Liletta®
(levonorgestrel-releasing intrauterine system) 52 mg

A Review of LILETTA

LLT51211
06/16

Chapter 1

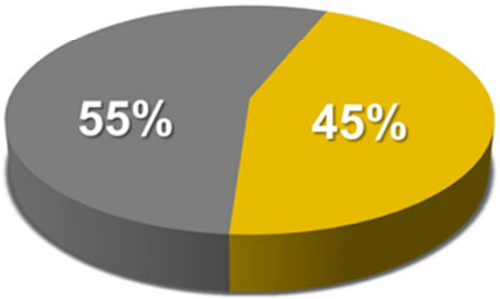
Long Acting Reversible Contraceptives – Overview

The following slides provide general information about long-acting reversible contraceptives (LARCs), including IUDs and implants, and are not intended to make claims about any specific treatment.

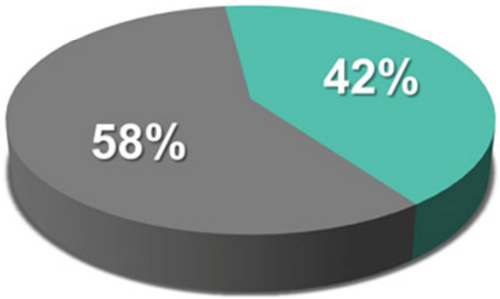
Following the overview of IUDs and implants, we will discuss a contraceptive option. For product-specific information, please consult the full Prescribing Information.

Unintended Pregnancies in the U.S.

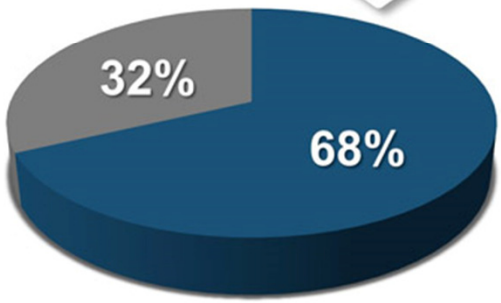
45% of pregnancies (2.8 million) in the U.S. are ***unintended***[1]



42% of unintended pregnancies end in ***abortion***[1]



68% of unplanned births are paid for by ***public insurance programs***, primarily Medicaid[2]



Annual government expenditures for births, abortions, and miscarriages resulting from ***unintended pregnancies*** equals

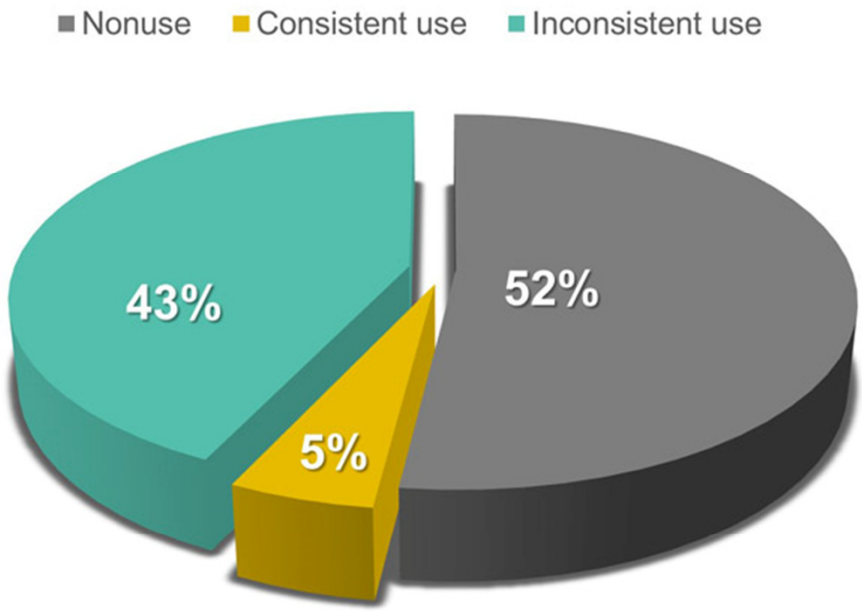
$21 billion

1. Guttmacher Institute. Unintended Pregnancy in the United States. Fact Sheet March 2016. Available at: https://www.guttmacher.org/fact-sheet/unintended-pregnancy-united-states. Accessed June 13, 2016.
2. Guttmacher Institute. Public Costs from Unintended Pregnancies and the Role of Public Insurance Programs in Paying for Pregnancy-Related Care National and State Estimates for 2010. Available at: https://www.guttmacher.org/sites/default/files/report_pdf/public-costs-of-up-2010.pdf. Accessed June 13, 2016.

Reasons for Unintended Pregnancies

- Inconsistent, or lack of, contraceptive use

95% of unintended pregnancies are due to ***Nonuse*** or ***Inconsistent use*** of contraceptives



Guttmacher Institute. Unintended Pregnancy in the United States. New York:. December 2013:1-6. Available at: http://www.guttmacher.org/pubs/FB-Unintended-Pregnancy-US html. Accessed Nov 3, 2014.

Reasons for Unintended Pregnancies

- Low adherence to reversible contraceptives

10

The number of times a typical woman discontinues contraceptive use for method-related reasons in her lifetime*[1]

1.3 million

The number of unintended pregnancies resulting from inconsistent or incorrect use of contraceptives[2]

* A woman continuously using reversible contraception from her 15th to her 45th birthday

1. Trussell J, et al. *Fam Plann Perspect*. 1999 Mar-Apr;31(2):64-72, 93.
2. Guttmacher Institute. Improving Contraceptive Use in the United States. Available at: http://www.guttmacher.org/pubs/2008/05/09/ImprovingContraceptiveUse.pdf. Accessed Feb 11, 2015.

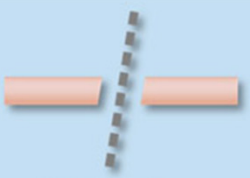
Contraceptive Methods: Tiered Effectiveness

More Effective

Less than 1 pregnancy per 100 women in one year

Less Effective

About 30 pregnancies per 100 women in one year



Sterilization

Injectable

Pill

Patch

Vaginal Ring

Male/Female condom

Sponge

Diaphragm

Fertility Awareness

Withdrawal

Spermicide

1. World Health Organization. Do You Know Your Family Planning Choices? Available at: https://www.fphandbook.org/sites/default/files/wallchart_english_2012.pdf. Accessed March 17, 2015.
2. Centers for Disease Control and Prevention. U.S. Selected Practice Recommendations for Contraceptive Use,2013: MMWR. 2013;62(5):1-46.

Recommendations for LARC (IUD and Implant) Use

American Congress of Obstetricians and Gynecologists (ACOG)[1]

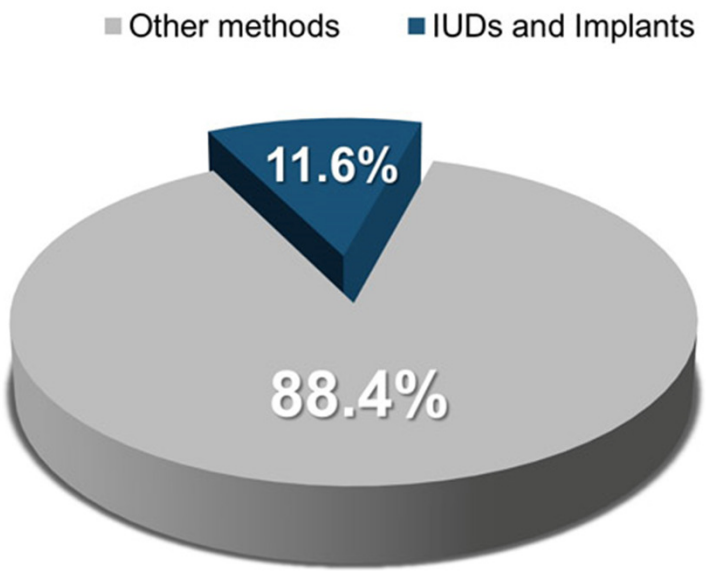
- "LARC methods are the best tool we have to fight against unintended pregnancies, which currently account for 49% of U.S. pregnancies each year."
- "The major advantage is that after insertion, LARCs work without having to do anything else. There's no maintenance required."

Centers for Disease Control and Prevention (CDC)[2]

- "All women should be counseled about the full range and effectiveness of contraceptive options for which they are medically eligible so that they can identify the optimal method."
- "LARC methods are appropriate for most women."
- "Among healthy women, few examinations or tests are needed before initiation of an IUD. Bimanual exam and cervical inspection are necessary before IUD insertion."

1. The American College of Obstetricians and Gynecologists. Committee Opinion. UDs Implants are Most Effective Reversible Contraceptives Available. Available at: http://www.acog.org/About-ACOG/News-Room/News-Releases/2011/IUDs-Implants-Are-Most-Effective-Reversible-Contraceptives-Available. Accessed March 6, 2015.
2. CDC. U.S. Selected Practice Recommendations for Contraceptive Use. MMWR. 2013;62(5):1-60.

Rates of IUD and Implant Use in the U.S. are Low



Despite their effectiveness, IUD and implant use in the U.S. is ***lower*** than any other developed nation

In the United States, IUD and implant users make up only *11.6%* of total contraceptive users

Kavanaugh ML, et al. *Obstet Gynecol.* 2015;126(5):917-27.

Barriers to Access and Use of IUDs and Implants

Clinicians

Patients

Insurance

Barriers to Access and Use of IUDs and Implants

- **Clinician Barriers**
  - Misconceptions of appropriateness[1,2]
  - Lack of insertion training[2,3]
  - Lack of availability on-site[4,5]
- **Patient Barriers**
- **Insurance Provider Barriers**

1. Luchowski AT, et al. *Contraception*. 2014;89(6):572-7.
2. ACOG Committee Opinion. Increasing Use of Contraceptive Implants and Intrauterine Devices To Reduce Unintended Pregnancy. Number 450, 2009.
3. Speidel J, et al. *Contraception*. 2008 Sep;78(3):197-200.
4. Beeson T, et al. *Contraception*. 2014;89(2):91-6.
5. CDC. *MMWR*. 2011;Jan;60(1):1-4

Barriers to Access and Use of IUDs and Implants

- Clinician Barriers
- **Patient Barriers**
  - Lack of LARC awareness[1]
  - High up-front costs[2]
  - Low accessibility[3]
- Insurance Provider Barriers

1. Fleming KL, et al. *Contraception*. 2010;82(2):178-82.
2. Eisenberg D, et al. *J Adolesc Health*. 2013;52(4 Suppl):S59-63
3. Beeson T, et al. *Contraception*. 2014;89(2):91-6.

