Name of Policy:
Levonorgestrel-releasing Intrauterine System (LNG-IUS) (Mirena®) for Heavy Menstrual Bleeding

Policy #: 209
Category: OB/Gyn Reproductive

Latest Review Date: September 2018
Policy Grade: A

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
Description of Procedure or Service:
Levonorgestrel-releasing intrauterine system (LNG-IUS), (Mirena®), is a device that releases levonorgestrel into the uterine cavity at a rate of approximately 20mcg per day for five years. It is indicated for intrauterine contraception for up to five years. It may also cause significant reduction in menstrual blood loss, thus it has been used for the treatment of menorrhagia and dysfunctional uterine bleeding. It has also been used to treat endometrial hyperplasia, as an effective method for suppression of the endometrium and as an alternative to hysterectomy.

Policy:
Levonorgestrel-releasing intrauterine system (LNG-IUS (Mirena®) meets Blue Cross and Blue Shield of Alabama’s medical criteria for coverage for the following medical conditions:

- Idiopathic menorrhagia
- Dysfunctional uterine bleeding
- Premenopausal menorrhagia
- Adenomatous hyperplasia
- Metrorrhagia

It is currently covered for groups which provide coverage for contraception.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member’s contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:
Menorrhagia represents a major burden in terms of women’s quality of life and health care resources. Menorrhagia is defined as menstrual blood loss (MBL), of at least 80 ml per cycle and is a common cause of iron deficiency anemia. Treatment options include drugs that can reduce heavy MBL, such as tranexamic acid, NSAIDS, combined oral contraceptives, progestogens, and the LNG-IUS. Surgery options include hysterectomy or endometrial resection, but these usually result in infertility. Some factors that may influence treatment choice are whether cycles are ovulatory or anovulatory, the need for contraception, patient preference, and contraindications to treatment.

The levonorgestrel-releasing intrauterine system (LNG-IUS) was developed primarily as a contraceptive device. It causes a reduction in menstrual blood loss with comparatively few side effects. It has been used as a treatment for menorrhagia and, unlike surgical treatments, preserves fertility.
Endrikat et al (2009) evaluated the efficacy of a levonorgestrel-releasing intrauterine system (LNG-IUS) compared with a combined oral contraceptive containing 1mg norethindrone acetate and 20 mg ethinyl estradiol (OC1/20) in reducing menstrual blood loss (MBL) in women over 30 years of age with idiopathic menorrhagia. Women were randomized to either with LNG-IUS (n = 20) or with OC1/20 (n = 19) over 12 months. The primary endpoint was the change in MBL from baseline to 12 months. Secondary endpoints included treatment success (defined as a MBL score < 100 after 12 months), hemoglobin levels, and the menorrhagia severity score. In both treatment groups, MBL decreased significantly from baseline to 12 months. For the primary endpoint, the MBL score decreased significantly more in the LNG-IUS group (median from 228 to 13, mean percent change-83%) compared to the OC1/20 group (median from 290 to 72; mean percent change-68%) after 12 months. In the LNG-IUS group, 80% of subjects had treatment success compared with 36.8 % in the OC1/20 group. Both treatments increased hemoglobin concentrations significantly between baseline and 12 months. The menorrhagia severity score was consistently lower in the LNG-IUS group at all study time points and was significantly lower at six months. Both treatments were well tolerated.

Kaunitz et al (2009) performed a systematic review and meta-analysis comparing the LNG-IUD to endometrial ablation in the treatment of heavy menstrual bleeding. Six randomized controlled trials that included 390 women (levonorgestrel intrauterine system, n=196; endometrial ablation, n=194) where menstrual blood loss was reported using pictorial blood loss assessment chart (PBAC) scores were identified. 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 six 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.

In 2013, Gupta et al compared the levonorgestrel releasing intrauterine system (levonorgestrel IUS) with usual medical treatment in 571 randomly assigned women with menorrhagia. The primary outcome was the patient-reported score on the Menorrhagia Multi-Attribute Scale (MMAS) (ranging from 0 to 100, with lower scores indicating greater severity), assessed over a 2-year period. Secondary outcomes included general quality-of-life and sexual-activity scores and surgical intervention. MMAS scores improved from baseline to 6 months in both the levonorgestrel-IUS group and the usual-treatment group (mean increase, 32.7 and 21.4 points, respectively; P<0.001 for both comparisons). The improvements were maintained over a 2-year period but were significantly greater in the levonorgestrel-IUS group than in the usual-treatment group (mean between-group difference, 13.4 points; 95% confidence interval, 9.9 to 16.9; P<0.001). Improvements in all MMAS domains (practical difficulties, social life, family life, work and daily routine, psychological well-being, and physical health) were significantly greater in the levonorgestrel-IUS group than in the usual-treatment group, and this was also true for seven of the eight quality-of-life domains. At 2 years, more of the women were still using the levonorgestrel-IUS than were undergoing the usual medical treatment (64% vs. 38%, P<0.001). There were no significant between-group differences in the rates of surgical intervention or sexual-activity scores. There were no significant differences in serious adverse events between groups. The authors concluded that levonorgestrel IUS was more effective than usual medical treatment in reducing the effect of heavy menstrual bleeding on quality of life.
In 2014, Qiu et al conducted a systematic review and meta-analysis comparing the effects of the levonorgestrel IUS with conventional medical treatment in reducing heavy menstrual bleeding. A total of 8 RCTs (1170 women, L-IUS, n=562, conventional medical treatment, n=608) met inclusion criteria. The LNG-IUS was superior to conventional medical treatment in reducing menstrual blood loss (as measured by the alkaline hematin method or estimated by pictorial bleeding assessment chart scores). More women were satisfied with the LNG-IUS than with the use of conventional medical treatment (odds ratio [OR] 5.19, 95% confidence interval [CI] 2.73-9.86). Compared with conventional medical treatment, the LNG-IUS was associated with a lower rate of discontinuation (14.6% vs. 28.9%, OR 0.39, 95% CI 0.20-0.74) and fewer treatment failures (9.2% vs. 31.0%, OR 0.18, 95% CI 0.10-0.34). Serious adverse events were statistically comparable between treatments. The authors concluded by stating L-IUS was more effective for management of menorrhagia than medical treatment.

