A Pharmacist's Update on the Efficacy, Safety and Role of Long-acting Reversible Contraception

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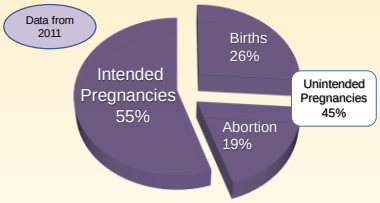
Educational Objectives

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

- Explore the efficacy and safety of various types of non-hormonal and hormonal long-acting reversible contraception (LARC) measures
- Identify the role of the pharmacist in the education and management of patients who elect to use LARCs

U.S. Pregnancies Unintended vs Intended



Guttmacher Institute. https://www.guttmacher.org/fact-sheet/unintended-pregnancy-united-states. Accessed January 10, 2017.

Patient Case

TL is a 32-year-old woman who is 38 weeks pregnant and is scheduled for a planned repeat C-section at 39 weeks. She is seeking contraception postpartum. She has 3 children, and she and her husband have decided not to have anymore children in the near future, but may consider having another child again in a few years.

She has a history of GERD, TMJ and seasonal allergies, but, otherwise, she is healthy. Her medications prior to pregnancy include omeprazole 20 mg PO daily, fluticasone 50 mcg 2 sprays intranasally daily, carbamazepine 200 mg PO BID for TMJ. Her BMI is 34. She has used condoms in the past but would like something more long-term. She plans to breastfeed and prefers to stay away from hormonal contraception for concerns with hormones in the breastmilk and because her mother had a DVT in the past. TL works full-time and is very busy. She is thinking about an intrauterine device and asks her pharmacist if it is a good option for her.

What are some contraceptive options for TL and some considerations regarding therapy choice for TL?

Ideal Contraceptive

- Very effective
- Easily accessible
- Long duration of action
- No adverse effects
- Reversible
- Discrete in use
- STI Protection

Hatcher RA, et al. *Contraceptive Technology*. 20th ed. New York: Ardent Media; 2011.

Factors in Choosing a Contraceptive

Effectiveness	• Theoretical (Perfect) vs Actual (Typical)
Accessibility	• Cost • Adherence ability • Acquisition
Patient Factors	• Age • Health/comorbidities and lifestyle choices • Medication history • Frequency of intercourse • Importance of not becoming pregnant • Perceptions and misperceptions
Product Consideration	• Adverse effects • Duration of action • Return to fertility time • Risks vs benefits

Hatcher RA, et al. *Contraceptive Technology*. 20th ed. New York: Ardent Media; 2011.

Contraceptive Methods

- Female/male sterilization
- Long-acting (IUD: copper, progestin; progestin implant)
- Shorter-acting hormonal contraceptives: combined, progestin-only
- Emergency contraceptives
- Barrier contraceptives
- Spermicides
- Natural family planning

Types of Long-Acting Reversible Contraception (LARC)

- Non-hormonal LARC
  - Intrauterine copper contraceptive

- Hormonal LARC
  - Progestin intrauterine systems
  - Progestin implant

Printed with permission from CDC. http://www.cdc.gov/reproductivehealth/unintendedpregnancy/pdf/family-planning-methods-2014.pdf. Accessed January 10, 2017

Characteristics of LARC

Ideal Contraceptive	Characteristics of LARC Answer	 Details
Highly Effective?	Yes	Low typical failure rates
Long Duration of Action?	Yes	3 to 10 years
Easily Reversible?	Yes	Return to fertility similar to non-LARC users
Adverse Effects?	Yes	Varies
Privacy of Use?	Yes	Not easily seen by others
STI Protection?	No	Need other protection
Easily Accessible? (able to attain, cost, availability)	Depends	Provider access for administration

Paragard T380A [package insert]. North Wales, PA: Teva Women's Health Inc.; Sept. 2014. .; Mirena [package insert]. Wayne, NJ: Bayer Healthcare Pharmaceuticals; December 2016.; Skyla [package insert]. Wayne, NJ: Bayer Healthcare Pharmaceuticals; December 2016.; Liletta [package insert]. Parsippany, NJ: Actavis Pharma, Inc.; Feb 2015.; Stoddard AM, et al. *Eur J Contracept Reprod Health Care*. 2015;20 (3):223-30.

Who is a Candidate for LARC?

Any healthy reproductive age woman who is seeking effective, reversible contraception. Includes those that are:

- Nulliparous or parous
- Adolescents
- History of sexually-transmitted infection (STI)
- Postpartum

ACOG. http://www.acog.org/-/media/Committee-Opinions/Committee-on-Gynecologic-Practice/co642.pdf?dmc=1. Accessed January 12, 2017.; ACOG. http://www.acog.org/~/media/Committee%20Opinions/Committee%20on%20Adolescent%20Health%20Care/co639.pdf. Accessed January 12, 2017.