Barriers to Access and Use of IUDs and Implants

- Clinician Barriers
- Patient Barriers
- **Insurance Provider Barriers**
  - Patient out of pocket costs[1,2]
  - Billing and reimbursement[3]

1. Sonfield A. *Guttmacher Policy Review*. 2013;16:4 Available at: http://www.guttmacher.org/pubs/gpr/16/4/gpr160408.html Accessed December 30th 2014
2. Eisenberg D, et al. *J Adolesc Health*. 2013;52(4 Suppl):S59-63.
3. Thompson KM, et al. *Contraception*. 2011;83(1):41-7

Contraceptive CHOICE Study

- A study of 9,256 women in the St. Louis area
- Provided consultation and access to contraceptives at no cost to the patient

75%

Of women in the CHOICE Study chose IUDs or implants when barriers of ***cost***, ***knowledge***, and ***access*** were removed

McNicholas C, et al. *Clin Obstet Gynecol.* 2014;57(4):635-43

Colorado Family Planning Initiative (CFPI)

- Beginning in 2009, CFPI aimed to increase access to IUDs and implants by providing training for providers and financing IUD and implant provision at publicly-funded clinics

19%

Of 15-24 year olds use IUDs or implants, up from 5%

Change in Fertility and Abortion Rates Since CFPI Began

Age	15-19	20-24
Fertility Rate	**-29%**	**-14%**
Abortion Rate	**-34%**	**-18%**

**2011 data*

Ricketts S, et al. *Perspect Sex Reprod Health.* 2014;46(3):125-32

California Family Planning, Access, Care, and Treatment (PACT) Program

- Introduced in 1997, the Family PACT serves uninsured reproductive age men and women at or below 200% of the federal poverty line[1]
- Between 2007-2010, IUD training was provided for clinicians[2]

+25%

Increase in IUD provision in clinics after Family PACT sponsored training[2]

+7%

Increase in IUD provision at clinics not provided training[2]

1. Bixby Center for Global Reproductive Health. Fact Sheet on Family PACT: An Overview. Available at: http://bixbycenter.ucsf.edu/publications/files/FPACT_Overview_2012.pdf. Accessed March 6, 2015.
2. Lewis CL, et al. *Contraception.* 2013;88(2):226-31.

Summary

- IUDs and implants are highly effective reversible contraceptives
- IUDs and implants should be recommended as first line for all appropriate women of reproductive age[1,2]
- IUDs and implants decrease unintended pregnancies and abortions
- Use of IUDs and implants remains low despite effectiveness
- Removing the barriers to IUDs and implants may increase their use

1. The American College of Obstetricians and Gynecologists. Committee Opinion. Number 539, October 2012.
2. American Academy of Pediatrics. *Pediatrics* . 2014;134; e1244.

The preceding slides provided general information about IUDs and implants, and are not intended to make claims about any specific treatment.
We will now discuss a specific IUD.

For product-specific information, please consult the full Prescribing Information.

Medicines360 and Allergan Partnership

- Medicines360 is a global nonprofit pharmaceutical company
  - Mission: To expand access to contraception for women regardless of their socioeconomic status or insurance status
  - Began the largest hormonal IUS trial conducted exclusively in the U.S.: ACCESS IUS, which studied the efficacy and safety of LILETTA in 1751 women
- To expand access to LILETTA, Medicines360 formed a partnership with Allergan
  - Medicines360 focused their efforts in the public sector
  - Allergan drives sales and marketing efforts in both the public and private sectors

Medicines360 and Allergan Partnership

- Programs and services designed to increase the availability of LILETTA
  - A $50 price for public sector entities participating in the 340B Drug Pricing Program
  - 24/7 practice support through LILETTA AccessConnect℠, an online portal
- Innovative patient support programs for women with private insurance
  - LILETTA Patient Savings Program℠
  - LILETTA + LILETTA Patient Commitment Program℠

Medicines360 and Allergan Partnership

Expanding access to an effective, long-acting reversible form of birth control such as LILETTA.

- Medicines360:
  - Reinvests their proceeds into advocacy, education, and additional product and partnership development
- Allergan:
  - Continues to invest in innovative programs and solutions to simplify access to LILETTA

Liletta®
(levonorgestrel-releasing intrauterine system) 52 mg

Chapter 2

Clinical Review & Insertion Procedure

LLT51211
06/16

Liletta®

Clinical Review

LILETTA IUD
(levonorgestrel-releasing intrauterine system)

Indications and Usage

- LILETTA is indicated for prevention of pregnancy for up to 3 years
- The system should be replaced after 3 years if continued use is desired

LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016

LILETTA Important Safety Information

Who is not appropriate for LILETTA

Use of LILETTA is contraindicated in women with: known or suspected pregnancy and cannot be used for post-coital contraception; congenital or acquired uterine anomaly, including fibroids if they distort the uterine cavity; known or suspected breast cancer or other progestin-sensitive cancer, now or in the past; known or suspected uterine or cervical neoplasia; acute liver disease or liver tumors; untreated acute cervicitis or vaginitis, including lower genital tract infections (eg, bacterial vaginosis) until infection is controlled; postpartum endometritis or infected abortion in the past 3 months; unexplained uterine bleeding; current IUS; acute pelvic inflammatory disease (PID) or history of PID (except with later intrauterine pregnancy); conditions increasing susceptibility to pelvic infection; or hypersensitivity to any component of LILETTA.

Please see additional Important Safety Information throughout this presentation and full prescribing information from your speaker

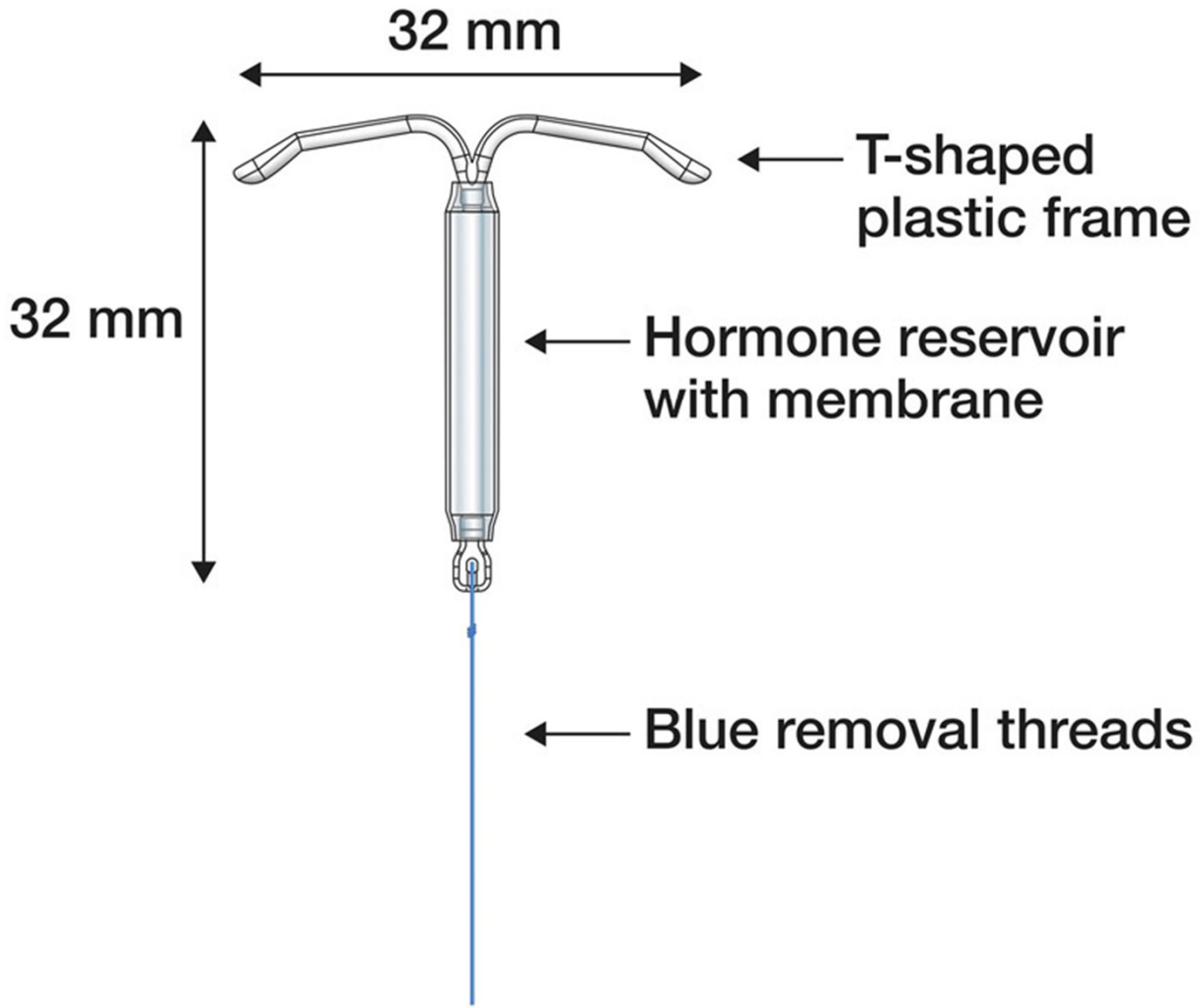
LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.

LILETTA– Dosage and Administration

- LILETTA contains 52 mg of levonorgestrel
  - Initial rate of levonorgestrel release is 18.6 mcg/day
  - Rate decreases progressively after insertion
  - The average release rate over a period of 3 years is ~15.6 mcg/day
- LILETTA can be removed at any time but must be removed by the end of the third year
- LILETTA can be replaced at the time of removal with a new LILETTA if continued contraceptive protection is desired

LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.

LILETTA Intrauterine System



LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.

LILETTA Important Safety Information (continued)

Clinical considerations for use and removal of LILETTA

Use LILETTA with caution after careful assessment in patients with coagulopathy or taking anticoagulants; migraine, focal migraine with asymmetrical visual loss, or other symptoms indicating transient cerebral ischemia; exceptionally severe headache; marked increase of blood pressure; or severe arterial disease such as stroke or myocardial infarction. Consider removing the intrauterine system if these or the following arise during use: uterine or cervical malignancy or jaundice. Because irregular bleeding/spotting is common during the first months of LILETTA use, exclude endometrial pathology (polyps or cancer) prior to the insertion of LILETTA in women with persistent or uncharacteristic bleeding. If the threads are not visible or are significantly shortened, they may have broken or retracted into the cervical canal or uterus. If LILETTA is displaced (eg, expelled or perforated the uterus), remove it.

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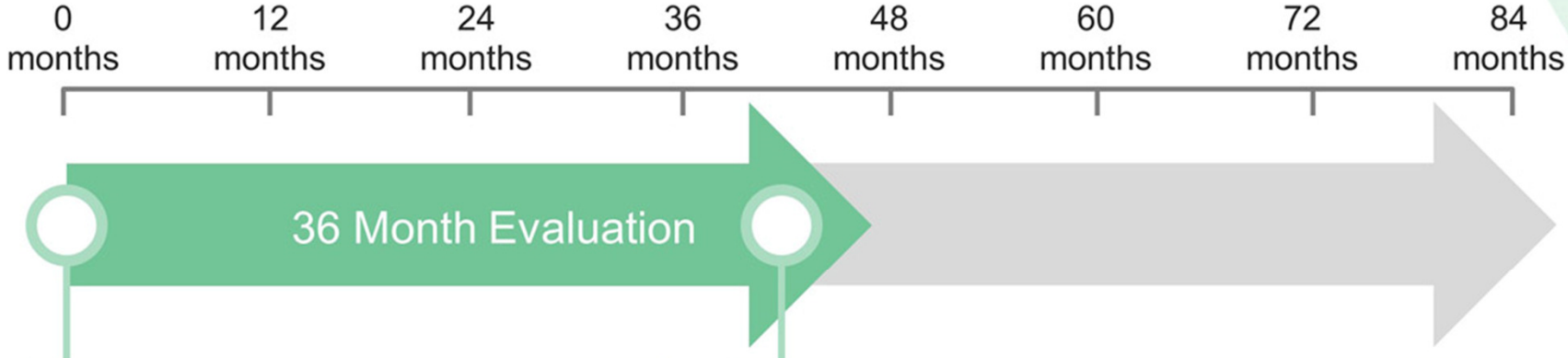
LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.

