms and ameliorate acne. (Evidence Level A - based on good and consistent scientific evidence.)

- Hormonal contraception should be considered for the treatment of menorrhagia in women who may desire further pregnancies. (Evidence Level B - based on limited or inconsistent scientific evidence.) (ACOG, 2010)

In an updated practice bulletin, ACOG states that the levonorgestrel intrauterine system leads to minimal systemic effects, and the localized endometrial effect is beneficial for treatment of menorrhagia. Small studies suggest that the levonorgestrel intrauterine system may be effective for treatment of heavy uterine bleeding in women with leiomyomas. However, these women may have a higher rate of expulsion and vaginal spotting. (ACOG, 2008; reaffirmed 2010)

**Uterine Artery Embolization**

**American College of Obstetricians and Gynecologists (ACOG)**

In a practice bulletin on alternatives to hysterectomy in managing uterine fibroids, ACOG states that based on long- and short-term outcomes, uterine artery embolization is a safe and effective option for appropriately selected women who wish to retain their uteri (ACOG, 2008).

**U.S. Food and Drug Administration (FDA):**

**Endometrial Ablation**

Devices for thermal ablation of the endometrium are regulated by the FDA as Class III devices that are subject to the most extensive regulations enforced by the FDA. See the following website for more information (use product codes MNB or MKN):


The HerOption Uterine Cryoblation Therapy System received premarket approval (PMA) on April 20, 2001. The device is a closed-cycle cryosurgical device intended to ablate the endometrial lining of the uterus in premenopausal women with menorrhagia due to benign causes for whom childbearing is complete. See the following website for more information:


Accessed August 2, 2011.

ThermaChoice received premarket approval (PMA) on December 12, 1997 for the treatment of menorrhagia (excessive uterine bleeding) due to benign causes in premenopausal women for whom child bearing is complete. See the following website for more information:


Accessed August 2, 2011.

Hydro ThermAblator received premarket approval (PMA) on April 20, 2001 to ablate the endometrial lining of the uterus in premenopausal women with menorrhagia (excessive uterine
bleeding) due to benign causes for whom child bearing is complete. See the following website for more information: [link]. Accessed August 2, 2011.

The NovaSure® Impedance Controlled Endometrial Ablation System (Hologic, Inc.) received premarket approval (PMA) on September 28, 2001 for ablation of the endometrial lining of the uterus in premenopausal women with menorrhagia due to benign conditions for whom childbearing is complete. See the following website for more information: [link]. Accessed August 2, 2011.

The Microsulis® Microwave Endometrial Ablation (MEA) System received premarket approval (PMA) on September 23, 2003 for ablation of the endometrial lining of the uterus in premenopausal women with menorrhagia due to benign conditions for whom childbearing is complete. See the following website for more information: [link]. Accessed August 2, 2011.

The Cryo-Hit System (Galil Medical) first received 510(k) approval from the FDA on July 1, 1998. Modified versions of the device received 510(k) approval on July 12, 1999 and October 30, 2001. The device is intended for the cryosurgical destruction of tissue during gynecological procedures as well as in general, dermatological, neurosurgical, thoracic, oncological, rectal, and urological surgeries. See the following website for more information: [link]. Accessed August 2, 2011.

Magnetic Resonance Imaging-Guided Focused Ultrasound
The ExAblate 2000 System received premarket approval (PMA) on October 22, 2004 for ablation of uterine fibroid tissue in pre- or perimenopausal women with symptomatic uterine fibroids who desire a uterine sparing procedure. See the following website for more information: [link]. Accessed August 2, 2011.

Levonorgestrel-Releasing Intrauterine Device
MIRENA® received FDA approval on December 8, 2000 for use as an intrauterine contraceptive. Treatment of heavy menstrual bleeding for women who choose to use intrauterine contraception as their method of contraception was approved as an additional indication on October 1, 2009. See the following Web site for more information: [link]. Accessed August 2, 2011.

Uterine Artery Embolization
Uterine artery embolization (UAE) is a procedure and, therefore, not subject to FDA regulation. However, the embolic agents used are subject to FDA oversight. A number of agents are approved by the FDA for embolization procedures of the neurological system, but several have been specifically approved for UAE. See the following website for additional information: [link]. Accessed August 2, 2011.

Policy and Rationale
Oxford will provide coverage for treatments of dysfunctional uterine bleeding and uterine fibroids as indicated in the Treatment/Application Guidelines below.

Treatment/Application Guidelines

Recommended Guidelines
The following procedures do not require medical director review:
• Endometrial ablation, using the following techniques, are medically necessary for treating menorrhagia or metrorrhagia in premenopausal women:
  o Cryoablation (HerOption®)
  o Thermal balloon ablation (Gynecare Thermachoice®)
  o Hydrothermal ablation (Hydro ThermAblator®)
  o Radiofrequency ablation (NovaSure®)
  o Microwave ablation (Microsulis® Microwave Endometrial Ablation (MEA) System)
  o Manual endometrial ablation techniques such as resectoscopic ablation or laser ablation

• Levonorgestrel-releasing intrauterine device (LNG-IUD) is medically necessary for the treatment of menorrhagia in premenopausal women. Refer to policy: Contraceptives and members certificate of coverage for additional information.

• Uterine artery embolization (UAE) is medically necessary for the treatment of symptomatic uterine fibroids for women who do NOT wish to preserve their childbearing potential.

• Uterine artery embolization (UAE) is not medically necessary for treating symptomatic uterine fibroids for women who wish to preserve their childbearing potential.

The effects of UAE on ovarian and uterine function and on fertility are relatively unknown. Further studies of safety and/or efficacy in published, peer-reviewed medical literature are necessary.

