Abnormal Uterine Bleeding and Uterine Fibroids

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➲ Instructions for Use

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Application

UnitedHealthcare Commercial

This Medical Policy applies to UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange

This Medical Policy applies to Individual Exchange benefit plans in all states except for Colorado.

Coverage Rationale

➲ See Benefit Considerations

Endometrial Ablation

Endometrial ablation is proven and medically necessary for treating abnormal uterine bleeding in premenopausal individuals. For medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Hysteroscopy, Operative.

Click here to view the InterQual® criteria.

Levonorgestrel-Releasing Intrauterine Device

Levonorgestrel-releasing intrauterine devices (LNG-IUD) (e.g., Mirena®, Skyla®, Liletta®, or Kyleena™) are proven and medically necessary for treating menorrhagia. Refer to the U.S. Food and Drug Administration (FDA) section for additional information.

Uterine Fibroids

Uterine artery embolization (UAE) is proven and medically necessary for treating symptomatic uterine fibroids, postpartum or post hysterectomy bleeding, or uterine arteriovenous malformation (AVM). For medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Uterine Artery Embolization (UAE).

Click here to view the InterQual® criteria.

UAE is unproven and not medically necessary for the purpose of preserving childbearing potential for individuals with symptomatic uterine fibroids due to insufficient evidence of efficacy.

Magnetic resonance-guided focused ultrasound ablation (MRgFUS) is unproven and not medically necessary for treating uterine fibroids due to insufficient evidence of efficacy.

Medical Records Documentation Used for Reviews

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. Medical records documentation may be required to assess whether the member meets the clinical criteria for coverage but does not guarantee coverage of the service requested; refer to the protocol titled Medical Records Documentation Used for Reviews.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
Uterine Fibroids	
0071T	Focused ultrasound ablation of uterine leiomyomata, including MR guidance; total leiomyomata volume less than 200 cc of tissue
0072T	Focused ultrasound ablation of uterine leiomyomata, including MR guidance; total leiomyomata volume greater or equal to 200 cc of tissue
37243	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction
58563	Hysteroscopy, surgical; with endometrial ablation (e.g., endometrial resection, electrosurgical ablation, thermoablation)

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HCPCS Code	Description
Levonorgestrel-Releasing Intrauterine Device	
J7296	Levonorgestrel-releasing intrauterine contraceptive system, (Kyleena), 19.5 mg
J7297	Levonorgestrel-releasing intrauterine contraceptive system (Liletta), 52 mg
J7298	Levonorgestrel-releasing intrauterine contraceptive system (Mirena), 52 mg
J7301	Levonorgestrel-releasing intrauterine contraceptive system (Skyla), 13.5 mg
J7306	Levonorgestrel (contraceptive) implant system, including implants and supplies
S4981	Insertion of levonorgestrel-releasing intrauterine system

Description of Services

Abnormal uterine bleeding (AUB) 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, AUB includes vaginal bleeding 12 months or more after the cessation of menstruation, or unpredictable bleeding in those who have been receiving hormone therapy for 12 months or more. AUB 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). 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 considered AUB. All these

conditions associated with menorrhagia can be referred to as AUB, 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 AUB includes watchful waiting and pharmacological therapy. Hormone therapy may cause the fibroids to shrink; however, they will quickly return to their original mass once therapy has been discontinued. Another treatment option is dilation and curettage. Hysterectomy is available when symptoms cannot be controlled by conservative treatment.

According to the American College of Obstetricians and Gynecologists (ACOG), fibroids are most commonly found in women aged 30-40 years but can occur at any age. 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. Uterine fibroid embolization (UFE) is indicated for individuals with clinically documented fibroids and fibroid-related symptoms and a viable alternative to hysterectomy surgery. Recommendations prior to UFE treatment include an endometrial biopsy to rule out malignancy or hyperplasia (Bradley 2018). Alternate minimally invasive procedures such as UFE are performed in an outpatient setting resulting in shorter recovery times, less complications and elimination of overnight hospital stays.

Levonorgestrel-Releasing Intrauterine Device (LNG-IUD)

The local administration of the progestin levonorgestrel is delivered via an intrauterine device (IUD). 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.

Uterine Artery Embolization (UAE)

This procedure injects particles via the uterine arteries to block blood supply to uterine fibroids, causing them to shrink.

Magnetic Resonance-Guided Focused Ultrasound (MRgFUS)

This procedure combines real-time MR-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.

Benefit Considerations

Levonorgestrel-Releasing Intrauterine Device (LNG-IUD)

Some plan documents exclude coverage for contraception. In these plan documents, coverage for intrauterine devices (IUD), including the LNG-IUD, is excluded when used for contraceptive purposes. However, in these plan documents, coverage exists for the LNG-IUD when used for a non-contraceptive purpose, including treatment of abnormal uterine bleeding. Refer to the Coverage Rationale section above for medically necessary indications for coverage.

Clinical Evidence

Levonorgestrel-Releasing Intrauterine Device (LNG-IUD)

As a long-term follow-up study of a multicenter randomized controlled trial (RCT) MIRA trial, Huijs et al. (2024) sought to assess the long-term differences in the reintervention risk and menstrual blood loss for women with the symptoms of heavy menstrual bleeding (HMB) treated according to a strategy starting with a 52-mg levonorgestrel-releasing intrauterine system (LNG-IUS) or radiofrequency nonresectoscopic endometrial ablation. The participants of the trial were separated into two groups: those receiving 52-mg LNG-IUD (n = 132) or radiofrequency on resectoscopic endometrial ablation (n = 138). The outcomes measured were the reintervention rate, menstrual bleeding, quality of life (QOL), sexual function, and patient satisfaction. The results of the trial showed that from the 270 women who were randomized in the original trial, 196 (52-mg LNG-IUS group: n = 94; radiofrequency nonresectoscopic endometrial ablation group: n = 102) took part in this long-term follow-up study. The cumulative reintervention rate (including both medical and surgical reinterventions) was 40.0% (34/85) in the 52-mg LNG-IUS group and 28.7% (27/94) in the radiofrequency nonresectoscopic endometrial ablation group (relative risk, 1.39; 95% confidence interval (CI), 0.92-2.10). The cumulative rate of surgical reinterventions only was significantly higher among those with a treatment strategy starting with a 52-mg LNG-IUS compared with radiofrequency nonresectoscopic endometrial ablation (35.3% [30/85] vs 19.1% [18/94]; relative risk, 1.84; 95% CI, 1.11-3.10). However, the hysterectomy rate was similar (11.8% [10/94] in the 52-mg LNG-IUS group and 18.1% [17/102] in the radiofrequency nonresectoscopic endometrial ablation group; relative risk, 0.65; 95% CI, 0.32-1.34). Most reinterventions occurred during the first 24 months of follow-up. A total of 171 Pictorial Blood Loss

Assessment Chart scores showed a median bleeding score of 0.0. No clinically relevant differences were found regarding QOL, sexual function, and patient satisfaction. The limitation of the study is the possibility that the responders to the long-term follow-up may only represent part of the original study population. Additionally, the cause of the symptom of HMB was not assessed at baseline following the Federation of Gynecology and Obstetrics (FIGO) classification. Lastly, a natural consequence of the long-term follow-up is that participants became postmenopausal during this period, given that the average age at baseline was approximately 45 years. The high proportion of postmenopausal women is another limitation of the current study, given that postmenopausal status could be conflated with optimal treatment effect. The authors concluded that the overall risk of reintervention after long-term follow-up was not different between women treated according to a treatment strategy starting with a 52-mg LNG-IUS and those treated using a strategy starting with radiofrequency nonresectoscopic endometrial ablation. However, women given a treatment strategy starting with a 52-mg LNG-IUS had a higher risk of surgical reintervention, which was driven by an increase in later endometrial ablation. Both treatment strategies effectively lower menstrual blood loss over the long term. The results of this long-term follow-up study can support physicians in improving the counseling of women with HMB, thus promoting informed decision-making regarding the choice of treatment.