LILETTA ACCESS IUS Trial

Designed to demonstrate the efficacy and safety of LILETTA in sexually active U.S. women, age 16-45



- Open-label, multi-center trial conducted at 29 U.S. study centers
- Including private practice, Planned Parenthood, and academic centers
- N = 1751

Primary Outcome

- Efficacy of LILETTA in nulliparous and parous females of childbearing potential (16-35 years old)

Secondary Outcomes Included

- Safety, bleeding patterns, and continuation rates
- Return to fertility after discontinuation
- Return of menses after discontinuation

1. LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.
2. Eisenberg DL, at al. *Contraception.* 2015;92(1):10-6. 3. Data on File, Medicines360. San Francisco, CA.

Study Entry Criteria

Key Inclusion Criteria*

- Generally healthy 16- to 45-year-old women
- Enrollment was not restricted by weight/BMI, race, or parity
- Regularly sexually active in a mutually monogamous relationship at study entry

Key Exclusion Criteria*

- History of ectopic pregnancy without a subsequent intrauterine pregnancy
- Pelvic inflammatory disease without a subsequent intrauterine pregnancy
- Trophoblastic disease without a subsequent intrauterine pregnancy
- Less than 4 weeks post-pregnancy
- HIV positive

**This is not a comprehensive list of all criteria subjects were required to fulfill to be eligible for study entry or excluded from study entry*

1. LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.
2. Data on File, Medicines360. San Francisco, CA.

Baseline Demographics

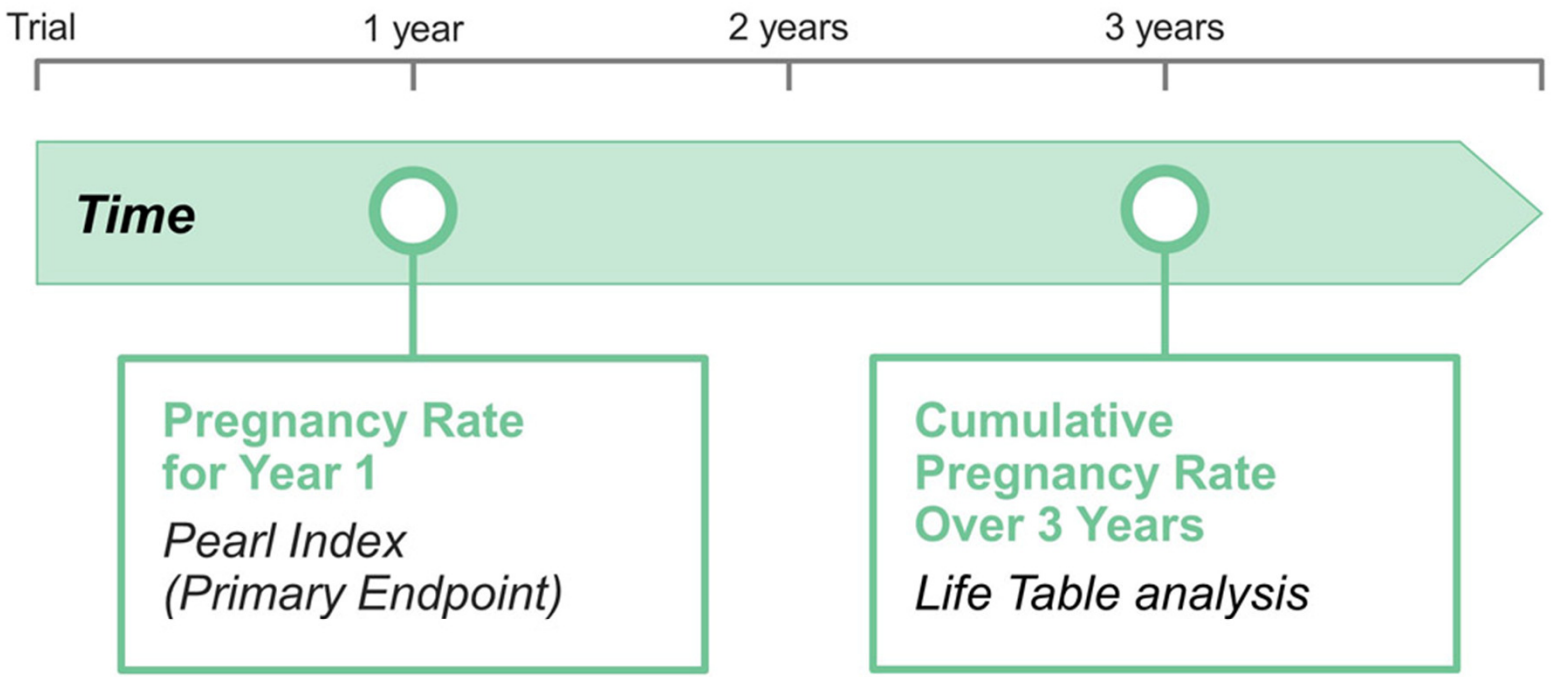
Women 16 – 45 years of age were enrolled, irrespective of race, BMI, and parity – 1751 received LILETTA

Age	Race	Ethnicity	BMI	Parity Status
16-45 years • **Mean: 27 yrs** • **n=1751** *The population included 1600 women aged 16-35* years and 151 women aged 36-41 years†*	**White** 78% **Black** 13% **Asian** 4% **Other** 5%	**Hispanic or Latina** 15% **Not Hispanic or Latina** 85%	**Mean: 26.9 kg/m²** Range: 15.8 - 61.6 kg/m² • 24% overweight • 24% obese • 5% morbidly obese	**Nulliparous** 58% n=1011 **Parous** 42% n=740

**Mean age of women aged 16-35 years was 26 years*
†Mean age of women aged 36-41 years was 40 years

1. LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.
2. Eisenberg DL, at al. *Contraception.* 2015;92(1):10-6.

Efficacy Endpoints



LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.

LILETTA Efficacy

- Contraceptive protection did not appear to vary by parity, race, or body-mass index

	Year 1 Pearl Index	Cumulative 3-Year Life Table
Cumulative number of 28-day cycles of exposure	**17,125**	**34,711**
Number of pregnancies	**2**	**6**
Pregnancy Rate (95% CI)	**0.15 (0.02, 0.55)**	**0.55 (0.24, 1.23)**

LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.

LILETTA Important Safety Information (continued)

Pregnancy related risks with LILETTA

If pregnancy should occur with LILETTA in place, remove the intrauterine system because leaving it in place may increase the risk of spontaneous abortion and preterm labor. Removal or manipulation may result in pregnancy loss. Evaluate women for ectopic pregnancy because the likelihood of a pregnancy being ectopic is increased with LILETTA. Tell women about the signs of ectopic pregnancy and associated risks, including loss of fertility. Women with a history of ectopic pregnancy, tubal surgery, or pelvic infection carry a higher risk of ectopic pregnancy.

Please see additional Important Safety Information throughout this presentation and full prescribing information from your speaker

LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.

LILETTA Important Safety Information (continued)

Educate her about PID

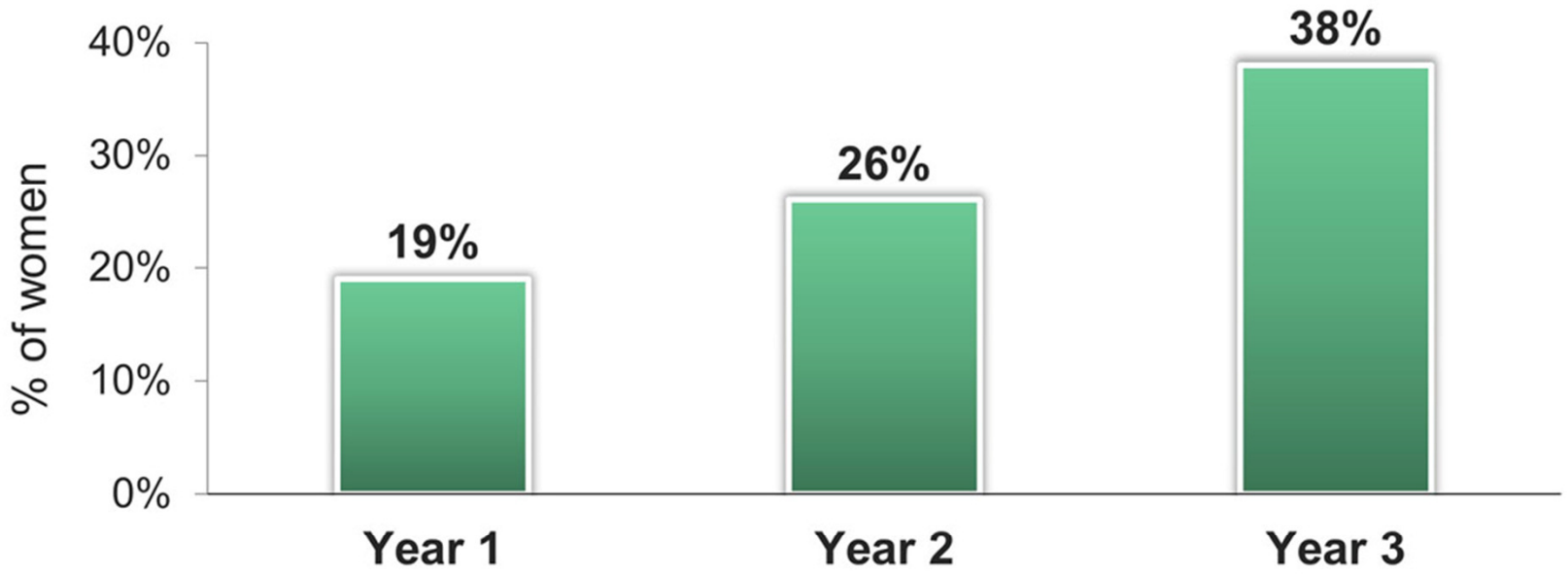
Insertion of LILETTA is contraindicated in the presence of known or suspected PID or endometritis or a history of PID unless there has been a subsequent intrauterine pregnancy. IUSs have been associated with an increased risk of PID, most likely due to organisms being introduced into the uterus during insertion. About 1/3 of women diagnosed with PID developed the infection within a week of LILETTA insertion, while the remainder were diagnosed more than six months after insertion. Counsel women who receive LILETTA to notify a healthcare provider if they have complaints of lower abdominal or pelvic pain, odorous discharge, unexplained bleeding, fever, or genital lesions or sores. PID is often associated with sexually transmitted infections (STIs); LILETTA does not protect against STIs, including HIV. PID or endometritis may be asymptomatic but still result in tubal damage and its sequelae. Inform women about the possibility of PID and that PID can cause tubal damage leading to ectopic pregnancy or infertility, or infrequently can necessitate hysterectomy, or cause death.

Please see additional Important Safety Information throughout this presentation and full prescribing information from your speaker

LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.