Intrauterine Copper Contraceptive

US product name	• ParaGard T 380A
Description	• T-shaped IUD (32 mm x 36 mm), frame - polyethylene with barium sulfate • 2 flexible arms for insertion that open in uterus to hold solid sleeves of copper against fundus • Surface area of copper: 380 mm²
Effectiveness	• Works for 10 years • Perfect use failure rate: 0.6% • Typical use failure rate: 0.8%

Paragard T380A [package insert]. North Wales, PA: Teva Women's Health Inc.; Sept. 2014.

Intrauterine Copper Contraceptive: Mechanism of Action

- Primary action: spermicide
- Copper ions
  - Inhibit sperm motility by inhibiting acrosomal enzyme activation
- Presence of device may prevent implantation
- Does not interfere with ovulation

Paragard T380A [package insert]. North Wales, PA: Teva Women's Health Inc.; Sept. 2014.; Zieman M, et al. *Managing Contraception*. 2016. Tiger, Georgia: Bridging the Gap Foundation, 2016.

Types of LARC

- Non-hormonal LARC
  - Intrauterine copper contraceptive

- Hormonal LARC
  - Progestin intrauterine systems
  - Progestin implant

Printed with permission from CDC. http://www.cdc.gov/reproductivehealth/unintendedpregnancy/pdf/family-planning-methods-2014.pdf. Accessed January 10, 2017

LARC- Progestins

Progestin	Description
Levonorgestrel	• Used in intrauterine systems, oral combined hormonal contraception, OTC emergency contraception • Second generation progestin
Etonogestrel	• Found in contraceptive implant, contraceptive vaginal ring • Active metabolite of desogestrel • Third generation progestin

Station, NJ: Merck; December 2016.; Dickey RP. *Managing Contraceptive Pill Patients*. 15th ed. Dallas, TX: EMS Inc; 2014.

Progestins

Mechanisms of action

- Thicken cervical mucus
- Inhibit sperm travel
- Alter endometrium

Some progestin adverse effects

- Headache
- Increased appetite
- Depression
- Changes in libido
- Hair loss*
- Hirsutism*
- Acne, oily skin*

*Androgen-mediated

Dickey RP. *Managing Contraceptive Pill Patients*. 15th ed. Dallas, TX: EMIS Inc; 2014.; Zieman M, et al. *Managing Contraception*. 2016. Tiger, Georgia: Bridging the Gap Foundation, 2016.

Levonorgestrel Intrauterine Systems

5-Yr. LNG-IUS (Mirena)	• Effective for 5 years • Releases 20 mcg/day • Also has indication for heavy menses in women who would like contraception • Size = 32 mm wide/32 mm
3-Yr. LNG-IUS (Liletta)	• Effective for 3 years • Releases 18.6 mcg/day • 16.3 mcg/day after 1 year • 14.3 mcg/day at 2 years • 12.6 mcg/day at 3 years • Size = 32 mm wide/32 mm
3-Yr. Low dose LNG-IUS (Skyla)	• Effective for 3 years • Releases 14 mcg/day after 24 days • 10 mcg/day after 60 days • Avg. release is 6 mcg/day over 3 years • Size = 28 mm wide/30 mm

LNG – IUS Failure Rates: Typical Use = Perfect Use (0.2%)

Mirena. http://www.mirena-us.com/index.php. Accessed January 12, 2017.; Liletta. https://www.liletta.com/about/what-it-looks-like. Accessed January 17, 2017.; Skyla. http://www.skyla-us.com/what-is-skyla.php?. Accessed January 12, 2017.; Mirena [package insert]. Wayne, NJ: Bayer Healthcare Pharmaceuticals; December 2016. Skyla [package insert]. Wayne, NJ: Bayer Healthcare Pharmaceuticals; December 2016.; Liletta [package insert]. Parsippany, NJ: Actavis Pharma, Inc.; May 2016. Zieman M, et al. *Managing Contraception*. 2016. Tiger, Georgia: Bridging the Gap Foundation, 2016.

Some Adverse Reactions of IUDs

- Uterine bleeding irregularities
  - Unscheduled bleeding
  - Decreased bleeding
  - Increased scheduled bleeding
- Amenorrhea
- Abdominal pain
- Headache/migraine
- Intrauterine conception
- Vaginal discharge
- Vaginitis
- Hormone-mediated effects
  - Acne
  - Depression/mood changes
  - Breast tenderness
  - Ovarian cysts

Mirena [package insert]. Wayne, NJ: Bayer Healthcare Pharmaceuticals, December 2016.; Skyla [package insert]. Wayne, NJ: Bayer Healthcare Pharmaceuticals, December 2016.; Liletta [package insert]. Parsippany, NJ: Actavis Pharma, Inc., Dec 2016.; Paragard T380A [package insert]. North Wales, PA: Teva Women's Health Inc. Sept. 2014.