In a 2024 systematic review and single-arm meta-analysis, Oliveira and associates examined the LNG-IUS in women with inherited bleeding disorders and HMB. The exploration uncovered six observational studies (n = 156) that met inclusion criteria. The results of the review showed that LNG-IUS use in those with inherited bleeding disorders and HMB was associated with amenorrhea in 60% of people and a significant increase of 1.40 g/dL in hemoglobin and 19.75 ng/mL in ferritin levels when comparing post- and pre-treatment levels. The post-treatment mean hemoglobin was 13.32 g/dL, and the mean ferritin was 43.22 ng/dL. The rate of IUD expulsion or removal due to malposition was low (13%), as was the need for IUD removal due to lack of efficacy (14%). The limitations include the need for more of a control group, the small number of studies, and the lack of individual patient-level data, which precludes a more robust analysis of personal factors that may be associated with better or worse efficacy of LNG-IUS in this group. The authors concluded that the LNG-IUS may improve bleeding patterns and QOL in those with inherited bleeding disorders and HMB.

Lee et al. (2024) conducted a systematic review and meta-analysis to investigate the effectiveness of high intensity focused ultrasound (HIFU) combined with Gonadotropin-Releasing Hormone Agonist (GnRH-a) or LNG-IUS for people with adenomyosis. The outcomes measured were the treatment efficacy rate of dysmenorrhea, the effective rate of menorrhagia severity, and the reduction rate of adenomyosis lesion. Adverse events were also assessed. The results uncovered that HIFU plus LNG-IUS showed lower dysmenorrhea (within six months: risk ratio [RR] 0.88, 95% CI 0.83-0.93, $p < 0.00001$; over one year: RR 0.73, 95% CI 0.65-0.82, $p < 0.00001$) and less menorrhagia severity (RR 0.63, 95% CI 0.60-0.66, $p < 0.00001$) than HIFU plus GnRH-a. Both groups showed equal efficacy in adenomyotic lesion reduction rate (RR 1.03, 95% CI 0.97-1.09, $p = 0.30$). Adverse effects happened equally in both groups. The limitations of the study included significant heterogeneity, retrospective nature of research, lack of randomization, allocation, and blinding process. The authors concluded that combination therapy of HIFU and LNG-IUS showed better results in the effectiveness of treating dysmenorrhea and menorrhagia than that of HIFU and GnRH-a.

Chen et al. (2022) compares the safety and efficacy of the LNG-IUS with other medical treatments for women with HMB . A search was conducted using Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Embase, and Wanfang databases. A total of thirteen RCTs were retrieved for the systematic review and twelve were included for meta-analyses. A total of 1677 individuals were included with the average age ranging from 28 to almost 42 years of age and all diagnosed with HMB. Included RCTs compared LNG-IUS against medical treatments. The LNG-IUS used was a continuous release system of intrauterine progesterone and comprised of 52 mg of levonorgestrel, which was released at a rate of approximately 20 µg/day during the first year. The medical treatments included oral hormonal drugs and tranexamic acid. The primary outcome assessed was clinical response to treatment and secondary outcomes included menstrual blood loss, QOL, adverse events, and patient satisfaction. The Cochrane Risk of Bias Tool was used for assessment for the risk of bias for the included RCTs. The authors found that the number of clinical responders was greater in the LNG-IUS group than that of the medical treatment groups. It was concluded the evidence was superior for LNG-IUS in the short- and medium-term clinical responses, blood loss control, compliance, and satisfaction when compared to that of medical treatments. Limitations included lack of long-term data, high-risk of performance bias due to the blinding of participants and personnel, and self-reported data.

Evidence from a Cochrane Systematic Database Review by Bofill Rodriguez et al. (2022) suggests LNG-IUS is the best first-line action for reducing menstrual blood loss. The authors synthesized the results of studies that focused on different treatments for HMB. Treatments were categorized based on patient characteristics, including the desire for future pregnancy, failure of previous treatment or having been referred for surgery. The data analyzed included 9950 participants from 85 studies. The medical treatments included nonsteroidal anti-inflammatory drugs (NSAIDs), antifibrinolytics, combined oral contraceptives, combined vaginal ring, long-cycle and luteal oral progestogens, the LNG-IUS, ethamsylate and danazol and were compared to a sham treatment. Surgical interventions included open, minimally

invasive, and unspecified routes for hysterectomy, resectoscopic endometrial ablation, non-resectoscopic endometrial ablation and unspecified endometrial ablation. In non-surgical candidates, LNG-IUS was the most effective first-line treatment to reduce menstrual blood loss. For surgical candidates, hysterectomy was the most effective treatment for reducing menstrual blood loss and to avoid further surgery for HMB. Future research should assess the efficacy and safety of progestogen-only contraceptives and compare it to different combined hormonal contraceptives for treatment of HMB in addition to assessment of QOL.

A 2020 Cochrane Systematic Database Review by Bofill et al. found that the LNG-IUS had a greater reduction in menstrual blood loss for women with HMB when compared to other medical treatments or placebos; the authors' conclusion was LNG-IUS appears to be more effective than oral medical therapies and results in better QOL and higher satisfaction. The analysis included 25 RCTs which included a total of 2511 women; most studies did not provide long-term data beyond 2 years. Limitations included the small number of participants in the differing trials and a high-risk of bias for blinding.

Cim et al. (2018) reported two-year follow-up data of people with AUB after insertion of the LNG-IUS. One hundred and six parous women aged 33-48 years with recurrent HMB participated in this study, and were followed for 1, 3, 6, 12, 18, and 24 months following the insertion. The authors reported that the LNG-IUS was well tolerated by all women. Pre-treatment of the use of the LNG-IUS, endometrial biopsy patterns for irregular proliferative endometrium and for atypical simple hyperplasia were 34/106 (32.08%) and 61/106 (57.55%) respectively and after treatment no abnormal pathologic findings were determined ($p < 0.001$).