Amenorrhea Rates

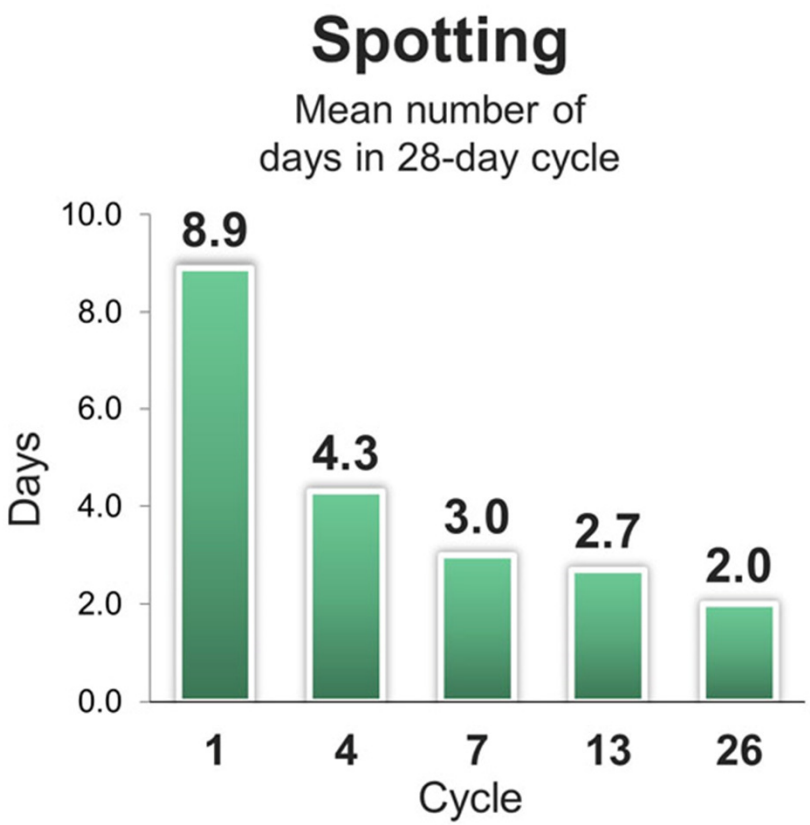
Users experiencing amenorrhea* at the end of each study year

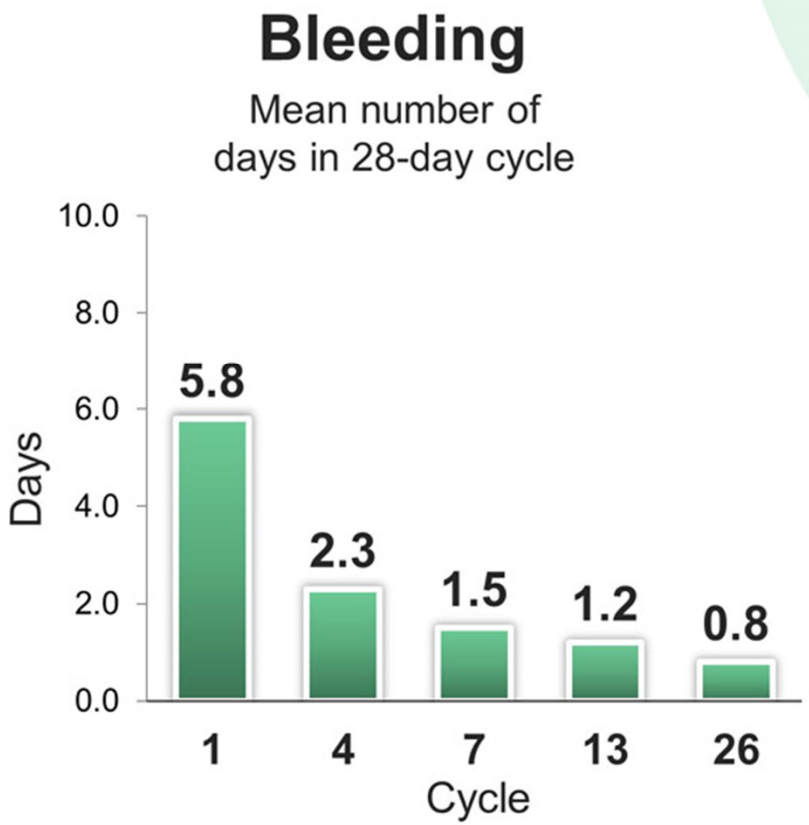


**No bleeding/spotting in the previous 90 days*

LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.

Spotting and Bleeding



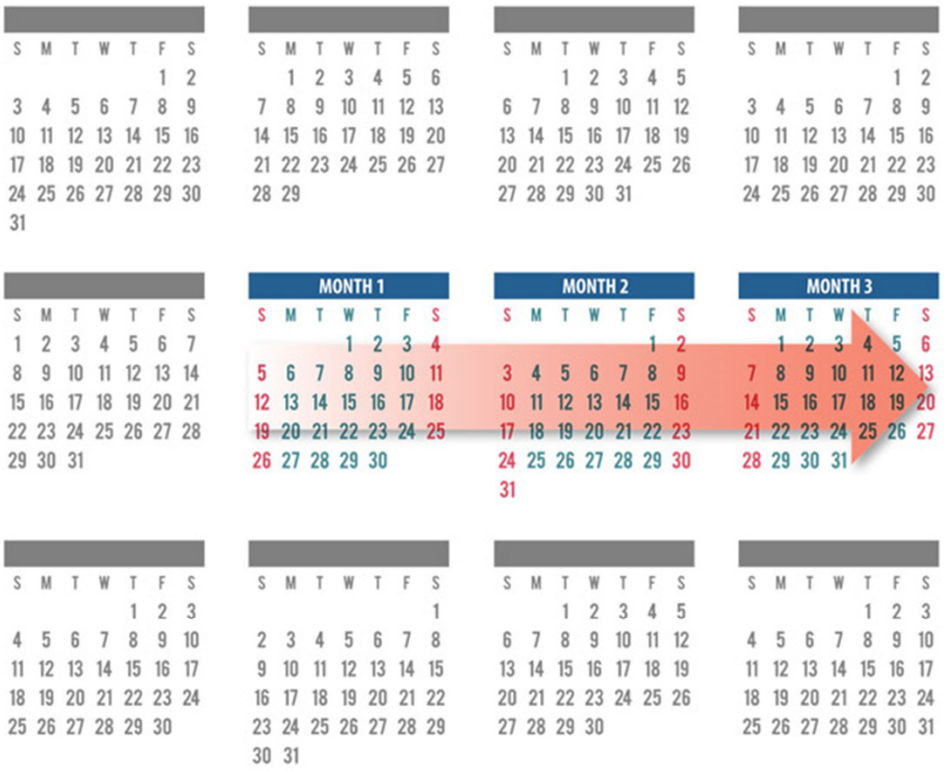


Spotting and bleeding data were obtained from subjects' daily diary

N = 1691 (Cycle 1), 1525 (Cycle 4), 1223 (Cycle 7), 791 (Cycle 13), 438 (Cycle 26)

1. LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.
2. Data on File, Medicines360. San Francisco, CA.

Menses After LILETTA Removal



97.3%

(248 of 255 women) experienced menses within *3 months* after LILETTA removal

1. LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.
2. Eisenberg DL, at al. *Contraception.* 2015;92(1):10-6.

LILETTA Important Safety Information (continued)

Expect changes in bleeding patterns with LILETTA

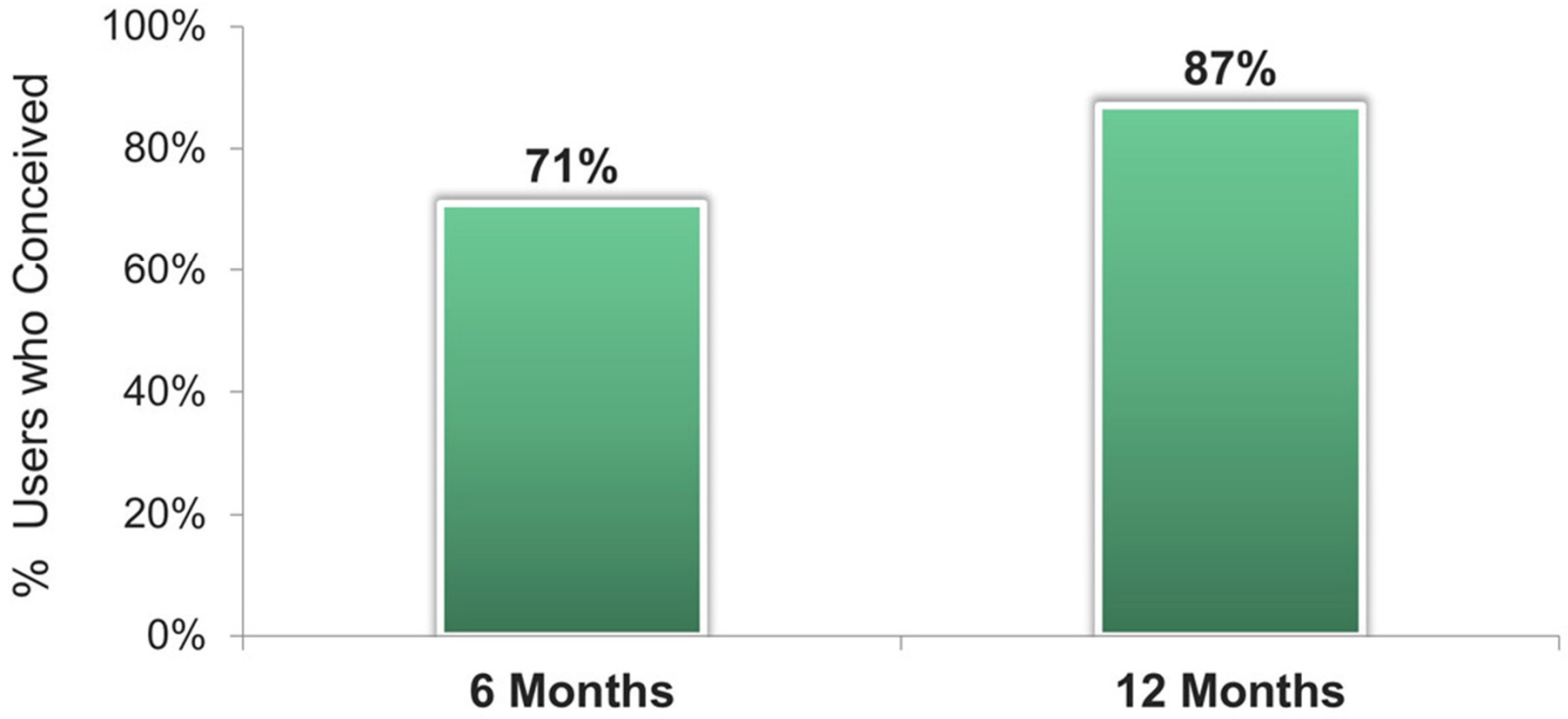
Spotting and irregular or heavy bleeding may occur during the first 3 to 6 months. Periods may become shorter and/or lighter thereafter. Cycles may remain irregular, become infrequent, or even cease. Consider pregnancy if menstruation does not occur within 6 weeks of the onset of previous menstruation.

If a significant change in bleeding develops during prolonged use, take appropriate diagnostic measures to rule out endometrial pathology.

Please see additional Important Safety Information throughout this presentation and full prescribing information from your speaker

LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.

Pregnancy After LILETTA Removal



N = 68

LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.

