continuing education for pharmacists

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Long-Acting Reversible Contraceptives

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Goal. The goal of this lesson is to provide an overview of contraception and of long-acting reversible contraceptives including the present usage, pathophysiology, adverse effects and treatment recommendations.

Objectives. At the completion of this activity, the participant will be able to:

1. recognize the normal physiology of female hormones;
2. list the indications, drug interactions and adverse effects of long-acting reversible contraceptives;
3. identify important counseling points for long-acting reversible contraceptives; and
4. compare and contrast the risks and benefits of various contraception formulations.

Introduction

Nearly three million, or about 50 percent, of pregnancies annually in the United States are unintended. Unintended pregnancies result in nearly 1.2 million abortions yearly, and approximately half of these unintended pregnancies are a result of failure of the chosen contraceptive method. The remaining unintended pregnancies are due to nonuse of contraception. This presents a significant problem in the U.S. with unintended pregnancies resulting in significant financial burden and negative effects on women's health. In 2002, unintended pregnancies resulted in five billion dollars in direct medical costs in the United States. In light of this significant problem, in 2010, the Centers for Disease Control and Prevention (CDC) released guidance on contraceptive method choice, *The U.S. Medical Eligibility Criteria for Contraceptive Use, 2010* (U.S. MEC). The U.S. MEC is based on guidelines released by the World Health Organization (WHO) and is intended to help practitioners in counseling women, men and couples about contraceptive choice.

Sixty-two percent of women of reproductive age are currently using some form of contraception. Oral contraceptives are the most popular form of birth control with 10.6 million women (28 percent) utilizing them in the United States. Oral contraceptives contain either an estrogen and progestin (combination oral contraceptives [COCs]) or progestin alone. The most common estrogen available in oral contraceptives is estradiol.

Failure rates of contraceptives are calculated by *perfect-use* and *typical-use*. Perfect-use refers to when the contraceptive methods are used consistently and correctly. Typical-use takes into account when methods are not used correctly (i.e., missed doses). Oral contraceptives have a failure rate of 0.3 percent with perfect-use, but a 9 percent failure rate with typical-use. Long-acting reversible contraceptives (i.e., implants, intrauterine devices [IUDs] and injectable depo-medroxyprogesterone acetate [DMPA]) have a much lower failure rate with fewer than one in one hundred women becoming pregnant yearly with typical-use.Table 1 lists various forms of birth control by effectiveness based on typical-use.

Use of long-acting reversible contraceptive (LARC) methods has increased significantly in the last several years. In 2002, only 2.4 percent of women utilized LARCs. This increased in 2007 to 5.5 percent and again in 2009 to 8.5 percent. IUDs and implants are most commonly used by women aged 25 to 39 years, married or cohabiting. The use of IUDs has increased sevenfold from 1995 to 2010 (0.8 percent to 5.6 percent), according to CDC. Injectable DMPA has become more popular with an increase in the percentage of women who have ever used it, from 4.5 percent in 1995 to 23 percent in 2006-2010. A recent study, The Contraceptive CHOICE Project by Secura, *et al.* indicates that as long-acting reversible contraceptive methods become more readily available financially, individuals are more likely to select them as their primary form of contraception. In the study, 10,000 women 14 to 45 years of age who wanted to avoid pregnancy for at least one year were read a script informing them about long-acting reversible contraceptive options to

Table 1
Form of contraception/ pregnancies per 100 women per year*

No Contraception	85
Spermicide	28
Fertility-Awareness Methods	28
Sponge	24
Withdrawal	22
Male Condom	18
Diaphragm	12
Ring	9
Patch	9
Pill	9
Injectable (DMPA)	6
Female Sterilization	0.5
Cu-IUD	0.8
LNG-IUD	0.2
Implant	0.05

*Adapted from U.S. Selected Practice Recommendations for Contraceptive Use, 2013.

increase their awareness. Participants in the study were then provided their choice of contraceptive method at no cost. In a report of the first 2,500 women enrolled, 67 percent (95 percent confidence interval, 65.3 to 69.0) chose long-acting methods, 56 percent selected an IUD, and 11 percent selected the subdermal implant. As these methods of contraception become increasingly popular, it is critical that pharmacists have a good understanding of them in order to counsel their patients.