Louie et al. (2017) evaluated comparative clinical outcomes after placement of LNG-IUS, ablation, or hysterectomy for AUB. A decision tree was generated to compare clinical outcomes in a hypothetical cohort of 100,000 premenopausal women with nonmalignant AUB. Complications, mortality, and treatment outcomes were evaluated over a 5-year period, with calculated cumulative quality-adjusted life years (QALYs), and probabilistic sensitivity analysis. The LNG-IUS had the highest number of QALYs (406, 920), followed by hysterectomy (403, 466), non-resectoscopic ablation (399, 244), and resectoscopic ablation (395, 827). Ablation had more treatment failures and complications than LNG-IUS and hysterectomy. According to the authors, findings were robust in sensitivity analysis.

A Cochrane review (Marjoribanks et al., 2016) compared the effectiveness, safety, and acceptability of surgery versus medical therapy for HMB. Fifteen RCTs (n = 1289) comparing surgery versus oral medication or LNG-IUD for treating HMB were included. The authors concluded that hysterectomy, endometrial surgery, and the LNG-IUD were all effective in reducing HMB, though surgery was most effective, at least over the short term. These treatments suited most women better than oral medication. Although hysterectomy will stop HMB, it is associated with serious complications. Both conservative surgery and LNG-IUD appear to be safe, acceptable, and effective.

An updated Cochrane systematic review by Lethaby et al. (2015) evaluated the safety and efficacy of the LNG-IUD for HMB. Twenty-one RCTs in women of reproductive age treated with progesterone or progestogen-releasing intrauterine devices versus no treatment, placebo or other medical or surgical therapy for HMB were included. The authors concluded that the LNG-IUD is more effective than oral medication as a treatment for HMB. The device is associated with a greater reduction in HMB, improved QOL and appears to be more acceptable long term but is associated with more minor adverse effects than oral therapy. When compared to endometrial ablation, it is not clear whether the LNG-IUD offers any benefits regarding reduced HMB, and satisfaction rates and QOL measures were similar. Limitations included inconsistency and inadequate reporting of study methods.

In a systematic review of twenty-six studies, Matteson et al. (2013) compared the effectiveness of nonsurgical AUB treatments for bleeding control, QOL, pain, sexual health, patient satisfaction, additional treatments needed and adverse events. Interventions included the levonorgestrel intrauterine system, combined oral contraceptive pills (OCPs), progestins, NSAIDs and antifibrinolytics. For reduction of menstrual bleeding in women with AUB presumed secondary to endometrial dysfunction, the levonorgestrel intrauterine system (71-95% reduction), combined OCPs (35-69% reduction), extended cycle oral progestins (87% reduction), tranexamic acid (26-54% reduction) and NSAIDs (10-52% reduction) were all effective treatments. The levonorgestrel intrauterine system, combined OCPs and antifibrinolytics were all superior to luteal phase progestins (20% increase in bleeding to 67% reduction). The levonorgestrel intrauterine system was superior to combined OCPs and NSAIDs. Antifibrinolytics were superior to NSAIDs for menstrual bleeding reduction. Data were limited on other important outcomes such as QOL for women with AUB presumed secondary to endometrial dysfunction and for all outcomes for women with AUB presumed secondary to ovulatory dysfunction.

In another systematic review, Matteson et al. (2012) compared hysterectomy with less-invasive alternatives for AUB. Nine RCTs comparing bleeding, QOL, pain, sexual health, satisfaction, need for subsequent surgery and adverse events were included. Endometrial ablation, levonorgestrel intrauterine system and medications were associated with lower risk of

adverse events but higher risk of additional treatments than hysterectomy. Compared to ablation, hysterectomy had superior long-term pain and bleeding control. Compared with the levonorgestrel intrauterine system, hysterectomy had superior control of bleeding. No other differences between treatments were found. The review group concluded that less-invasive treatment options for AUB result in improvement in QOL but carry significant risk of retreatment caused by unsatisfactory results. Although hysterectomy is the most effective treatment for AUB, it carries the highest risk for adverse events.

Uterine Artery Embolization (UAE)

There is insufficient evidence to conclude that treatment of fibroids with UAE preserves childbearing potential. Most studies on UAE's impact on fertility are low quality and small sample size limiting the generalizability of the findings. There is also a scarcity of long-term follow up data on fertility and pregnancy outcomes after UAE, with some studies suggesting a higher risk of pregnancy complications. Additional research involving larger, robust RCT's is needed to establish safety, effectiveness, and long-term outcomes.

In 2023, Yan and associates conducted a systematic review with trial sequential analysis aimed at focusing on pregnancy rate and outcomes for females after UAE. A subgroup analysis was also performed based on different patient populations or various control treatments. The overall results revealed that UAE significantly decreased postoperative pregnancy rate (RR [95% CI]: 0.721 [0.531–0.979], 95% PI: 0.248–2.0970 and was associated with an increased risk of postoperative postpartum hemorrhage (PPH) (RR [95% CI]: 3.182 [1.319–7.675], 95% PI: 0.474–22.089). Analysis grouped by population indicated that UAE decreased the risk of preterm delivery (RR [95% CI]: 0.326 [0.128–0.831], $p = 0.019$) and cesarean section (RR [95% CI]: 0.693 [0.481–0.999], $p = 0.050$) and increased the risk of placenta previa (RR [95% CI]: 8.739 [1.580–48.341], $p = 0.0130$ in those with uterine fibroids, cesarean scar pregnancy (CSP), and PPH, respectively. When compared with myomectomy, HIFU, and non-use of UAE, UAE treatment was associated with the reduced risks of preterm delivery (RR [95% CI]: 0.296 [0.106–0.826]) and cesarean section ([95% CI]: 0.693 [0.481–0.999], $p = 0.050$) and increased placenta previa risk (RR [95% CI]: 10.682 [6.859–16.636]), respectively. Limitations of the study include heterogeneity, lack of specificity whether the participants in the research suggested exclusively from a single disease, and an insufficient number of studies to continue sub-analysis by subgroup 1 and subgroup 2. The authors concluded that UAE treatment was associated with a lower postoperative pregnancy rate and increased risk of PPH. The subgroup analysis suggested that UAE was shown to decrease the risk of preterm delivery and cesarean section and increase placenta previa risk.

Akhatova et al. (2023) conducted a systematic review that compared and assessed UAE, USgHIFU and MRgHIFU, and transcervical radiofrequency ablation (TFA) procedures. A search using PubMed, Google Scholar, ScienceDirect, Cochrane Library, Scopus, Web of Science and Embase was performed and returned 25 articles. The number of pregnancies varied considerably amongst the studies, as well as the mean age of the women which usually included women > 40 years of age. The rates of live births for UAE, HIFU, and TFA were similar at 70.8%, 73.5%, and 70%, respectively. Miscarriage rate was the greatest in the UAE group which accounted for 19.2%. Overall, the delivery rate by cesarean section was greater in these minimally invasive procedures when compared to that for the general population rate (31.8%); this was most likely due to the greater risks associated with women with uterine fibroids. Upon analysis, the authors found the estimation of pregnancy was found to be higher after UAE and HIFU when compared to TFA. The evidence confirmed that minimally invasive uterine-sparing treatment options for uterine fibroids, such as UAE, HIFU, and TFA, are a good approach for those wishing to preserve their fertility. Future studies should include additional robust studies to help identify which subpopulation would benefit most from receiving one technique versus another. Limitations included retrospective design, low total number of pregnancies after TFA available for analysis, and lack of data around the size, location and number of fibroids which are known to influence treatment.

