Name of Policy:
Levonorgestrel-releasing Intrauterine System (LNG-IUS) (Mirena®)

Policy #: 209
Category: OB/Gyn Reproductive
Latest Review Date: January 2013
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.
There have been several articles published in the literature that support the use of this device. Some of them are summarized below.

Stewart, et al (2001), published a systematic review looking at whether the use of LNG-IUS for menorrhagia results in better outcomes than other treatments for menorrhagia, in terms of reducing menstrual blood loss, patient satisfaction, quality of life, and cost effectiveness. Ten studies were identified that fulfilled the criteria, five were randomized controlled trials and five were case series. Nine studies recorded statistically significant average menstrual blood loss reductions with LNG-IUS (range 74%-97%). One study reported a 70% reduction in menstrual disturbance score compared to a 2% reduction in controls. Other studies reported mean menstrual blood loss reduction at 12 months was greater for LNG-IUS users (96%) compared to flurbiprofen (21%) or tranexamic acid (44%). Also, another study reported mean menstrual blood loss reduction at 12 months was less for LNG-IUS users (90%) compared to endometrial resection (98%), although this was not significant. One study reported 82% of LNG-IUS users were taken off surgery wait lists by 12 months. In another study, 64% of LNG-IUS users canceled surgery at six months.

The authors concluded that these studies showed that LNG-IUS can reduce menstrual blood loss in women with confirmed menorrhagia. However, further research is needed to compare it with other treatments, to see if it is effective long-term, to see its impact on demand for surgery, and to determine its cost effectiveness.

Barrington, et al (2002) compared the effectiveness of endometrial thermal ablation and LNG-IUS to manage menorrhagia. Fifty women were randomized to either surgical treatment using thermal ablation or medical treatment using a LNG-IUS. A menstrual chart was done before and six months after treatment. There was no significant difference in the follow up menstrual scores. The authors concluded that thermal balloon ablation and the LNG-IUS are equally effective in reducing menstrual blood loss.

Hurskainen, et al (2002) published a report comparing costs and quality of life after treatment of menorrhagia with the LNG-IUS (n=119) and hysterectomy (n=117). At 12 months after treatment, in the LNG-IUS group, 68% still had the device in place, 20% had undergone hysterectomy and 8% had the device removed. Of those with the device, 53% had little or no menstrual bleeding. For the quality of life scores, the improvement in pain score was greater for the hysterectomy group, but for the other seven categories, there was no significant difference between the groups.

Wildemeersch and Dhont (2003) reported on 12 women with abnormal uterine bleeding and non-atypical and atypical endometrial hyperplasia who were treated with a “frameless” LNG-IUS, which releases 14 mcg/d of levonorgestrel. The cure rate was 100%, as confirmed by repeat endometrial biopsy at 12 months. The authors concluded this is an effective method for suppression of the endometrium and may be considered as an alternative to hysterectomy.

Vereide, et al (2003) reported on 57 women with endometrial hyperplasia and compared treatment with LNG-IUS (n=26) and per-oral gestagen (n=31, historic group). Only patients with low or uncertain risk of cancer development were included. After 3 months of treatment, all
the LNG-IUS patients showed regression of hyperplasia, whereas 14 of 31 of the per-oral patients still had disease. The authors concluded that LNG-IUS was a superior treatment for endometrial hyperplasia.

October 2007 Update
A review of the literature and the manufacturer information identified no new information. The policy statement remains unchanged.

October 2009 Update
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.

January 2013 Update
In January 2010, the American College of Obstetricians and Gynecologist (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.”
de Souza et al (2010) compared levonorgestrel-releasing intrauterine system (LNG-IUS) \( n=30 \) women with thermal balloon ablation (TBA) \( n=28 \) women for the treatment of heavy menstrual bleeding (HMB) in a prospective randomized trial. The investigators reported that hemoglobin levels increased \( p<.001 \) and blood loss was reduced \( p<.001 \) in both groups after one year of treatment. Menstrual bleeding was less in the LNG-IUS group compared to the TBA group at six and 12 months of treatment \( p=.035 \) and \( p=.048 \), respectively. Intermenstrual bleeding was significantly less in the TBA group at six months compared to the LNG-IUS group \( p=.044 \); however, there was no significant difference at 12 months \( p=.129 \). No difference was found in psychological aspects between pre- and posttreatment variables in either of the groups \( p=.537 \). The investigators concluded both the LNG-IUS and TBA appear to be effective in controlling HMB; however, posttreatment uterine bleeding patterns are different.

Heliövaara-Peippo et al (2009) evaluated the changes in lower abdominal pain and back pain among women with menorrhagia treated by hysterectomy or LNG-IUS in a randomized controlled trial of 236 women. Women were randomly assigned to treatment by hysterectomy \( n = 117 \) or LNG-IUS \( n = 119 \). Main outcome measures, frequency and intensity of lower abdominal pain and back pain, were evaluated by questionnaires at baseline and after six months, 12 months and five years. The investigators reported by six months, women in both groups had less frequent back pain than before treatment \( p < 0.001 \). Lower abdominal pain decreased only in the hysterectomy group \( p = 0.02 \) with significant differences between the groups. Between 12 months and five years, frequency of lower abdominal pain \( p = 0.05 \) and back pain \( p = 0.002 \) decreased more in the LNG-IUS group than in the hysterectomy group. Between baseline and five years, the lower abdominal pain score (including frequency and intensity of pain) decreased in both groups \( p < 0.001, p = 0.01 \). Back pain score decreased only in the LNG-IUS group and the difference between the groups was significant \( p = 0.02 \). However, some women experienced more pain after both treatments than before treatment. In multivariate analyses, LNG-IUS use was associated with a decrease in lower abdominal pain and back pain. The investigators concluded in the treatment of menorrhagia, both hysterectomy and LNG-IUS decrease lower abdominal pain. LNG-IUS use, but not hysterectomy, has beneficial effects on back pain.

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

**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.

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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.