Most Common Adverse Reactions

Adverse reactions occurring in ≥5% of users

System Organ Class/Preferred Term	% LILETTA Subjects (N = 1751)
Vaginal infections	13.6%
Vulvovaginal infections	13.3%
Acne	12.3%
Headache or migraine	9.8%
Nausea or vomiting	7.9%
Dyspareunia	7.0%
Abdominal discomfort or pain	6.8%
Breast tenderness or pain	6.7%
Pelvic discomfort or pain	6.1%
Depression or depressed mood	5.4%
Mood changes	5.2%

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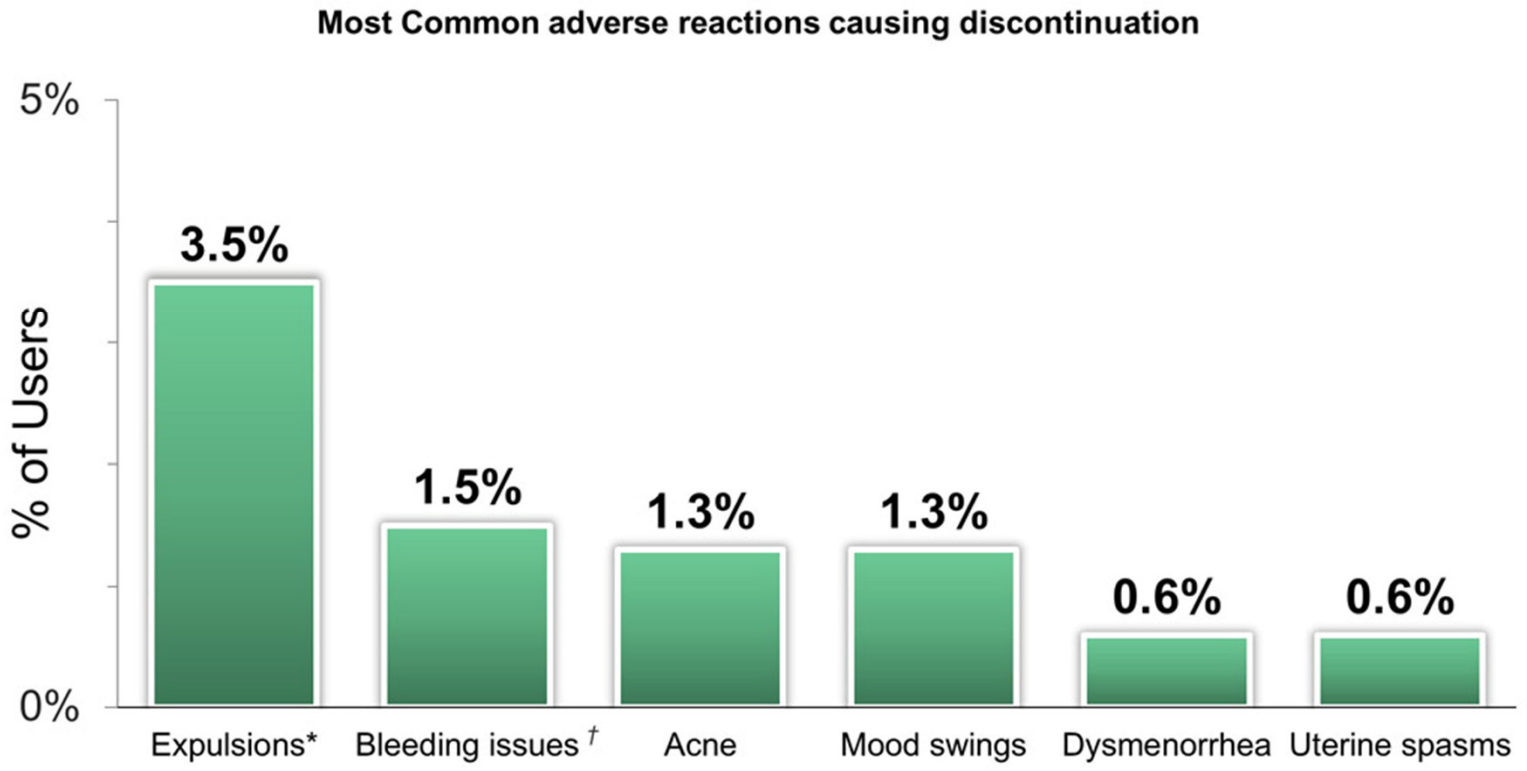
Most Common Adverse Reactions Leading to Discontinuation

12.3% of LILETTA users discontinued prematurely due to an adverse reaction



***Expulsion rate was 2.0% in nulliparous women and 5.6% in parous women**

***†Bleeding issues include events such as dysfunctional uterine bleeding and irregular menstruation**

N = 1751

LILETTA (levonorgestrel-releasing intrauterine system) 52 mg [Prescribing Information]. Parsippany, NJ: Allergan and Medicines360; 2016.

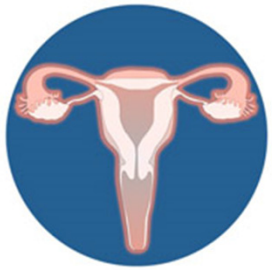
Incidence of Pelvic Infection in LILETTA Trial

Pelvic Infection

0.6%

Pelvic Inflammatory Disease

0.4%



Endometritis

0.2%

About 1/3 of women diagnosed with PID developed the infection within a week of LILETTA insertion, while the remainder were diagnosed more than six months after insertion

n = 10 (PID: 7, Endometritis: 3)

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Data on File, Medicines360. San Francisco, CA.

LILETTA Important Safety Information (continued)

Be aware of other serious complications and most common adverse reactions

Some serious complications with IUSs like LILETTA are sepsis, perforation, and expulsion. Severe infection or sepsis, including Group A streptococcal sepsis (GAS), have been reported following insertion of other LNG-releasing IUSs. Aseptic technique during insertion of LILETTA is essential in order to minimize serious infections such as GAS.

Perforation (total or partial, including penetration/embedment of LILETTA in the uterine wall or cervix) may occur, most often during insertion, although the perforation may not be detected until sometime later. Perforation may reduce contraceptive efficacy. If perforation occurs, locate and remove LILETTA. Surgery may be required. Delayed detection or removal of LILETTA in case of perforation may result in migration outside the uterine cavity, adhesions, peritonitis, intestinal perforations, intestinal obstruction, abscesses, and erosion of adjacent viscera. The risk of perforation is higher if inserted in lactating women and may be higher if inserted in women who are postpartum or when the uterus is fixed retroverted.

Partial or complete expulsion of LILETTA may occur, resulting in the loss of contraceptive protection.

Please see additional Important Safety Information throughout this presentation and full prescribing information from your speaker

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LILETTA Important Safety Information (continued)

Be aware of other serious complications and most common adverse reactions (continued)

Delay LILETTA insertion a minimum of 6 weeks or until uterine involution is complete following a delivery or a second trimester abortion. Remove a partially expelled LILETTA. If expulsion has occurred, a new LILETTA may be inserted within 7 days after the onset of a menstrual period after pregnancy has been ruled out.

Ovarian cysts may occur and are generally asymptomatic, but may be accompanied by pelvic pain or dyspareunia. Evaluate persistent ovarian cysts.

In the clinical trial of LILETTA the most common adverse reactions (≥5% users) were vaginal infections (13.6%), vulvovaginal infections (13.3%), acne (12.3%), headache or migraine (9.8%), nausea or vomiting (7.9%), dyspareunia (7.0%), abdominal pain or discomfort (6.8%), breast tenderness or pain (6.7%), pelvic discomfort or pain (6.1%), depression or depressed mood (5.4%), and mood changes (5.2%).

Teach patients to recognize and immediately report signs or symptoms of the aforementioned conditions. Evaluate patients 4 to 6 weeks after insertion of LILETTA and then yearly or more often if clinically indicated.

Please see additional Important Safety Information throughout this presentation and full prescribing information from your speaker

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Insertion Procedure

Timing of LILETTA Insertion

Population	Insertion Timing Recommendations
Women not using contraception	• Can be inserted any time provided pregnancy is ruled out
After abortion or miscarriage	• First trimester: May be inserted immediately • Second trimester: After at least 6 weeks or until uterus is involuted. Pregnancy should be ruled out before insertion
After childbirth	• After at least 6 weeks or until uterus is involuted • Pregnancy should be ruled out before insertion – Increased risk of perforation in lactating women

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Timing of LILETTA Insertion

Population	Insertion Timing Recommendations
Switching from oral, transdermal or vaginal hormonal contraceptive	• May be inserted at any time • Continue previous method for 7 days after LILETTA insertion or until the end of the current treatment cycle
Switching from injectable progestin contraceptive	• Can be inserted at any time • If LILETTA is inserted more than 3 months (13 weeks) after the last injection, a barrier method of contraception (such as condoms and spermicide) should also be used for 7 days after insertion
Switching from contraceptive implant or another IUD	• On the same day the implant or IUD is removed

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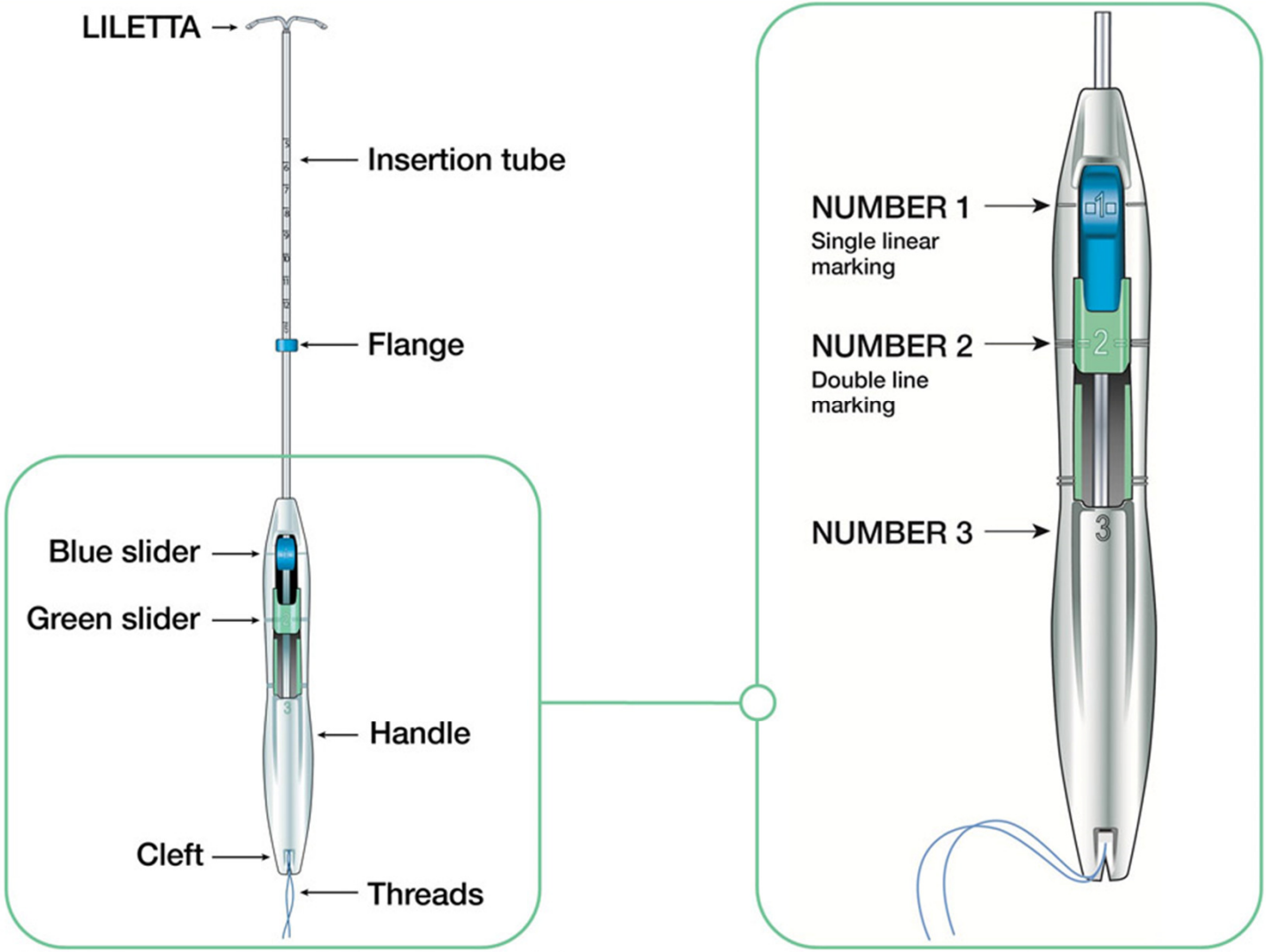
LILETTA IUD and Inserter



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LILETTA Insertion Video

- Insertion Video

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Planning for LILETTA Insertion

- Be thoroughly familiar with the product, product educational materials, product insertion instructions, prescribing information, and patient labeling before attempting insertion of LILETTA
- Obtain a complete medical & social history
- Check the expiration date on the box before opening it. Do not insert LILETTA after the expiration date
- Visually inspect the packaging to verify that the packaging has not been damaged
- Ensure that the patient understands the contents of the Patient Information Booklet and obtain consent

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Planning for LILETTA Insertion (Contd.)