Pathophysiology

The typical menstrual cycle is 28 days, but may range from 21 to 35 days in adults, and 21 to 45 days in young teens. Bleeding generally lasts two to seven days with an average of five days. Average blood loss during the cycle is 30 mL with a normal range of 13 to 80 mL. Bleeding is typically greatest on the second day. The menstrual cycle is separated into three distinct phases characterized by the hormones released during each phase. The three phases are the follicular phase, ovulatory phase and luteal phase. The menstrual cycle begins with day one of bleeding which corresponds with the first day of the follicular phase.

Follicular Phase. During the follicular phase, follicles are developed in the ovaries through an increase in the production of the follicle-stimulating hormone (FSH) by the pituitary gland. One to two days following the slight increase in FSH, there begins a slow increase in luteinizing hormone (LH). FSH stimulates the growth of follicles in the ovaries, each containing an egg. As the cycle progresses, one of the follicles, known as the *dominant follicle*, continues to grow and the other follicles break down. The dominant follicle then produces estrogen, beginning preparation of the uterus and stimulating a surge in luteinizing hormone. During this time, levels of estrogen, especially estradiol, increase exponentially. The follicular phase typically lasts 13 to 14 days, although the length varies more than the other phases. The follicular phase ends when the level of luteinizing hormone surges, resulting in the release of the egg.

Ovulatory Phase. The ovulatory phase is signaled by an increase in luteinizing hormone which causes the release of the egg from the dominant follicle. As the ovulatory phase begins, estradiol levels peak and trigger LH secretion through positive feedback mechanisms. The level of FSH also increases, but to a lesser degree. During the LH surge, levels of estradiol decrease, but progesterone levels continue to increase. The ovulatory phase typically lasts 16 to 32 hours, as the LH surge stimulates enzymes which break down the follicle wall and release the mature egg. The ovulatory phase ends upon release of the egg which occurs about 10 to 12 hours after the luteinizing hormone surge. The window for fertilization is narrow, with an egg able to be fertilized for only about 12 hours after its release.

Luteal Phase. The luteal phase follows ovulation and lasts about 14 days, ending just before the menstrual period. During the luteal phase, the dominant follicle becomes the corpus luteum which releases progesterone, causing the uterine lining to thicken and prepare for implantation of the fertilized egg. The corpus luteum secretes progesterone with a peak of about 25mg/day six to eight days post-ovulation. If implantation does not occur, the levels of estrogen and progesterone rapidly decrease, resulting in the sloughing of the endometrial lining.

The mechanism by which contraceptive methods work vary based on the dose of the hormones involved. Progestin-only based hormonal contraceptives work both through the inhibition of ovulation and thickening of the cervical mucus. Hormonal contraceptives containing both estrogen and progesterone work by inhibiting follicular development and the prevention of ovulation. Many combination hormone contraceptives utilize withdrawal bleeding to simulate a normal cycle. By discontinuing the use of the contraceptives (i.e., using placebos or removing the patch or ring for a week) for a short period, the uterine lining sheds as it does when the progesterone and estrogen levels drop during the normal cycle following an ovulated egg that does not implant.

Prior to the initiation of contraceptives, a provider needs to be reasonably certain a woman is not pregnant. According to the U.S. MEC, it is unlikely a woman is pregnant if she does not have any symptoms of pregnancy and meets any one of the following: 1) is less than or equal to seven days after the start of normal menses, 2) has not had sexual intercourse since the start of last normal menses, 3) has been correctly and consistently using a reliable method of contraception, 4) is less than or equal to seven days after a spontaneous or induced abortion, 5) is within four weeks postpartum, 6) is fully or nearly fully breast feeding, 7) is amenorrheic and <6 months postpartum.