In 2016, Kai et al preformed a multicenter, open label, long term, randomized controlled trial that assessed the effectiveness of the L-IUS versus usual medical treatments for women presenting with heavy menstrual bleeding. A total of 571 women were randomized into L-IUS or usual medical treatment groups. The primary outcome was the patient reported Menorrhagia Multi-Attribute Scale (MMAS, measuring effect of HMB on practical difficulties, social life, psychological and physical health, and work and family life; scores from 0 to 100). Secondary outcomes included surgical intervention (endometrial ablation/hysterectomy), general quality of life, sexual activity, and safety. At 5 years post-randomization, 424 (74%) women provided data. While the difference between LNG-IUS and usual treatment groups was not significant (3.9 points; 95% confidence interval = -0.6 to 8.3; P = 0.09), MMAS scores improved significantly in both groups from baseline (mean increase, 44.9 and 43.4 points, respectively; P<0.001 for both comparisons). Rates of surgical intervention were low in both groups (surgery-free survival was 80% and 77%; hazard ratio 0.90; 95% CI = 0.62 to 1.31; P = 0.6). There was no difference in generic quality of life, sexual activity scores, or serious adverse events. The authors concluded that large improvements in symptom relief across both groups show treatment for heavy menstrual bleeding can be successfully initiated with long term benefit and only a modest need for surgery.

**Summary of Evidence**

For women who are experiencing heavy menstrual bleeding and receive a levonorgestrel releasing IUS (i.e. Mirena), the evidence consists of meta-analyses and randomized controlled trials. The primary endpoints were quality of life, safety, and surgical reinterventions. Overall, studies have shown more patient satisfaction with LNG-IUDs compared to medical treatment. In a systematic review and meta-analysis conducted, the LNG-IUS was superior to conventional medical treatment in reducing menstrual blood loss and more women were satisfied with the LNG-IUS than with the use of conventional medical treatment. In other trials, the LNG-IUS group was more satisfied compared to medical treatment. The evidence is sufficient to determine that the device results in a meaningful improvement in the net health outcome.
Practice and Position Statements
In January 2010 (reaffirmed in 2018), the American College of Obstetricians and Gynecologists (ACOG) replaced Committee Opinion number 337 (Noncontraceptive uses of the Levonorgestrel Intrauterine System) with a Practice Bulletin (Number 110), “Noncontraceptive uses of Hormonal Contraception.” Per the bulletin, “The levonorgestrel intrauterine system is a highly effective contraceptive method with significant noncontraceptive benefits in women with excessive menstrual bleeding and dysmenorrhea. Numerous studies have confirmed the effectiveness of the levonorgestrel intrauterine system for reduction of menstrual blood loss from idiopathic menorrhagia, adenomyosis, leiomyomas, pain due to endometriosis and hemostatic disorders with commensurate reduction in dysmenorrhea and anemia.”

Key Words:
Mirena®, levonorgestrel-releasing intrauterine system, LNG-IUS, menorrhagia, premenopausal menorrhagia, endometrial hyperplasia, adenomatous hyperplasia, dysfunctional uterine bleeding, hysterectomy, IUS, menstrual bleeding, heavy menstrual bleeding

Approved by Governing Bodies:
The FDA approved Mirena® (levonorgestrel-releasing intrauterine device) in December 2000 as a hormone-releasing system for intrauterine contraception.

The FDA approved Mirena® (levonorgestrel-releasing intrauterine device) October 1, 2009 for the treatment of heavy menstrual bleeding in women who use intrauterine contraception as a method of pregnancy prevention.

Benefit Application:
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable. The use of this device for contraceptive management is a group specific benefit.
ITS: Home Policy provisions apply
FEP contracts: Special benefit consideration may apply. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Current Coding:
CPT codes:
58300 Insertion of intrauterine device (IUD)

HCPCS codes:
J7298 Levonorgestrel-releasing intrauterine contraceptive system, 52mg, 5 year duration (Effective 01/01/2016)
S4981 Insertion of levonorgestrel-releasing intrauterine system
Previous Coding:
J7302 Levonorgestrel-releasing intrauterine system (Mirena®) (Deleted 12/31/2015)

References:

**Policy History:**
Medical Policy Group, October 2004 (3)
Medical Policy Administration Committee, October 2004
Available for comment November 24, 2004-January 7, 2005
Medical Policy Group, October 2007 (1)
Medical Policy Group, January 2009 (3)
Medical Policy Administration Committee, February 2009
Available for comment January 14-February 27, 2009
Medical Policy Group, October 2009 (3)
Medical Policy Administration Committee, October 2009
Medical Policy Group, January 2013 (1): Update to Key Points and References related to annual review process; no change in policy statement
Medical Policy Group, February 2016: 2016 Annual Coding Update. Created Previous coding section and moved HCPCs code J7302 to this section. Added HCPCs code J7298 to current coding.
Medical Policy Group, April 2016 (2): Update to Current coding; code J7298 updated to 5 year duration.

Medical Policy Group, September 2018 (4): Updates to Title, Key Points, Key Words, and References. No policy statement change. Added Key Words: IUS, menstrual bleeding, heavy menstrual bleeding. Added “for Heavy Menstrual Bleeding” to the title.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.