Mailli et al. (2023) conducted a literature review on UAE treatment for symptomatic fibroids, which included a focus on post-procedure fertility outcomes. A search of the literature was performed using the PubMed/Medline, Google scholar, Cochrane and EMBASE databases. The search resulted in seventeen articles for review: two RCTs, two prospective controlled studies, seven prospective cohorts, four retrospective cohorts and three case series. One key factor identified during the research was the age of the participants and the effect on fertility; studies that included women over the age of forty had a negative impact on fertility. However, the overall mean age was 35.9 years thus the authors suggested UAE could be considered in younger people who have a desire to preserve fertility. The authors concluded that the evidence does support UAE as a viable treatment option in women with large fibroids and seeking to preserve fertility, however future RCTs are warranted.

Karlsen et al. (2018) conducted a systematic review of the reported rates of pregnancy and miscarriage after treatment of uterine fibroids with UAE. RCTs, controlled clinical trials, comparative before-after trials, cohort studies, case-control studies, and case series where UAE treatment of premenopausal women was performed for uterine fibroids with and

where a control intervention was included. The PRISMA guideline was used to do a systematic review using the main outcomes pregnancy rate and miscarriage rate. Risk of bias was assessed by the Cochrane risk of bias tool or by ROBINS-I. The quality of evidence was assessed by the GRADE approach. 17 studies comprising 989 patients were selected and included 1 RCT, 2 cohort studies, and 14 case series. The results showed pregnancy rates after UAE were 50% in the RCT and 51 and 69% in the cohort studies. Among the case series median pregnancy rate was 29%. Miscarriage rates were 64% in the RCT. Miscarriage rates at 56 and 34% were found in the cohort studies after UAE. The median miscarriage rate was 25% in the case series. The authors concluded that pregnancy rate was found to be lower and miscarriage rate higher after UAE than after myomectomy. However, they found very low quality of evidence regarding the assessed outcomes and the reported proportions are uncertain. There is a need for improved prospective randomized studies to improve the evidence base.

The Agency for Healthcare Research and Quality (AHRQ) published a comparative effectiveness review on management of uterine fibroids that was designed to review the treatment effectiveness and the risk of leiomyosarcoma in women with fibroids. The review found high strength evidence that UAE is effective for reducing the size of fibroids and total fibroid volume. Improvements in bleeding and QOL had a moderate strength of supporting evidence. Over half of the women who received UAE did not require a subsequent intervention after a 5-year follow-up period. Insufficient evidence was found to determine safety of the UAE on reproductive outcomes. Additionally, the uncertainty in estimates of leiomyosarcoma prevalence and evolving data about methods for tissue extraction requires exploration(Hartmann et al., 2017).

Pisco et al. (2017) conducted a retrospective analysis of prospectively collected data of 359 women with uterine fibroids and/or adenomyosis who were unable to conceive. The purpose of the study was to determine pregnancy rates after conventional and partial UFE. The mean follow-up period was 69 months. During follow-up, 149 women became pregnant, 131 women had live births, and 16 women had several pregnancies, resulting in a total of 150 live newborns. It was the first pregnancy for 85.5% (112 of 131) of women. Spontaneous pregnancy rates at 1 year and 2 years after UFE were 29.5% and 40.1%. A dominant submucosal fibroid and ischemia greater than or equal to 90% had greater likelihood of spontaneous pregnancy. Complication rates for individuals treated with partial UFE (14.6%) were not greater than rates in those treated with conventional UFE (23.1%, p = .04). The authors concluded that partial UFE may be safe and effective outpatient procedures for women with uterine fibroids who want to conceive. Limitations included the study was performed at a single center along with a non-standardized technique utilized by the radiologists; additional RCTs comparing UFE to myomectomy are needed.

Panagiotopoulou et al. (2014) evaluated the effectiveness of uterine-sparing interventions for women with symptomatic uterine fibroids who wish to preserve their uterus. Five trials, involving 436 women were included. Two compared UAE with myomectomy and three compared UAE with laparoscopic uterine artery occlusion. Indirect treatment comparison showed that myomectomy and UAE resulted in higher rates of patient satisfaction and lower rates of clinical failure than laparoscopic uterine artery occlusion. Myomectomy resulted in a lower reintervention rate than UAE and laparoscopic uterine artery occlusion even though the latter techniques had an advantage over myomectomy because of shorter hospitalization and quicker recovery. There was no evidence of difference between the three techniques in ovarian failure and complications rates. The evidence for reproductive outcomes is poor. The authors concluded that these results suggest that laparoscopic uterine artery occlusion is less effective than UAE and myomectomy in treatment of symptomatic fibroids. The choice between UAE and myomectomy should be based on individuals' expectations and fully informed discussion. Limitations of the study included the relatively low number of included studies and low number of participants; further RCTs providing longer follow up and assessing the safety and efficacy of the interventions are warranted.

In a retrospective analysis, Pisco et al. (2011) evaluated the outcome of pregnancy after UFE in 74 individuals who wanted to conceive. The length of the follow-up period was 4.5 years; however, all the pregnancies occurred between 4 and 22 months after UFE. Of the study participants, 44 became pregnant (59.5%). There are five (11.3%) ongoing pregnancies and 39 (88.7%) finished pregnancies, with 33 successful live births (84.6%), four spontaneous abortions (10.3%), one induced abortion, and one stillbirth. There were 22 cesarean deliveries (66.6%), two preterm deliveries at 36 weeks (6.1%), and five low birth weights. Although the authors concluded that UFE appears to be safe, study limitations include non-randomization in comparison with myomectomy, and small patient population.

Magnetic Resonance-Guided Focused Ultrasound Ablation (MRgFUS)

There is insufficient evidence to conclude that MRgFUS is effective for treating fibroids. There is a paucity of long-terms studies on the durability of symptom relief and fibroid recurrence after MRgFUS treatment. There is a lack of standardization of treatment protocols which can lead to variability in outcomes. Additional research involving larger, robust RCTs is needed to establish its safety, efficacy, and long-term outcomes.