Injectable Contraceptives

Depo-medroxyprogesterone acetate

(Depo-Provera [DMPA] manufactured by Pfizer) is indicated for the prevention of pregnancy in adolescents and adults. DMPA is *not* recommended before menarche, in post-menopausal women, and for long-term use, defined by the package insert as greater than two years. It is available in a 1 mL vial and 1 mL prefilled syringe of 150 mg for intramuscular injection, or 104 mg/0.65 mL for subcutaneous injection. The subcutaneous injection is formulated to provide a slower and more sustained absorption of DMPA. This allows for a 30 percent lower dose and reduces peak blood levels while maintaining the same duration of action. Administration of the subcutaneous dose is reportedly less painful than the intramuscular injection; otherwise profiles are similar for the two medications.

DMPA is administered every three months intramuscularly in the gluteal or deltoid muscle, or subcutaneously into the anterior thigh or abdomen. It is not recommended for use longer than two years, unless other birth control methods are considered inadequate. The first dose should be administered within five days of the start of a normal menstrual cycle in order to ensure the woman is not pregnant. If the timing between doses is greater than 13 weeks, pregnancy should be ruled out before administering the medication. DMPA is contraindicated in patients with 1) known or suspected pregnancy, 2) active thrombophlebitis, 3) known or suspected breast cancer, hypersensitivity to Depo-Provera or any of its components, 4) significant liver disease, and 5) undiagnosed vaginal bleeding.

There is a boxed warning for loss of bone mineral density (BMD). This is especially prevalent in adolescents; risks and benefits should be weighed before starting therapy. DMPA reduces serum estrogen levels and has been associated with significant bone mineral density loss. In adolescents and young women who have not reached maximum bone accumulation, this is of particular concern. The rate of bone density loss is non-linear with the greatest loss occurring in the first one to two years of use. There is no evidence whether this loss in bone mineral density will be fully recovered, although studies have shown remarkable reversal. Compared to the hip, reversal of bone loss at the spine occurs sooner. It is postulated that this may reduce peak bone mass in these women, and could increase the risk of osteoporotic fracture later in life. At the time of writing this lesson, however, it is unknown whether this is true. Observational studies have reported an increased risk of fracture in current DMPA users compared to non-users. However, it is difficult to draw clinical conclusions from these studies as DMPA users also have significant behavioral differences from non-users which may increase their risk of fracture. A retrospective cohort study of the two groups reported that DMPA users had a higher incidence of fracture than never-users prior to DMPA use, and that this rate did not significantly increase after starting DMPA. Comparison studies of the intramuscular and subcutaneous injection show no statistically significant differences in bone mineral density loss or efficacy over two years. This risk does not seem to indicate a need for BMD testing, as the effect of DMPA on BMD is similar to the decrease seen with pregnancy or lactation. It is recommended that women taking DMPA receive an adequate daily dose of calcium and vitamin D and should follow recommendations for good bone health (i.e., regular exercise).

DMPA is highly efficacious. Following a single dose of DMPA, the drug level increases for three weeks until it reaches a peak serum concentration of 7 ng/mL. It then declines until it becomes undetectable. The contraception mechanism is the prevention of ovulation in most patients. The intramuscular injection yields plasma levels high enough to inhibit the secretion of LH and FSH which in turn prevents the development of mature follicles. It is also thought to work by thickening the cervical mucus which decreases sperm penetration, and by impairing implantation. Ovulation typically resumes at DMPA levels <0.1 ng/mL.