- Complete the pelvic examination, speculum placement, tenaculum placement, and sounding of the uterus before opening the LILETTA tray
- Do not open the tray to insert LILETTA if the cervix is unable to be properly visualized, if the uterus cannot be adequately instrumented (during sounding), or if the uterus sounds to less than 5.5 cm
- Exclude pregnancy and confirm that there are no other contraindications to the insertion and use of LILETTA
- Follow the insertion instructions exactly as described in order to ensure proper insertion

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Planning for LILETTA Insertion (Contd.)

- If you encounter cervical stenosis at any time during uterine sounding or LILETTA insertion, use cervical dilators, not force, to overcome resistance. If necessary, dilation, sounding, and insertion may be performed with ultrasound guidance
- Insertion may be associated with some pain and/or bleeding or vasovagal reactions (e.g., diaphoresis, syncope, bradycardia, or seizure), especially in patients with a predisposition to these conditions. Consider administering analgesics prior to insertion
- Use aseptic technique during the entire insertion procedure. If at any step, there is a need to touch a sterile surface, sterile gloves should be used

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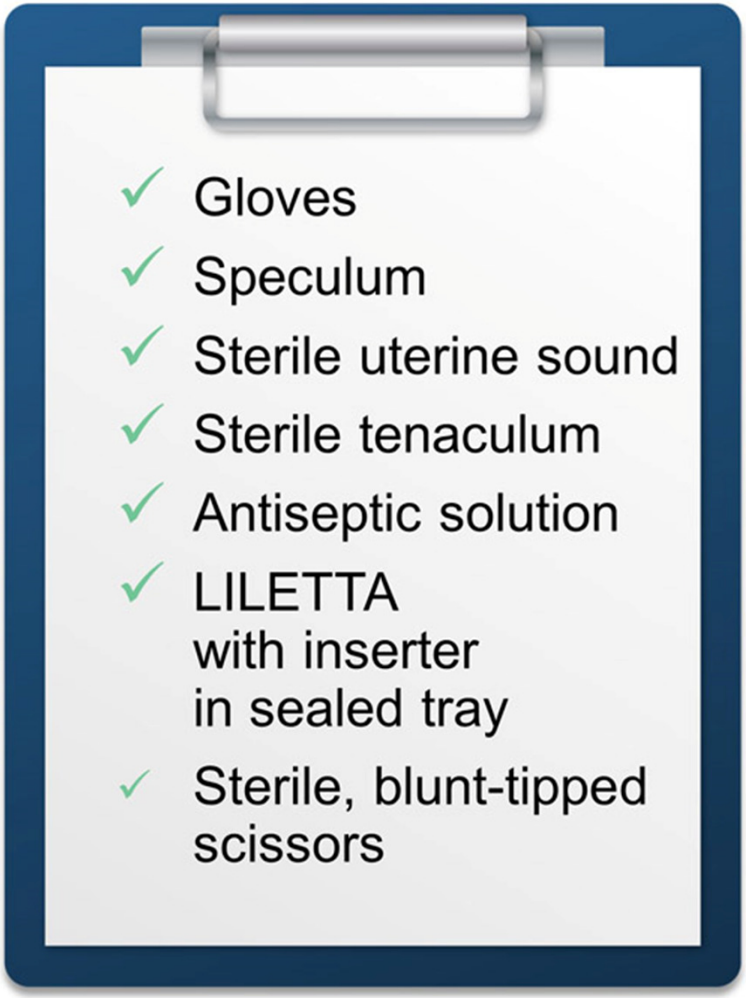
Items for Insertion



Additional items that may be useful could include:

- Local anesthesia, needle, and syringe
- Os finder and/or cervical dilators
- Ultrasound with abdominal probe

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Step 1: Preparation of Patient for Insertion

- Perform a bimanual exam to establish the size, shape, and position of the uterus and to evaluate any signs of uterine infection
- Gently insert a speculum to visualize the cervix
- Thoroughly cleanse the cervix and vagina with antiseptic solution
- Administer cervical anesthetic, if needed
- Apply a tenaculum to the cervix and use gentle traction to align the cervical canal with the uterine cavity
  - If the uterus is retroverted, it may be more appropriate to grasp the lower lip of the cervix. Keep the tenaculum in position and maintain gentle traction on the cervix throughout the insertion procedure

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Step 1: Preparation of Patient for Insertion (Continued)

Carefully sound the uterus to measure its depth

- The uterus should sound to a depth of at least **5.5 cm**
- Insertion of LILETTA into a uterine cavity that sounds to less than 5.5 cm may increase the incidence of expulsion, bleeding, pain, perforation, and possibly pregnancy. LILETTA should not be inserted if the uterus sounds to less than 5.5 cm
- After ascertaining that the patient is appropriate for LILETTA, replace contaminated glove(s), and open the tray containing LILETTA

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Step 2: Opening the Sterile LILETTA Packaging

- Remove the insertion tray containing LILETTA from the box
- Inspect the insertion tray and do not use the product if the tray is damaged
- Lay the tray on a flat surface with the sealed peel-off lid side up.
- Lay the tray on a flat surface, with the peel-off lid side up, open the sealed peel-off lid from the handle end toward the inserter tip

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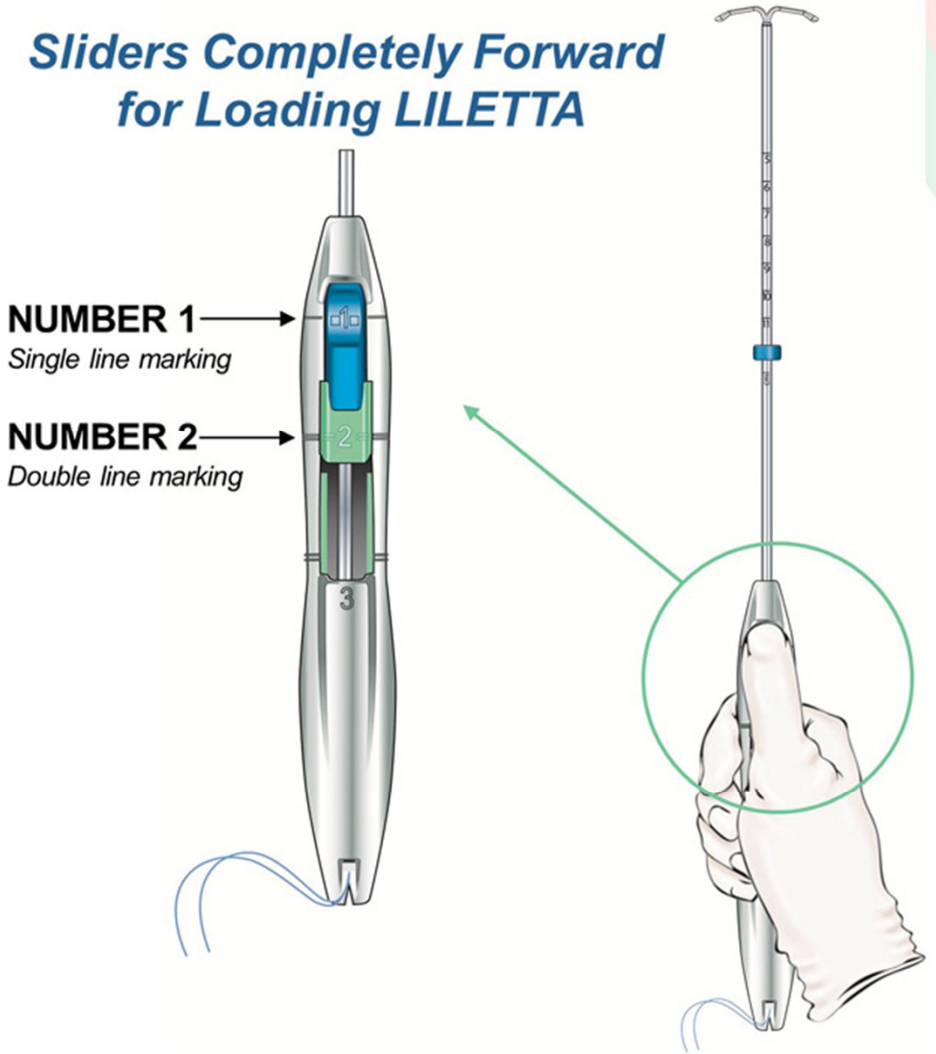
Step 3: Loading LILETTA into the Inserter

- Remove the inserter from the tray
- Ensure both sliders are fully forward
- Grip the handle keeping your thumb or finger in the groove of the BLUE slider (over the numeral 1) and apply forward pressure while ensuring both sliders are fully forward



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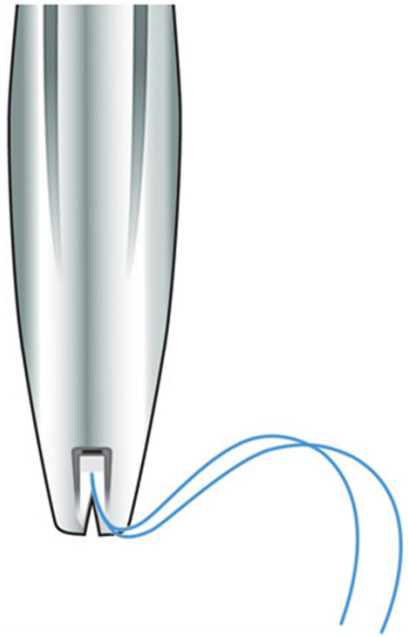
Step 3: Loading LILETTA into the Inserter (Continued)

- Ensure the arms of the IUS are horizontal; adjust the rotation of the IUS as needed using the flat sterile surface of the tray
- While maintaining forward pressure on the blue slider, pull the threads straight back until you feel a hard stop
- Pull the threads upward or downward to lock the threads into the cleft at the bottom end of the handle