The following procedures require MD review:

• Magnetic resonance imaging (MRI)-guided cryoablation is not medically necessary for the treatment of uterine fibroids.

The published evidence on MRI-guided cryoablation for uterine fibroids is very limited, as the procedure has been evaluated in very few patients. The long-term outcomes and overall health benefits remain unknown. Further long-term studies on larger samples published in peer-reviewed medical literature are necessary to demonstrate the safety and efficacy of this technology.

• Magnetic resonance imaging (MRI)-guided focused ultrasound ablation (FUA) is not medically necessary for the treatment of uterine fibroids.

Further studies are needed to determine the long-term efficacy of this procedure and to evaluate the efficacy and safety of this procedure relative to other treatments for uterine fibroids.

**PAYMENT GUIDELINES**

The below procedures **DO NOT REQUIRE** Medical Director Review:

<table>
<thead>
<tr>
<th>CPT® Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>37210</td>
<td>Uterine fibroid embolization (UFE, embolization of the uterine arteries to treat (uterine fibroids, leiomyomata), percutaneous approach inclusive of vascular access, vessel selection, embolization, and all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the procedure</td>
</tr>
<tr>
<td>58353</td>
<td>Endometrial ablation, thermal, without hysterscopic guidance</td>
</tr>
<tr>
<td>58356</td>
<td>Endometrial cryoablation with ultrasonic guidance, including</td>
</tr>
</tbody>
</table>
endometrial curettage, when performed

58563 Hysteroscopy, surgical; with endometrial ablation (eg. Endometrial resection, electrosurgical ablation, thermoablation)

CPT® is a registered trademark of the American Medical Association.

The below procedures REQUIRE Medical Director Review:

<table>
<thead>
<tr>
<th>CPT® Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0071T</td>
<td>Focused ultrasound ablation of uterine leiomyomata, including MR guidance; total leiomyomata volume less than 200 cc of tissue</td>
</tr>
<tr>
<td>0072T</td>
<td>Focused ultrasound ablation of uterine leiomyomata, including MR guidance; total leiomyomata volume greater or equal to 200 cc of tissue</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J7302</td>
<td>Levonorgestrel-releasing intrauterine contraceptive system, 52 mg</td>
</tr>
<tr>
<td>J3706</td>
<td>Levonorgestrel (contraceptive) implant system, including implants and supplies</td>
</tr>
<tr>
<td>S4981</td>
<td>Insertion of levonorgestrel-releasing intrauterine system</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-9 Procedure Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>626.2</td>
<td>Excessive or frequent menstruation</td>
</tr>
<tr>
<td>626.6</td>
<td>Metrorrhagia</td>
</tr>
<tr>
<td>627.0</td>
<td>Premenopausal menorrhagia</td>
</tr>
</tbody>
</table>

ICD-10 Codes (Preview Draft)
In preparation for the transition from ICD-9 to ICD-10 medical coding on October 1, 2014*, a sample listing of the ICD-10 CM and/or ICD-10 PCS codes associated with this policy has been provided below for your reference. This list of codes may not be all inclusive and will be updated to reflect any applicable revisions to the ICD-10 code set and/or clinical guidelines outlined in this policy. *The effective date for ICD-10 code set implementation is subject to change.

<table>
<thead>
<tr>
<th>ICD-10 Diagnosis Code (Effective 10/01/14)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N92.0</td>
<td>Excessive and frequent menstruation with regular cycle</td>
</tr>
<tr>
<td>N92.1</td>
<td>Excessive and frequent menstruation with irregular cycle</td>
</tr>
<tr>
<td>N92.4</td>
<td>Excessive bleeding in the premenopausal period</td>
</tr>
</tbody>
</table>

REFERENCES
The foregoing Oxford policy has been adapted from an existing UnitedHealthcare national policy that was researched, developed and approved by the UnitedHealthcare Medical Technology Assessment Committee. [2011T0442G]
References:

17. Cooper KG, Bain C, Lawrie L, Parkin DE. A randomised comparison of microwave endometrial ablation with transcervical resection of the endometrium; follow up at a minimum of five years. BJOG. 2005 Apr;112(4):470-5.


**POLICY HISTORY/REVISION INFORMATION**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action/Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>09/14/2012</td>
<td>- Added list of applicable ICD-10 codes (preview draft) in preparation for the transition from ICD-9 to ICD-10 medical coding on 10/01/14</td>
</tr>
</tbody>
</table>
| 11/01/2011    | - Updated description of services to reflect the most current clinical evidence, FDA information, and references
  - Updated/clarified coverage rationale:
    - Revised coverage statement for endometrial ablation; replaced language indicating "endometrial ablation, using the listed techniques, is medically necessary for treating menorrhagia in premenopausal women" with "endometrial ablation, using the listed techniques, is medically necessary for treating menorrhagia or metrorrhagia in premenopausal women"
    - Revised coverage statement for levonorgestrel-releasing intrauterine device (LNG-IUD); replaced language indicating "LNG-IUD is medically necessary for treating dysfunctional uterine bleeding in premenopausal women" with "LNG-IUD is medically necessary for treating menorrhagia in premenopausal women"
    - Revised coverage statement for uterine artery embolization (UAE):
      - Replaced language indicating "UAE is medically necessary for treating confirmed symptomatic uterine fibroids" with "UAE is medically necessary for treating symptomatic uterine fibroids for women who do not wish to preserve their childbearing potential"
      - Replaced language indicating "UAE is not medically necessary for women with symptomatic uterine fibroids who wish to preserve their childbearing potential" with "UAE is not medically necessary for treating symptomatic uterine fibroids for women who wish to preserve their childbearing potential"
    - Added list of applicable HCPCS and ICD-9 diagnosis codes
    - Archived previous policy version SURGERY 057.4 T2