The most common side effects of DMPA are headache, menstrual irregularities and weight gain. Headache was reported in 16.5 percent of individuals studied over 13 months. Menstrual irregularities were reported in 57.3 percent of women at 12 months and 32.1 percent at 24 months, and are the most common reason for discontinuation of DMPA. Menstrual irregularities include spotting, irregular or unpredictable bleeding, and amenorrhea. Amenorrhea is increasingly more common with longer duration of use. By 12 months, 55 percent of women report amenorrhea, and by 24 months that number increases to 68 percent.

Delays in return to fertility after stopping DMPA are likely. In one study of 188 women who discontinued DMPA to become pregnant, data are available for 61 percent of them. Of those women, the median time to conception post-DMPA use was 10 months following the last injection. The range was four months to 31 months and was unrelated to duration of DMPA use. Based on analysis of data from this trial, it is expected that within 12 months, 68 percent of women may conceive, 83 percent may conceive within 15 months, and 93 percent within 18 months from the last injection.

Intramuscular DMPA is administered as a 1 mL injection by deep intramuscular injection into the gluteal or deltoid muscle. Subcutaneous DMPA is administered as a 0.65 mL injection into the anterior thigh or abdomen. Subcutaneous administration into the upper arm is an off-label use; however, studies have shown that administration at this site provides sufficient drug levels to provide contraceptive protection. Both products should be shaken vigorously prior to adminis-

Table 2
Initiation of contraception implants

Previous Contraception	Recommended Timing of Insertion	Use of Backup Birth Control
No previous hormonal contraception in past month	Between Day 1 and Day 5 of menstrual cycle	Not necessary
Combination hormonal contraceptives	•Day after last active tablet •Day of vaginal ring removal •Day of patch removal	Not necessary
Progestin-only contraceptives	•DMPA: day next injection due •Minipill: switch at any time within 24 hours of last tablet •IUD: same day as IUD is removed	Not necessary
Following abortion or miscarriage	•First trimester: within five days of abortion or miscarriage •Second trimester: between 21 to 28 days following abortion or miscarriage	Not necessary
Postpartum	•Not breastfeeding: between 21 to 28 days postpartum •Breastfeeding: after fourth postpartum week	No Yes, until 7 days post-insertion

tration to ensure a uniform suspension. DMPA may be administered at any time, as long as pregnancy has been excluded. If either formulation is administered within the first seven days of a menstrual cycle, backup birth control is not needed. If DMPA is administered greater than seven days from the last menstrual period or administered postpartum, backup contraception is recommended for seven days.

If a woman is transitioning from another form of birth control (pill, patch, and ring) to DMPA, begin DMPA while she is still using hormonal contraception. The hormonal contraception may be discontinued seven days after the injection and no backup birth control is needed. If switching from an IUD to DMPA, administer DMPA seven days prior to IUD removal.

Contraception Implants

Nexplanon (Merck) is a small, white, flexible implant 4 cm in length and 2 mm in diameter which contains 68 mg of etonogestrel. This implant, which is about the size of a matchstick, is inserted subdermally in the upper arm by a health care practitioner under aseptic conditions. It should be inserted in the non-dominant arm about eight to 10 cms above the medial epicondyle of the humerus (the inside bump of the elbow). Once inserted, both the practitioner and the patient should palpate the rod to verify the presence of the implant. Nexplanon must be removed by the end of the third year. If the patient would like to continue using Nexplanon after this time, a new implant may be inserted at the time of removal. Nexplanon may be removed at any time during the three years. Nexplanon asserts its contraceptive effect through the suppression of ovulation, increased viscosity of cervical mucus and alterations in the endometrium.

A previous version of the implant, Implanon (2001, Merck), is now being marketed under the name Nexplanon. Nexplanon is easier to insert due to changes to the insertion rod and is radiopaque, meaning it can be seen on x-ray in the case of non-palpable insertion. Both implants contain 68 mg of etonogestrel.