Securing the Threads in Cleft



Reminder: It's important to ensure even tension is applied to both threads when pulling

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Step 3: Loading LILETTA into the Inserter (Continued)

- After the IUS is loaded, continue to sustain forward pressure on the BLUE slider to maintain a hemispherical dome with the tips of the IUS
- If the IUS is not correctly loaded, do not attempt insertion. The LILETTA inserter can be reloaded

Close-up of Hemispherical Dome at Tip of Tube

When correctly loaded, the IUS is completely within the insertion tube with the tips of the arms forming a hemispherical dome at the top of the tube

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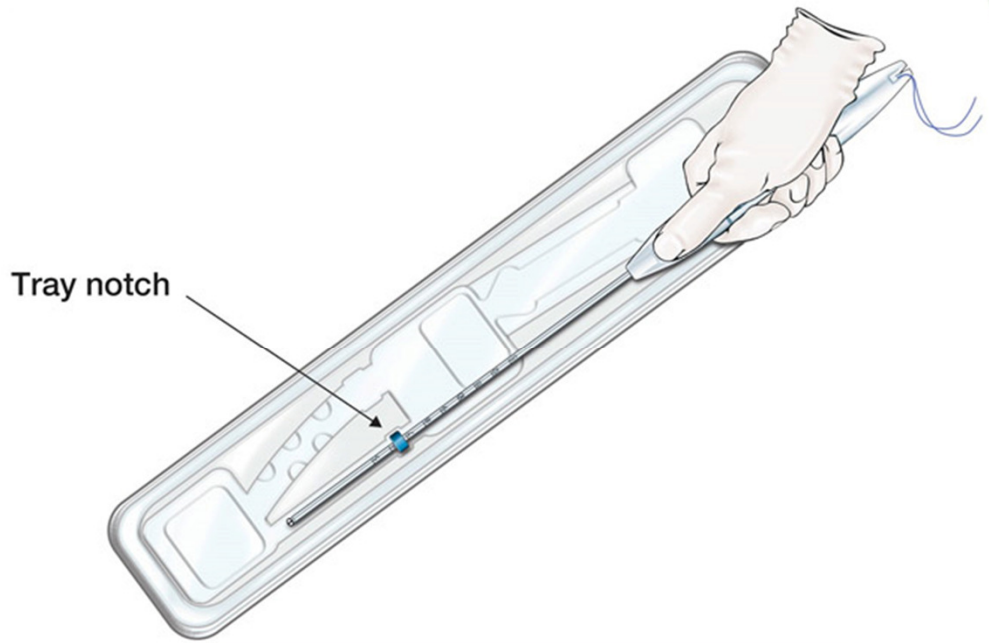
Step 3: Loading LILETTA into the Inserter (Continued)

- Adjust the flange to the measured uterine depth based on sounding
  - Place the flat side of the flange in the tray notch or against a sterile edge inside of the tray
  - Slide the insertion tube as necessary to move the flange to the correct measurement
  - Ensure the flat sides of the flange are in the same horizontal plane as the handle

Adjusting the Flange



Reminder: When bending the tube, be careful to avoid sharp bends to prevent kinking

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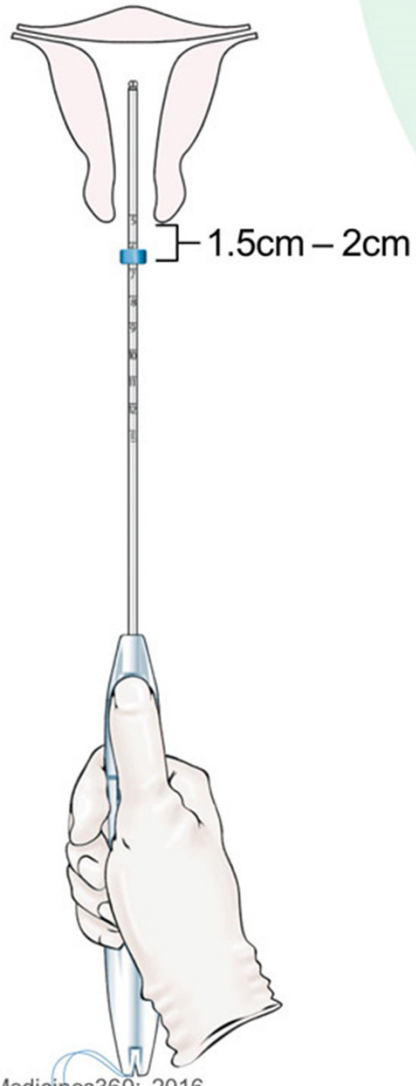
Step 4: Inserting LILETTA into the Uterus

- Apply gentle traction on the tenaculum while inserting the loaded insertion tube through the cervical os
- Advance the tube until the upper edge of the flange is 1.5-2 cm from the external cervical os
- Maintain forward pressure on the BLUE slider throughout the insertion process

Advancing Insertion Tube until Flange is 1.5 to 2 cm from the External Cervix



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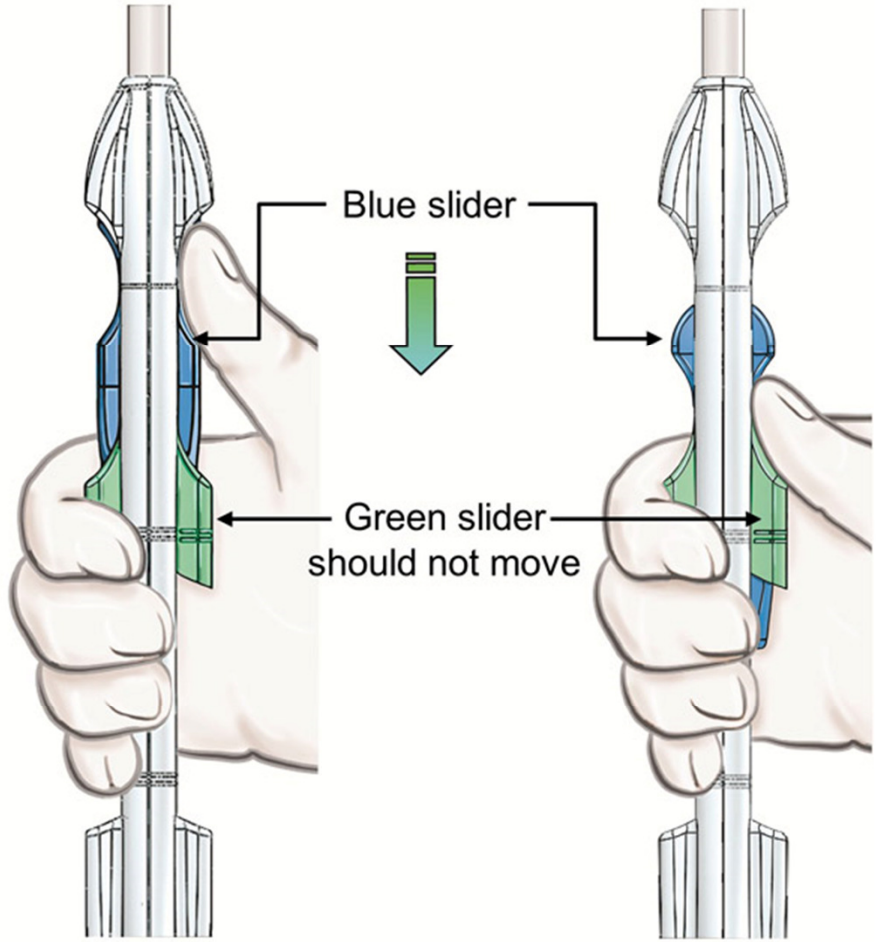
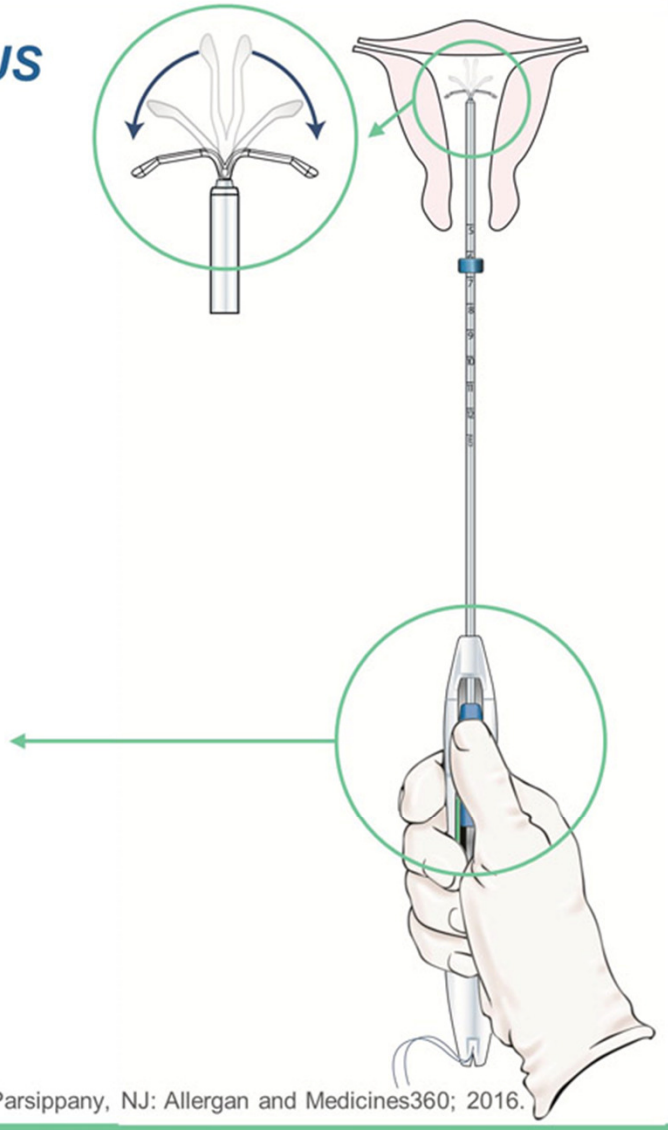
Step 4: Inserting LILETTA into the Uterus (Continued)

Releasing and Opening the Arms of the IUS





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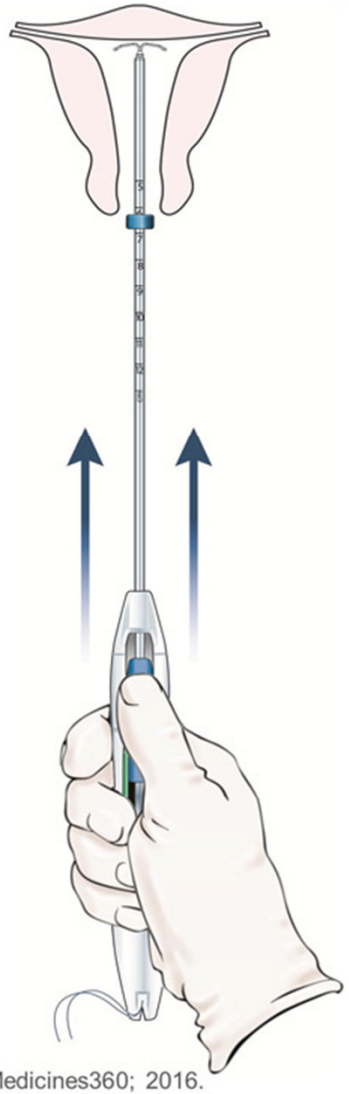
Step 4: Inserting LILETTA into the Uterus (Continued)