In a 2024 systematic review and meta-analysis, Dou and associates sought to quantify the reintervention rate and analyze the risk factors for reintervention after HIFU ablation of uterine fibroids. The study enrolled 5216 individuals with fibroids treated with HIFU. There were 3247, 1239, 1762, and 2535 women reaching reintervention rates of 1% (95% CI: 1-1), 7% (95% CI: 4-11), 19% (95% CI: 11-27), and 29% (95% CI: 14-44) at 12, 24, 36, and 60-month after HIFU. The reintervention rates of those treated with US-guided HIFU (USgHIFU) were significantly lower than those treated with MRgFUS. When the non-perfused volume rate (NPVR) of fibroids was over 50%, the reintervention rates at 12, 36, and 60-month after HIFU were 1% (95% CI: 0.3–2), 5% (95% CI: 3–8), and 15% (95% CI: 9–20). The reintervention risk for hypo-/iso-intensity fibroids on T2WI was 3.45 times higher (95% CI: 2.7–4.39) for hypo-/iso-intensity fibroids. The limitations of the study include the inclusion of several observation studies due to the limited availability of the literature on the long-term outcomes of this treatment. The authors concluded that the overall reintervention rates after HIFU were acceptable and provided consultative suggestions regarding treatment alternatives for those with fibroid. The subgroup analysis revealed that USgHIFU, NPVR ≥ 50%, and iso-intensity of fibroids on T2WI were significant factors in reducing intervention.

Through a systematic review and meta-analysis, Hu and colleagues (2023) compared high-intensity focused ultrasound and laparoscopic treatment of uterine fibroids. A total of 1375 articles were received in the literature, 14 of which were selected. The authors found that women who underwent HIFU surgery had higher rates of spontaneous pregnancy, higher rates of spontaneous delivery, and higher rates of full-term delivery but may have higher rates of miscarriage or postpartum complications than women who underwent laparoscopic myomectomy. Limitations of the study included insufficient controlled studies; therefore, single-group rates were counted in this study, subgroup analysis was used, and no comparisons were made between the two groups. No ratio data could be generated, leading to an absolute inability to discuss the sources of heterogeneity using regression analysis. The authors concluded that HIFU is not worse than laparoscopic myomectomy in terms of fertility and is even better regarding spontaneous pregnancy rates, spontaneous labor, and full-term delivery. HIFU is a better choice for women with fibroids with fertility requirements.

Kociuba et al. (2023) evaluated the most common adverse events (AEs) and complications in people following MRgFUS therapy for uterine fibroids. A literature search using PubMed/MEDLINE, Scopus and CENTRAL returned forty-three publications for analysis which totaled 3102 participants; most studies were cohorts with only two RCTs. Overall, the risk bias assessment categorized 23 studies as low, 8 studies as moderate, and 12 studies as high risk of bias based on the reported AEs. Three types of devices were identified for use in treating the uterine fibroids (ExAblate 2000/2100, Sonalleve V1/V2 and Chongqing Haifu JM 2.5 C/JM 5100), with the ExAblate 2000 device being the most popular (in 22 studies) which had a mean occurrence of 18.03% for AEs. Sonalleve was the second most popular device found in eleven studies with a mean occurrence of 40.3% for AEs. Pain (pelvic/abdominal) was the most common reported AE along with first- or second-degree skin burns, rashes or ulcerations being the next. The authors concluded that MRgFUS is a relatively safe choice in uterine fibroid therapy with the occurrence of AEs as rather low in addition to very few major AEs identified. However, the authors did find nerve damage as another clinical problem that should be considered as a potentially serious AE for a patient when performing MRgFUS. Limitations included small sample size with short follow-up time, lack of pain assessment tools, and unclear definition of an AE. Future prospective RCTs on larger populations and long-term outcomes are necessary to determine the safety and efficacy of the procedure.

An ECRI (2022) clinical evidence assessment for HIFU indicates the evidence may be somewhat favorable based on review of five systematic reviews with meta-analysis. Evidence assessment included results for symptom relief, QOL, reintervention rate, hospital stay, recovery time, post procedure pregnancy rate, and adverse events. When compared to surgery, HIFU was associated with fewer adverse events, shorter hospital stays, and a better QOL after one year. When compared to UAE, HIFU demonstrated less improvement in QOL, less symptom relief and a higher reintervention rate. Future high quality RCTs that assess long-term outcomes are warranted, in addition to standardized HIFU protocols.

A Hayes report (2019; updated 2022) concluded that, although evidence suggests that magnetic resonance-guided focused ultrasound (MRgFUS) reduces fibroid volume in women with symptomatic fibroids, the overall quality of the evidence is low due to the lack of well-designed controlled studies. Substantial uncertainty remains regarding the effect of magnetic resonance–guided focused ultrasound ablation of uterine fibroids on symptoms and the comparative effectiveness with other treatment alternatives.

Yu et al. (2021) conducted a comparative meta-analysis on the efficacy and safety of magnetic resonance-guided high intensity focused ultrasound (MR-HIFU) and ultrasound-guided HIFU. Forty-eight studies were included for review; twenty-eight addressed the MR-HIFU and 20 focused on US-HIFU. Uterine fibroids with of a volume of < 300 cm^3 were part of the inclusion criteria. NPVR is considered a significant parameter that is positively connected with clinical success rate. A NPVR for the MR-HIFU was 58.92% which was lower than that of the US-HIFU group which was 81.07%. A NPVR of greater than 80% is considered successful. The average treatment time for MR-HIFU was almost double that of US-HIFU which had a mean of 96.9 minutes. For treatment of symptomatic uterine fibroids, the author conclusions revealed

the US procedure had greater safety and efficacy than the MR procedure. Limitations included a loss of follow-up in the majority of the studies, poor documentation for number and location of fibroids, and lack of long-term outcomes.

In a 2019 systematic review (included in the 2019 Hayes report), Taheri et al. examined the change in uterine and fibroid volumes associated with UAE, focused ultrasound (FUS), and radiofrequency ablation (RFA). Eighty-one relevant papers were identified: 52 related to UAE, 11 to RFA, 17 to FUS, 1 compared UAE and FUS. Uterine volume and fibroid volume changes seen in these studies were at 1 to 36 months. The pooled fibroid volume reductions at six months seen with RFA were 70%, UAE 54% and FUS 32%. All three types of non-respective treatment result in fibroid volume reduction. However, fibroid volume reduction is most marked with RFA, with UAE resulting in the next most volume reduction. Additional larger cohort studies, including those that are randomized and/or comparative, would enable definitive conclusions.

Verpalen et al. 2019(included in the 2022 ECRI report) reassessed the effectiveness of MR-HIFU on reducing fibroid related symptoms. Individuals with fibroids containing a high T2 signal intensity or Funaki type 3 were excluded. Eighteen articles were included for review; sixteen of them were clinical trials and all were case series. The quality of evidence ranged from 9 to 16 using the 18-point criteria tool. The level of evidence for all included studies was IV according to Oxford Centre for Evidence-based Medicine (OCEBM) guidelines. Only 6 of the 18 studies were of acceptable quality. The author's concluded all studies displayed fibroid shrinkage and demonstrated that fibroids could continue shrink up to a years' time following the procedure. Adverse events were minimal and only two people experience a serious adverse effect (DVT and third-degree skin burn). The studies suggested that MRHIFU may be a cost-effective strategy however the topic of cost was not analyzed. Limitations included weaknesses of a meta-analysis design, potential high-risk bias related to specific study designs, different sample sizes and loss of follow-up in some sub-studies. The authors expressed additional future studies are needed, but because randomized trials are difficult to conduct and pose methodological challenges along with difficulty recruiting individuals, larger comparative controlled cohort studies with longer follow-up are warranted.