Initiation of the implant and use of backup birth control varies based on previous contraceptive use (Table 2). It is important to rule out pregnancy prior to the insertion of the implant. The implant may be inserted at any time as long as it is reasonably certain the woman is not pregnant. According to the package insert of Nexplanon, use of a secondary (backup) form of birth control is not necessary unless the timing of the implant insertion is not as recommended. In these cases, backup birth control is recommended for seven days following the insertion. According to the recommendations in the *U.S. Selected Practice Recommendations for Contraceptive Use 2013,* however, backup contraception or abstinence is recommended for seven days unless the implant is inserted within five days of the start of the menstrual cycle.

Nexplanon is contraindicated in women who are known or suspected to be pregnant. If a woman should become pregnant while using Nexplanon and wishes to maintain the pregnancy, Nexplanon should be removed as soon as possible. Nexplanon is also contraindicated in women with a history or thrombosis or thromboembolic disorders, liver tumors or active liver disease, undiagnosed genital bleeding, breast cancer or a history of breast cancer, or an allergic reac-

tion to any of the components of Nexplanon. Individuals should be warned of the potential for serious adverse events including thrombosis, liver disease, and uncontrolled, elevated blood pressure. In the event of any of these, Nexplanon should be removed. Patients should also be warned of potential metabolic effects including mild insulin resistance and elevated LDL levels. These are of unknown clinical significance but patients who have been diagnosed as prediabetic, diabetic or have hyperlipidemia should be monitored closely.

Similar to DMPA, the most common adverse effects reported were change in menstrual bleeding pattern, headache and weight gain. Changes in menstrual bleeding patterns include changes in frequency, intensity or duration. Women should be counseled regarding bleeding pattern changes prior to implant insertion. Irregular bleeding was the most common reason women discontinued therapy with Nexplanon. Other common adverse reactions (≥10 percent) were vaginitis, acne, breast pain, abdominal pain and pharyngitis. Migration of Nexplanon has been noted in post-marketing case reports. In some cases, implants have migrated into vessels of the arm or the pulmonary artery. In the case of an implant which becomes non-palpable, its location should be identified using x-ray or CT technology and removal is strongly recommended. Exploratory surgery without knowledge of the exact location of the implant is discouraged. Patients should be warned that complications may be associated with the insertion and/or removal of Nexplanon, including pain, paresthesia, bleeding, hematoma, scarring and infection.

Etonogestrel levels in the blood decrease below sensitivity of the assay within one week of removal of the implant. Pregnancies have been reported as soon as seven to 14 days post-removal.

Changes in efficacy have been noted in women on long-term treatment with hepatic enzyme inducing drugs including CYP3A4 inducers. Some of these drugs include: barbiturates, carbamazepine, oxcarbazepine, griseofulvin, phenytoin, rifampin, St. John's Wort and topiramate. HIV antiretrovirals have also been noted to interact with progesterone derivatives and may affect the efficacy of the implant. It is important to review all medications a patient may be taking for interactions before insertion of the implant. If a patient is to be on continuous treatment with an interacting medication, it is recommended to remove the implant and transition to a contraceptive method that is unaffected by the interacting medication. The efficacy of Nexplanon in overweight women may also be reduced. This is especially plausible if the woman is also currently using a medication which induces hepatic enzymes. Women who weighed more than 130 percent of their ideal body weight were not studied in clinical trials. It has been noted that serum concentrations of etonogestrel are inversely related to body weight and it is, therefore, possible that Nexplanon may be less effective in overweight women. Baseline measurement of weight and BMI may be useful for monitoring implant users over time.

IUD Contraceptives

Four different intrauterine devices (IUDs) are available at the time of publication, one non-hormonal (ParaGard) and three hormonal (Mirena, Liletta, Skyla).

Intrauterine devices are safe for women of all ages including adolescents. IUDs are very effective with only 0.8 pregnancies per 100 women per year. They can be inserted at any time, if it is reasonably certain the woman is not pregnant. An IUD can also be inserted at any time when a woman is transitioning from another form of birth control, as long as it is reasonably certain she is not pregnant. Waiting until the next menstrual cycle is not necessary. When transitioning from another birth control to an IUD, no additional contraception is necessary.