- Apply gentle traction on the tenaculum
- While maintaining the same slider position, advance the inserter until the flange touches the cervix
- If fundal resistance is encountered, do not continue to advance
- LILETTA is now in the fundal position

Move LILETTA into the Fundal Position



Reminder: Fundal position is important to prevent expulsions

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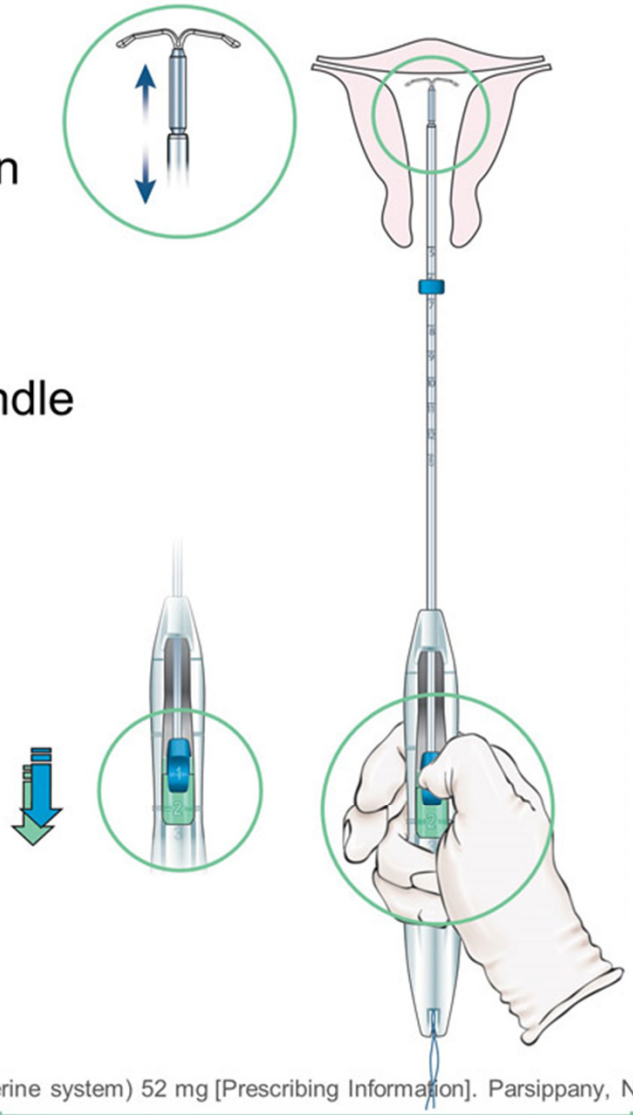
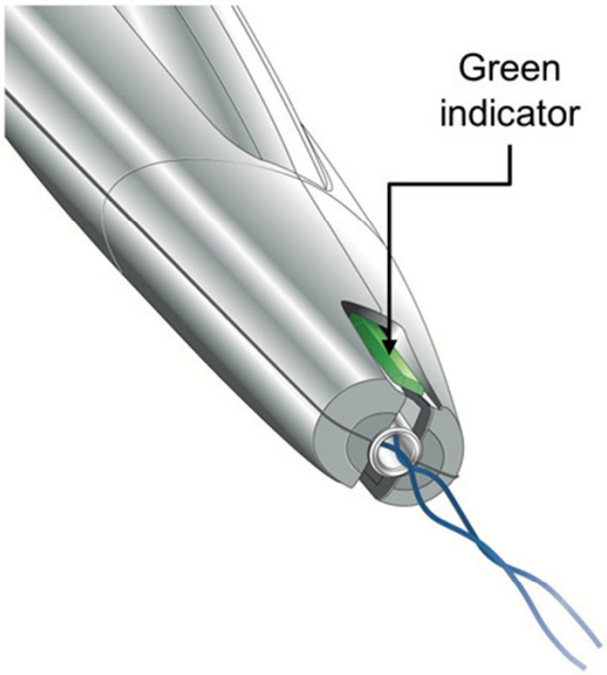
Step 5: Releasing LILETTA & Procedure Completion

While holding the inserter steady and maintaining its position relative to the cervix, move both sliders (BLUE and GREEN) together down the handle until a click is heard



Green indicator visible and threads released from cleft



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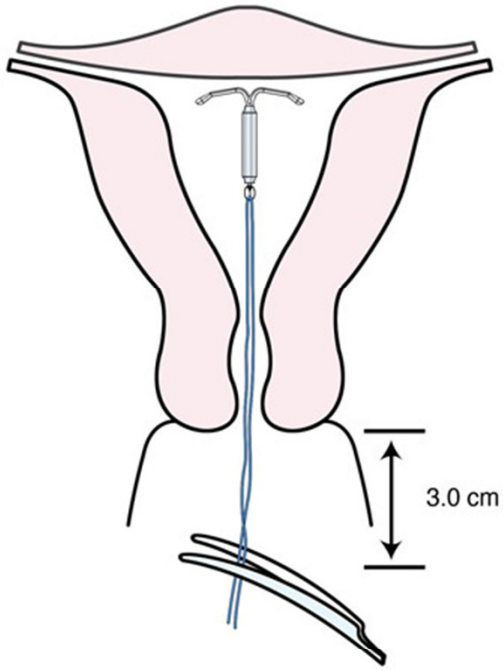
Step 5: Releasing LILETTA & Procedure Completion (Continued)

- Use blunt-tipped sharp scissors to cut the IUS threads perpendicular to the thread length, leaving about 3 cm outside of the cervix
  - Do not apply tension or pull on the threads when cutting to prevent displacing the IUS

Cut the Threads about 3 cm from the Cervix



Reminder: Do not cut threads at an angle as this may leave sharp ends

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After Insertion

Once insertion is complete, the patient should be re-examined and evaluated 4 to 6 weeks after and once a year thereafter, or more frequently if clinically indicated

Important information to consider during or after insertion:

If you suspect the IUS is not in the correct position:

- Check insertion with an ultrasound or other appropriate radiologic test
- If incorrect insertion is suspected, remove LILETTA
- A removed LILETTA must not be re-inserted

If insertion is difficult because the uterus cannot be appropriately instrumented, the following measures can be considered:

- Use of cervical anesthesia to make sounding and manipulation more tolerable
- Use of dilators to dilate the cervix if needed to allow passage of the sound or inserter
- Abdominal ultrasound guidance during dilation and/or insertion
- If there is clinical concern, exceptional pain, or bleeding during or after insertion, appropriate steps should be taken immediately to exclude perforation

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Timing of Removal of LILETTA

- If pregnancy is desired, LILETTA may be removed at any time
- If pregnancy is not desired, a contraceptive method should be started prior to removal of LILETTA
  - Counsel your patient that if she has intercourse the week prior to removal without a backup contraceptive method, she is at risk of pregnancy
- LILETTA should be removed after 3 years
  - LILETTA can be replaced at the time of removal with a new LILETTA if continued contraceptive protection is desired

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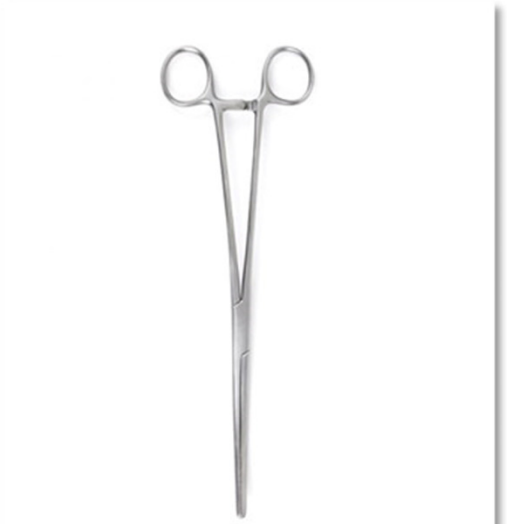
Items for Removal

Ensure all needed items for LILETTA removal are readily available:

- Gloves
- Speculum
- Sterile forceps

Additional items that may be required could include:

- Local anesthetic, needle, and syringe
- Os finder, and/or cervical dilators
- Ultrasound with abdominal probe
- Sterile tenaculum
- Antiseptic solution
- Long, narrow forceps (eg, Alligator forceps)



Packing forceps

Alligator forceps

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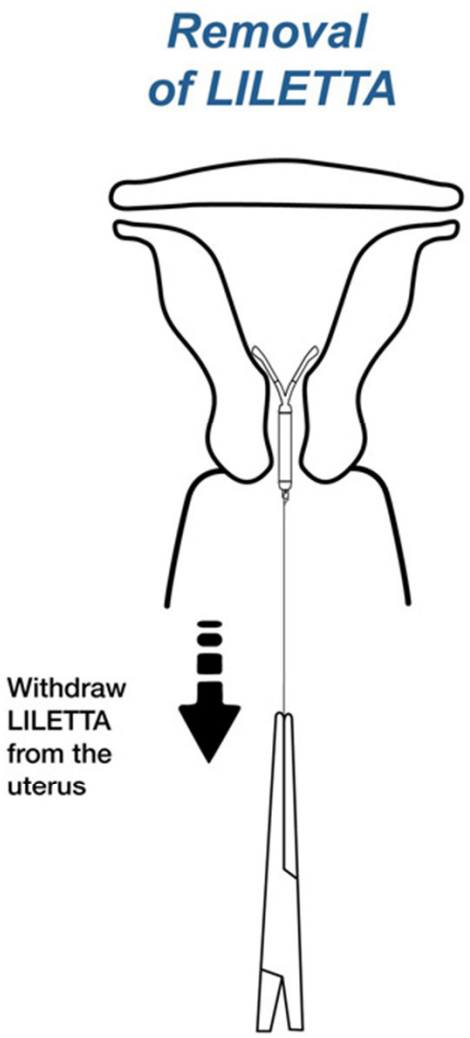
LILETTA Removal Instructions

- When the threads are visible remove LILETTA by applying gentle traction on the threads with forceps
- If the threads of LILETTA are not visible or if it cannot be removed with traction on the threads, perform an ultrasound examination to confirm location
- If the IUS is in the uterus, use a long, narrow forceps (eg, Alligator forceps) to grasp it
  - Consider use of a tenaculum, cervical anesthesia, cervical dilators, and/or ultrasound guidance as needed
- If the IUS cannot be removed using the above techniques, consider hysteroscopic evaluation for removal
- If the IUS is not in the uterine cavity, consider an abdominal x-ray or CT scan to evaluate if the IUS is in the abdominal cavity. Consider laparoscopic evaluation for removal, as clinically indicated
- After removal, examine the system to ensure it is intact



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Continuation of Contraception After Removal

- For women who desire to continue using LILETTA:
  - A new system can be inserted immediately after removal at any time during the cycle
- For women with regular cycles who desire a different contraceptive:
  - Either remove LILETTA during the first 7 days of the menstrual cycle and start the new method, OR start the new method at least 7 days prior to LILETTA removal
- For women with irregular cycles or amenorrhea who desire a different contraceptive:
  - Start the new method at least 7 days prior to LILETTA removal

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Continuation of Contraception After Removal

- A new contraceptive method can be started on the day LILETTA is removed. However, to prevent pregnancy, the patient should either:
  - Use a backup barrier method of contraception, or
  - Abstain from vaginal intercourse for 7 days

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Liletta®

(levonorgestrel-releasing intrauterine system) 52 mg

LLT51211 06/16