Ierardi et al. (2018) performed a systematic review for percutaneous ablation on uterine fibroids. The primary endpoint was to investigate feasibility and safety of the technique. Six articles containing 541 individuals were evaluated and no major complications of the procedure was found. After reviewing the data, the authors concluded microwave ablation of uterine fibroids to be safe and effective, however larger randomized prospective trials are needed to better demonstrate the benefits. The authors found a major limitation of MRgFUS is that many women are not eligible for the procedure due to potential challenges and risks associated with visceral injury.

Barnard et al. 2017 (included in the 2022 ECRI and the 2019 Hayes report and Kociuba et al. 2023 systematic review above) conducted a RCT and comprehensive cohort analysis to compare the periprocedural outcomes of fibroid embolization and focused ultrasound. Premenopausal women with symptomatic uterine fibroids seen at 3 US academic medical centers were enrolled in the RCT (n = 57). Women meeting identical criteria who declined randomization but agreed to study participation were enrolled in a nonrandomized parallel cohort (n = 34). The two treatment groups were analyzed by using a comprehensive cohort design. All women undergoing focused ultrasound and UAE received the same post procedure prescriptions, instructions, and symptom diaries for comparison of recovery in the first 6 weeks. Return to work and normal activities, medication use, symptoms, and adverse events were captured with post procedure diaries. Data were analyzed using the Wilcoxon rank sum test or $\chi 2$ test. Multivariable regression was used to adjust for baseline pain levels and fibroid load when comparing opioid medication, adverse events, and recovery time between treatment groups because these factors varied at baseline between groups and could affect outcomes. Adverse events were also collected. The results showed focused ultrasound surgery was a longer procedure than embolization, with 23 (over half) women undergoing focused ultrasound 2 treatment days. Immediate self-rated post procedure pain was higher after UAE than focused ultrasound. Compared with those having focused ultrasound (n = 39), women undergoing embolization (n = 36) were more likely to use outpatient opioid (75% vs 21%) and nonsteroidal anti-inflammatory medications (97% vs 67%) and to have a longer median recovery time (days off work, 8 vs 4; days until return to normal, 15 vs 10. There were no significant differences in the incidence or severity of adverse events between treatment arms; 86% of adverse events (42 of 49) required only observation or nominal treatment, and no events caused permanent sequelae or death. After adjustment for baseline pain and uterine fibroid load, UAE was still significantly associated with higher opioid use and longer time to return to work and normal activities. Results were similar when restricted to the RCT. The authors discussed the challenges that have inhibited mainstream adoption of MRgFUS, and they include the prolonged duration of most procedures, patient eligibility with numerous exclusion criteria and restrictive selection criteria and concluded that more comparative trials are needed to assess MRgFUS against other more established uterine-preserving treatments.

In a clinical assessment, ECRI concluded the evidence for the ExAblate Body System was inconclusive. The evidence suggests that the ExAblate reduces symptoms and improves the QOL in women up to three years, however the studies

have a high risk of bias and report on too few outcomes to be conclusive on how well it works. The evidence was limited by small sample size, retrospective design, high patient attrition, lack of control groups, randomization, and blinding. (ECRI 2017; updated August 2020).

According to a systematic review prepared for the AHRQ, HIFU reduced fibroid and uterine size, but strength of evidence is low because of short follow-up and poor quality of overall study design. Evidence related to patient reported outcomes is insufficient (Hartmann et al., 2017, included in the 2019 Hayes report).

Havryliuk et al. 2017 (included in the 2019 Hayes report) conducted a systematic review and meta-analysis from clinical studies that described populations of pre-menopausal women seeking surgical management (both uterine-sparing and hysterectomy) for their symptomatic fibroids. Procedures included in the analysis were myomectomy, UAE, Lap-RFA, MRgFUS, and hysterectomy. The complication rate for MRgFUS was 6.0% (1.3% major; 5.1% minor) (n = 298), and long-term follow-up averaged 12.6 months (n = 209). The reintervention rate was highest of all the procedures at 30.5% (145 combined patients). Based on their analysis, the authors concluded that MRgFUS carries low complication rates, no blood loss, and moderate improvement in HRQL scores. However, there is also a significant concern for injury of organs that may be in the way for focused ultrasound such as bowel, bladder, and sacral nerves. The authors state that limitations of this review include the inherent heterogeneity among studies; only a portion of the included studies were RCTs, most were not and were assigned an ACOG quality score of B; and lack of uniformity in reporting conventions. Further comprehensive prospective research, ideally in the form of well-powered RCTs, is needed to confirm the specific treatment modality preferred for specific anatomical variances of fibroids.

In a pilot study (PROMISe), Jacoby et al. 2016 (included in the 2019 Hayes report) assessed the feasibility of a full-scale, randomized, placebo-controlled trial to evaluate the safety and efficacy of MRgFUS in premenopausal women with symptomatic uterine fibroids. Twenty women (mean 44 years of age) were enrolled. Thirteen were randomly assigned to MRgFUS and 7 to sham therapy. The primary outcome was a change in fibroid symptoms from baseline to 4 and 12 weeks after treatment assessed by the UFS-QOL. Secondary outcome was incidence of surgery or procedures for recurrent symptoms at 12 and 24 months. Four weeks after treatment, all participants reported improvement in the UFS-QOL: a mean of 10 points in the MRgFUS group and 9 points in the placebo group. By 12 weeks, the MRgFUS group had improved more than the placebo group (mean 31 points and 13 points, respectively). The mean fibroid volume decreased 18% in the MRgFUS group with no decrease in the placebo group at 12 weeks. After unblinding at 12 weeks, 5 individuals in the sham group opted for treatment by MRgFUS and were followed for an additional 12 weeks. Two years after MRgFUS, 4 of 12 women who had a follow-up evaluation (30%) had undergone another fibroid surgery or procedure. The authors noted that a placebo effect may explain some of the improvement in fibroid-related symptoms observed in the first 12 weeks after MRgFUS. This study is limited by very small sample size and substantial loss to follow-up.

In a nonrandomized clinical trial, Froeling et al. 2013 (included in the 2019 Hayes report) compared the long-term outcome after UAE (n = 41) versus magnetic resonance-guided high-intensity focused ultrasound (MR-g HIFU) (n = 36) in women with symptomatic uterine fibroids. Symptom severity and total health-related QOL scores were assessed by questionnaire before treatment and at long-term follow-up after UAE (median 61.9 months) and after MR-g HIFU (median: 60.7 months). Reintervention was significantly lower after UAE (12.2%) than after MR-g HIFU (66.7%) at long-term follow-up. The authors reported that improvement of symptom severity and health-related QOL scores was significantly better after UAE resulting in a significant lower reintervention rate compared to MR-g HIFU.