All four IUDs are contraindicated in pregnancy. Women who are pregnant or suspected of being pregnant should not use an IUD. Women who become pregnant while using an IUD should have the IUD removed as soon as possible. Use of an IUD carries the risk of perforation of the uterine wall or cervix. Expulsion of an IUD has also been reported and patients should be warned that if this goes unnoticed, an unintended pregnancy may occur. Expulsion typically occurs during menses and is most often reported in the first few months after insertion. Women who have never had children (nulliparous) have a slight increased risk of expulsion, compared to those who have given birth.

ParaGard. ParaGard T 380A is an intrauterine copper contraceptive (Cu-IUD) manufactured by Teva. It is a T-shaped IUD 32mm by 36mm in size. It contains an exposed copper surface which allows copper to be continuously released into the uterine cavity. Copper enhances the contraceptive efficacy of the device by interfering with sperm transport and fertilization of an egg. It also potentially prevents implantation of a fertilized egg.

ParaGard is indicated for intrauterine contraception for up to 10 years. No additional contraception is necessary after insertion of a Cu-IUD. It is contraindicated in pregnant women or when there is a suspicion of pregnancy as it increases the risk of spontaneous abortion, premature delivery, sepsis and, rarely, death. ParaGard is also contraindicated when there are uterine abnormalities, acute pelvic inflammatory disease, postpartum or post-abortal endometritis, uterine or cervical malignancy, unexplained genital bleeding, mucopurulent cervicitis, Wilson's disease, allergy to any component of ParaGard, or a previously placed IUD that has not been removed. Common adverse effects of ParaGard include anemia, backache, dysmenorrhea, dyspareunia, expulsion, leukorrhea, prolonged men-

strual flow, menstrual spotting, pain and cramping, and vaginitis. The most serious adverse events are discussed further below and include intrauterine pregnancy, septic abortion, ectopic pregnancy, pelvic infection, perforation and embedment.

Women who become pregnant while using ParaGard should first be evaluated for ectopic pregnancy, as pregnancies that occur with a Cu-IUD in place are more likely to be ectopic than in the general population. If the pregnancy is intrauterine and ParaGard is in place with the string visible, ParaGard should be removed due to the increased risk of spontaneous abortion. However, removal may be followed by pregnancy loss. If the string is not visible and the woman decides to continue the pregnancy, an ultrasound should be performed to confirm that ParaGard is still in place. There are limited data regarding birth defects from copper exposure, but at the time of writing, studies have not detected a pattern of abnormalities and do not suggest a higher risk than baseline for birth defects.

Women using ParaGard should also be warned of the potential for pelvic infection. Although pelvic inflammatory disease is uncommon, IUDs may be associated with an increased risk when compared to other forms of birth control. Women who have AIDS should not have IUDs inserted unless they are clinically stable on antiretroviral therapy. Women should also be warned that partial penetration or embedment in the myometrium, partial or total perforation of the uterine wall or cervix, and expulsion of ParaGard have been reported.

Irregular bleeding and menstrual changes are the most common reason for discontinuing use of ParaGard. In one large clinical trial, 11.9 percent of patients who discontinued ParaGard cited bleeding/pain as the main reason. Women should be counseled that they may experience heavy bleeding and dysmenorrhea (painful menstruation including cramping) while using the device. Menstrual bleeding and cramping may initially increase, but usually decrease over time. There is strong evidence to support the use of nonsteroidal anti-inflammatory medications for the treatment of dysmenorrhea.

ParaGard is the only IUD which has been studied for use as emergency contraception. Insertion of a Cu-IUD is effective when inserted up to five days after unprotected intercourse. In a study of 1,963 women who underwent the insertion of Cu-IUD for emergency contraception, the pregnancy rate was 0.23 percent. Comparison studies of Cu-IUD and other forms of emergency contraception have not been conducted.

LNG-IUDs. Levonorgestrel (LNG)-IUDs prevent pregnancy through the thickening of the cervical mucus which prevents passage of sperm into the uterus, inhibition of sperm capacitation or survival, and alteration of the endometrium. The local effects of LNG as a means to enhance contraceptive effectiveness has not been conclusively established.

LNG-IUDs are contraindicated in patients who are pregnant or suspected to be pregnant. They are also contraindicated in patients with a congenital or acquired uterine anomaly if it distorts the uterine cavity. Other contraindications for LNG-IUD use include patients who have pelvic inflammatory disease; postpartum endometritis; known or suspected uterine, cervical, breast or liver cancer; uterine bleeding of unknown etiology; acute cervicitis/vaginitis or conditions associated with increased susceptibility to pelvic infections. Finally, LNG-IUDs are contraindicated in patients who have a previous IUD which has not been removed or have a history of hypersensitivity to any of the components in the respective IUD.

No drug interaction studies have been completed with LNG-IUDs; however, progestins may be decreased by CYP3A4 inducers including, but not limited to, carbamazepine, phenytoin, rifampin, St. John's Wort, and topiramate.

Mirena. Mirena (Bayer HealthCare Pharmaceuticals) is a progestin-containing intrauterine device indicated for contraception for up to five years. Mirena contains 52 mg of levonorgestrel released at a rate of 20 mcg/day. Mirena must be removed after five years because the rate of levonorgestrel release at this point is decreased by 50 percent. Mirena is recommended for women who have had at least one child, although current evidence suggests the benefits generally outweigh the risks in nulliparous women as well. Mirena should be inserted during the first seven days of the menstrual cycle or immediately after a first trimester abortion. Backup birth control is not needed if Mirena is inserted during this time period. Patients should be evaluated four to six weeks following insertion, then yearly afterwards.

Irregular bleeding patterns including spotting, heavy bleeding, increased frequency, and amenorrhea are common with Mirena. Within one year, 20 percent of women using Mirena will experience amenorrhea. Other common adverse reactions include abdominal/pelvic pain (22 percent), headache/migraine (16 percent), genital discharge (15 percent) and vulvovaginitis (10 percent).

Skyla. Skyla is a progestin-containing intrauterine device indicated for the prevention of pregnancy for up to three years. Skyla, like Mirena, is manufactured by Bayer HealthCare Pharmaceuticals. It contains 13.5 mg of levonorgestrel which is released at a rate of 14 mcg/day. This declines to 5 mcg/day after three years at which point Skyla must be removed or replaced. Adverse reactions associated with Skyla are (≥10 percent) irregular bleeding, vulvovaginitis, abdominal/pelvic pain, acne, ovarian cyst and headache. Skyla should be inserted during the first seven days of the menstrual cycle or immediately after a first trimes-

ter abortion. Backup birth control is not needed if Skyla is inserted during this time period. Skyla is the smallest IUD in size, about 28 mm horizontally and 30 mm vertically.

Liletta. Liletta is manufactured by Allergen and was initially approved for use in the United States in 2015. In addition to the contraindications listed for all LNG-IUDs, Liletta is contraindicated when used for emergency contraception. Liletta contains 52 mg of levonorgestrel and is indicated for the prevention of pregnancy for up to three years. It releases levonorgestrel at a rate of 18.6 mcg/day initially and declines to 12.6 mcg/day at three years post-insertion. The most common adverse reactions (>10 percent) are vaginal and vulvovaginal infections and acne.

Conclusion

LARCs offer a long-acting, reliable form of contraception without many of the adherence issues of oral contraceptives. Regardless of the form of contraception chosen, all women should be counseled on the risks of sexually transmitted diseases, including HIV, and the use of condoms.