In a prospective cohort study, Dobrotwir & Pun (2012) evaluated the efficacy and safety of MRgFUS in 100 people (mean age 42 years) with symptomatic fibroids (n = 104 treatments). Mean pretreatment fibroid volume was 185 cm^3 (range 2 to 1109). The authors reported that fibroid volume significantly decreased by the 12-month follow-up, and that the symptom severity score decreased by 55%. However, 14% of these individuals required reintervention for persistent or recurrent fibroid disease. This study is limited by lack of randomization and control and short-term follow-up.

Clinical Practice Guidelines

American Association of Gynecologic Laparoscopists (AAGL)

In a position statement on the treatment of submucous leiomyomas, the AAGL (2012) states that with currently available evidence, embolic and ablative therapies are not appropriate for women with submucous myomas who have current infertility or who wish to conceive in the future. These techniques include UAE and occlusion, as well as leiomyoma ablation with radiofrequency electricity, cryotherapy, and MRgFUS (based primarily on consensus and expert opinion [Level C]). The AAGL recommends long-term studies on the impact of various ablation techniques on the symptom of HMB in women with submucous leiomyomas.

American College of Obstetricians and Gynecologists (ACOG)

An ACOG committee opinion on uterine morcellation for presumed leiomyomas recommends women should be evaluated to determine increased risk of malignancy of the uterine corpus before considering morcellation of the uterus. The preoperative evaluation should include risk stratification and use of imaging, cervical cancer screening, and endometrial tissue sampling to identify malignancy. Additionally, the patient should be informed of the possible risk of disseminating and occult uterine malignancy by open morcellation, as well as the risk disseminating benign uterine tissue. Shared decision making, between the obstetrician-gynecologist and patient should include informed consent, explanation of risk and benefits of each approach to surgery for presumed leiomyomas, alternatives to morcellation, and the risk and benefits of morcellation (ACOG, 2021).

An ACOG committee opinion on acute AUB concludes that surgical management should be considered for those who are not clinically stable, are not suitable for medical management or have failed to respond appropriately to medical management. The choice of surgical management should be based on the patient's underlying medical conditions, underlying pathology, and desire for future fertility. (ACOG 2013; reaffirmed 2020).

Levonorgestrel-Releasing Intrauterine Device (LNG-IUD)

In a practice bulletin on management of symptomatic uterine leiomyomas, ACOG states that the LNG-IUD) may be considered for treatment of abnormal uterine bleeding, however there is insufficient evidence to support their use for the treatment of any other uterine leiomyoma symptoms other than bleeding (ACOG, June 2021).

An ACOG practice bulletin on the use of non-contraceptive uses of hormonal contraceptives says 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 (ACOG, 2010; reaffirmed 2020). (Evidence Level B – Based on limited or inconsistent scientific evidence.)

Magnetic Resonance Imaging-Guided Focused Ultrasound Ablation

In a practice bulletin on management of symptomatic uterine leiomyomas ACOG states that while limited, low quality data suggests MRgFUS is associated with a reduction in leiomyoma and uterine size, smaller randomized comparative data suggests when compared with UAE, MRgFUS is associated with less improvement in symptoms and a higher rate of reintervention (ACOG, 2008; reaffirmed 2021).

Uterine Artery Embolization (UAE)

In a practice bulletin for AUB, ACOG states an office endometrial biopsy is the first-line procedure for tissue sampling in the evaluation of people with AUB. Endometrial sampling should be performed on individuals younger than 45 years of age for persistent AUB and failed medical management. (ACOG 2012, reaffirmed 2016).

In a practice bulletin on management of symptomatic uterine leiomyomas, ACOG states UAE is recommended as a procedure for the treatment of uterine leiomyomas in women who desire uterine preservation and that they be counseled on the limited available data for reproductive outcomes (ACOG, 2008; reaffirmed 2021).

American College of Radiology (ACR)

The ACR revised its appropriateness criteria for managing uterine fibroids in 2023. A summary of recommendations is as follows:

- Laparoscopic or open myomectomy, medical management, MRgFUS, or UAE is usually appropriate for the initial therapy of a reproductive age patient with uterine fibroids, symptomatic with heavy uterine bleeding or bulk symptoms (e.g., pressure, pain, fullness, bladder, or bowel symptoms), and a desire to preserve fertility. In most cases, medical management should be trialed before pursuing more invasive therapies. The procedures are equivalent alternatives (i.e., only one procedure will be ordered to provide the clinical information to manage the patient's care effectively).
- Laparoscopic or open myomectomy, medical management, MRgFUS, or UAE is usually appropriate for the initial therapy for a reproductive age patient with uterine fibroids, symptomatic with heavy uterine bleeding or bulk symptoms (e.g., pressure, pain, fullness, bowel, or bladder symptoms), and no desire for future ACR Appropriateness Criteria® 15 Management of Uterine Fibroids fertility. In most cases, medical management should be trialed before pursuing more invasive therapies. The procedures are equivalent alternatives (i.e., only one procedure will be ordered to provide the clinical information to manage the patient's care effectively).

- Medical management or UAE is usually appropriate for the initial therapy for a reproductive-age patient with uterine fibroids and concurrent adenomyosis, symptomatic with heavy uterine bleeding or bulk symptoms (e.g., pressure, pain, fullness, bladder, or bowel symptoms), and no desire for future fertility. In most cases, medical management should be trialed before pursuing more invasive therapies.
- Hysteroscopic myomectomy or medical management is usually appropriate for the initial therapy for a reproductive-age patient with pedunculated submucosal uterine fibroids that are symptomatic with heavy uterine bleeding. In most cases, medical management should be trialed before pursuing more invasive therapies.
- Hysterectomy is usually appropriate as a next step for a postmenopausal patient with uterine fibroids, symptomatic with heavy uterine bleeding or bulk symptoms (e.g., pressure, pain, fullness, bladder, or bowel symptoms) and negative endometrial biopsy. These procedures are equivalent alternatives (i.e., only one procedure will be ordered to provide the clinical information to manage the patient's care effectively).
- Hysteroscopic myomectomy or laparoscopic or open myomectomy is usually appropriate for the initial therapy for a reproductive-age patient with uterine fibroids desiring pregnancy and experiencing reproductive dysfunction. These procedures are equivalent alternatives (i.e., only one procedure will be ordered to provide the clinical information to manage the patient's care effectively). The panel did not agree on recommending medical management for this clinical scenario. There is insufficient medical literature to conclude whether or not these individuals would benefit from this procedure in this scenario. Intervention with this procedure in this patient population is controversial but may be appropriate.

National Institute of Health and Care Excellence (NICE)

The NICE guidelines on ultrasound-guided high-intensity transcutaneous focused ultrasound for symptomatic uterine fibroids state that the current evidence on the safety of ultrasound-guided high intensity transcutaneous focused ultrasound for symptomatic uterine fibroids shows there are well-recognized complications, including skin burns. The evidence on efficacy is limited in quality. Therefore, NICE recommends only using this procedure with special arrangements for clinical governance, consent, and audit or research. NICE recommends that:

- Clinicians wishing to do ultrasound-guided high intensity transcutaneous focused ultrasound for symptomatic uterine fibroids should Inform the clinical governance leads in their NHS trusts.
- Ensure that individuals understand the procedure's safety and efficacy and any uncertainties about these, and provide them with clear written information to support shared decision-making. In addition, using NICE's information for the public is recommended.
- Audit and review clinical outcomes of all those having ultrasound-guided high-intensity transcutaneous focused ultrasound for symptomatic uterine fibroids. NICE has identified relevant audit criteria and has developed an audit tool (which is for use at local discretion).