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The author, the Ohio Pharmacists Foundation and the Ohio Pharmacists Association disclaim any liability to you or your patients resulting from reliance solely upon the information contained herein. Bibliography for additional reading and inquiry is available upon request.

This lesson is a knowledge-based CPE activity and is targeted to pharmacists in all practice settings.
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continuing education quiz

Long-Acting Reversible Contraceptives

1. Which of the following is the most effective in preventing pregnancy based on typical-use?
   a. Injectable DMPA c. Cu-IUD
   b. Implant d. LNG-IUD

2. The corpus luteum secretes which of the following hormones?
   a. Luteinizing hormone c. Estrogen
   b. Follicle stimulating hormone d. Progesterone

3. According to the package insert, DMPA may be administered subcutaneously into the:
   a. gluteus. c. deltoid.
   b. anterior thigh. d. all of the above.

4. Which of the following has a boxed warning for bone mineral density loss?
   a. Depo-Provera c. ParaGard
   b. Nexplanon d. Skyla

5. All of the following are common adverse reactions with DMPA EXCEPT:
   a. headache. c. genital discharge.
   b. weight gain. d. menstrual irregularities.

6. Which of the following is implanted subdermally into the upper arm?
   a. Depo-Provera c. ParaGard
   b. Nexplanon d. Skyla

7. All of the following are potential serious adverse effects of Nexplanon EXCEPT:
   a. weight gain.
   b. thrombosis.
   c. uncontrolled elevated blood pressure.
   d. liver disease.

Completely fill in the lettered box corresponding to your answer.

1.	[a]	[b]	[c]	[d]	6.	[a]	[b]	[c]	[d]	11.	[a]	[b]	[c]	[d]
2.	[a]	[b]	[c]	[d]	7.	[a]	[b]	[c]	[d]	12.	[a]	[b]	[c]	[d]
3.	[a]	[b]	[c]	[d]	8.	[a]	[b]	[c]	[d]	13.	[a]	[b]	[c]	[d]
4.	[a]	[b]	[c]	[d]	9.	[a]	[b]	[c]	[d]	14.	[a]	[b]	[c]	[d]
5.	[a]	[b]	[c]	[d]	10.	[a]	[b]	[c]	[d]	15.	[a]	[b]	[c]	

❑ **I am enclosing $5 for this month's quiz made payable to: Ohio Pharmacists Association.**

1. Rate this lesson: (Excellent) 5 4 3 2 1 (Poor)
2. Did it meet each of its objectives? ❑ yes ❑ no
   If no, list any unmet_____
3. Was the content balanced and without commercial bias?
   ❑ yes ❑ no If no, why?_____
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Return quiz and payment (check or money order) to Correspondence Course, OPA, 2674 Federated Blvd, Columbus, OH 43235-4990

8. The most common reason for discontinuation of Nexplanon was:
   a. weight gain. c. BMD loss.
   b. irregular bleeding. d. headache.

9. All of the following interact with a progestin-based contraceptive EXCEPT:
   a. phenytoin. c. St. John's Wort.
   b. carbamezapine. d. saw palmetto.

10. Which of the following is indicated for the prevention of pregnancy for up to 10 years?
   a. Depo-Provera c. Mirena
   b. Liletta d. ParaGard

11. After ParaGard insertion, backup contraception is necessary for seven days.
   a. True b. False

12. Which of the following IUDs may be used as emergency contraception?
   a. Liletta c. ParaGard
   b. Mirena d. Skyla

13. LNG-IUDs are contraindicated in all of the following EXCEPT:
   a. pregnancy. c. uterine abnormality.
   b. BMD loss. d. pelvic inflammatory disease.

14. Which of the following is the smallest IUD?
   a. Liletta c. ParaGard
   b. Mirena d. Skyla

15. In addition to the contraindications listed for all LNG-IUDs, Liletta is also contraindicated in/for:
   a. uncontrolled blood pressure. c. amenorrhea.
   b. emergency contraception.

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