Additionally, NICE recommends that during the consent process, clinicians should tell individuals that their symptoms may not be thoroughly relieved and may return and that further procedures may be needed. They should also inform patients about the risk of skin burns. Individuals considering pregnancy should be told that the effects of the procedure on fertility and future pregnancy are uncertain. A multidisciplinary team, including a gynecologist and an appropriate imaging specialist should do patient selection. The procedure should only be done in specialized centers by clinicians with specific training in this technique. NICE encourages further research and prospective data collection. Studies comparing ultrasound-guided high-intensity focused ultrasound with other therapies, such as UAE and MRI-guided high intensity transcutaneous focused ultrasound, would be helpful. Studies should report patient selection (including size, location, and number of fibroids), patient-reported outcome measures, long-term outcomes, and subsequent pregnancy rates (NICE, 2019).

A NICE guideline on assessment and management of HMB recommends LNG-IUS as the first treatment for women with no identified pathology, fibroids less than 3 cm in diameter, or suspected or diagnosed adenomyosis. If the treatment is unsuccessful, the patient declines pharmacological treatment, or symptoms are severe, referral to a specialist is recommended to discuss additional options. For women with fibroids greater than 3 cm in diameter, LNG-IUS is listed as a pharmacologic option (NICE, 2018; updated 2021).

The NICE guideline on the management of HMB lists UAE as an option for women with fibroids 3 cm or more in diameter. They recommend that the woman's uterus and fibroid(s) be assessed by ultrasound prior to the procedure, and if further information about fibroid position, size, number, and vascularity is needed, MRI should be considered (NICE, 2018; updated 2021).

A NICE guidance document states that current evidence on the efficacy of MRgFUS for uterine fibroids in the short term is adequate, although further treatment may be required and the effect on subsequent pregnancy is uncertain. There are well-recognized complications, but the evidence on safety is adequate to support the use of this procedure provided that

normal arrangements are in place for clinical governance and audit. NICE encourages further research into the efficacy of MRgFUS for uterine fibroids. Research studies should report long-term outcomes, including the need for further treatment (NICE, 2011).

The NICE guidance document states that current evidence on UAE for fibroids shows that the procedure is efficacious for symptom relief in the short and medium term for a substantial proportion of people. 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).

Society of Interventional Radiology (SIR)

SIR quality improvement guidelines (Dariushnia et al., 2014) state that UAE is indicated for the treatment of uterine leiomyomata that are causing significant symptoms, occasionally a single symptom, but more commonly a combination of symptoms. The most common of these are:

- Heavy or prolonged menstrual bleeding
- Severe menstrual cramping
- Pelvic pressure, discomfort, excessive bloating, or fullness, particularly perimenstrual, or bothersome abdominal wall distortion caused by the enlarged uterus
- Pelvic pain related to identified leiomyomas, including dyspareunia
- Urinary urgency, frequency, nocturia or retention related to the enlarged leiomyomatous uterus
- Hydronephrosis caused by the enlarged uterus

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Levonorgestrel-Releasing Intrauterine Device (LNG-IUD)

Mirena® received FDA approval on December 8, 2000, for use as an intrauterine contraceptive. Treatment of HMB for women who choose to use intrauterine contraception as their method of contraception was approved as an additional indication on October 1, 2009. Search the following website for more information: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. (Accessed August 8, 2024)

Skyla® received FDA approval on January 9, 2013, for use as an intrauterine contraceptive. Search the following website for more information: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. (Accessed August 8, 2024)

Liletta™ received FDA approval on February 26, 2015, for use as an intrauterine contraceptive. Search the following website for more information: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. (Accessed August 8, 2024)

Kyleena™ received FDA approval on September 16, 2016, for use as an intrauterine contraceptive. Search the following website for more information: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. (Accessed August 8, 2024)

Uterine Artery Embolization (UAE)

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. Search the following website for additional information: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. (Accessed August 8, 2024)

Magnetic Resonance-Guided Focused Ultrasound (MRgFUS)

The ExAblate 2000/2100 System (Insightec) received premarket approval (PMA) on October 22, 2004 (P040003); approval for updated labeling was given on August 9, 2011. The device is indicated for ablation of uterine fibroid tissue in pre- or perimenopausal women with symptomatic uterine fibroids who desire a uterine sparing procedure and whose uterine size is less than 24 weeks. On August 31, 2015, the indications were modified to remove the restriction of treatment to women who had completed childbearing. Refer to the following website for more information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P040003S009. (Accessed August 8, 2024)

Laparoscopic Power Morcellation Warning

Laparoscopic power morcellators are Class II medical devices used during laparoscopic (minimally invasive) surgeries to cut tissue into smaller pieces so the tissue can be removed through a small incision site (typically 2 cm long or less). An FDA Safety Communication issued on November 24, 2014, recommends that manufacturers of laparoscopic power morcellators with a general indication or a specific gynecologic indication prominently include the following black box warning and contraindications in their product labeling:

- **Warning**
  - Uterine tissue may contain unsuspected cancer. The use of laparoscopic power morcellators during fibroid surgery may spread cancer and decrease the individual's long-term survival. Because of this risk and the availability of alternative surgical options for most women, the FDA is warning against the use of laparoscopic power morcellators in the majority of women undergoing myomectomy or hysterectomy for treatment of fibroids. This information should be shared with individuals when considering surgery with the use of these devices.
- **Contraindications**
  - Laparoscopic power morcellators are contraindicated in gynecologic surgery in which the tissue to be morcellated is known or suspected to contain malignancy.
  - Laparoscopic power morcellators are contraindicated for removal of uterine tissue containing suspected fibroids in those who are peri- or post-menopausal, or are candidates for en bloc tissue removal, for example through the vagina or via a mini-laparotomy incision.

For FDA warnings, contraindications, final guidance, updates, and additional information, refer to the following website: https://www.fda.gov/medical-devices/surgery-devices/laparoscopic-power-morcellators.(Accessed August 8, 2024)

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Policy History/Revision Information

Date	Summary of Changes
01/01/2025	**Template Update** • Created shared policy version to support application to UnitedHealthcare West plan membership **Coverage Rationale** • Replaced reference to "*women*" with "*individuals*" **Medical Records Documentation Used for Reviews** *(previously titled Documentation Requirements)* • Replaced list of *Required Clinical Information* with instruction to refer to the protocol titled Medical Records Documentation Used for Reviews **Supporting Information** • Updated *Description of Services*, *Benefit Considerations*, *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy versions 2024T0442QQ and MMG002.DD

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.