Contraindications for IUDs
Per Package Labeling

- Pregnancy or suspected pregnancy
- Distortion of the uterus
- Acute pelvic inflammatory disease or current high risk
- Postpartum/postabortal endometritis in last 3 months
- Uterine or cervical cancer
- Unknown etiology of vaginal bleeding
- Mucopurulent cervicitis or vaginitis
- Allergic to product
- Current IUD that has not yet been removed
- Acute liver disease or liver tumor (benign or malignant)
- Breast cancer or other progestin-sensitive cancer

*Purple denotes levonorgestrel IUD

Paragard T380A [package insert]. North Wales, PA: Teva Women's Health Inc.; Sept. 2014.; Mirena [package insert]. Wayne, NJ: Bayer Healthcare Pharmaceuticals, December 2016.

IUD: Patient Counseling

- PAINS
  - P – Period late; abnormal spotting or bleeding
  - A – Abdominal pain, pain with intercourse
  - I – Infection exposure (STI); abnormal vaginal discharge
  - N – Not feeling well, fever, chills
  - S – String missing, shorter or longer
- Anticipated menstrual changes
- If expulsion occurs, back up contraception must be used

Zieman M, et al. *Managing Contraception*. 2016. Tiger, Georgia: Bridging the Gap Foundation, 2016.

Progestin Implant

Product Name	• Nexplanon (etonogestrel) • Inserted subdermally in upper arm
Description	• Single, soft, radiopaque, rod implant • 4 cm x 2 mm • Made of ethylene vinyl acetate • Contains 68 mg of etonogestrel and 15 mg of barium sulfate • Releases 25-45 mcg/day over 3 years
Effectiveness	• Typical use failure rate: 0.05% • Perfect use failure rate: 0.05%

Nexplanon [package insert]. Whitehouse Station, NJ: Merck; December 2016.

Progestin Implant

- Common adverse effects:
  - Irregular menses ~18% after 2 years
  - Amenorrhea occurs in ~22% after 2 years
  - Fibrosis
  - Insertion site pain, difficulty removing rods
  - Headache
  - Vaginitis
  - Consistent with progestins
  - Does not appear to affect BMD
  - Weight gain 2.8 lbs in first year, 3.7 lbs in second year

Nexplanon [package insert]. Whitehouse Station, NJ: Merck; December 2016.; Xu H, et al. *Obstet Gynecol*. 2012;120(1):21-26.

Contraindications for Progestin Implant
Per Package Labeling

- Pregnancy or suspected pregnancy
- Unknown etiology of vaginal bleeding
- History of thrombosis or thromboembolic disease
- Allergic to product
- Acute liver disease or liver tumor (benign or malignant)
- Breast cancer or other progestin-sensitive cancer

Nexplanon [package insert]. Whitehouse Station, NJ: Merck; December. 2016.

Studies: Decrease in Abortions/Pregnancy/Births

- Contraceptive CHOICE Project – St. Louis
  - -Over 9,000 women enrolled for 3 years, 75% chose LARC method
  - -Continuation rates higher than for short-acting methods
    - –86% vs 55% at 12 months
    - –77% vs 41% at 24 months
  - -71% of participants reported no change in partners at 6 and 12 months

Secura G, et al. *N Engl J Med*. 2014;371(14):1316-1323.; McNicholas C, et al. *Clin Obstet Gynecol*. 2014;5(4):635-643.; Turok DK, et al. *Fertil and Steril*. 2016;106(6):1273-1281.

Studies: Decrease in Abortions/Pregnancy/Births

- Contraceptive CHOICE Project – *continued*
  - Failure rates for pill, patch and ring users were higher (4.8–9.4%) than for LARC users (<1%) over the 3 years
  - Birth and abortion rates decreased by half compared to nation rates
    - Pregnancy 3.4% vs 5.74% (all US teens 15-19), 15.85% (sexually active US teens)
    - Abortion 0.97% vs 1.47% (all US teens 15-19), 4.15% (sexually active US teens)
    - Birth 1.97% vs 3.44% (all US teens 15-19), 9.4% (sexually active US teens)
- National Survey of Family Growth 2006-2010
  - 13% of postpartum women using short-acting contraceptives were pregnant within 18 months compared to 0.5% using LARC

Secura G, et al. *N Engl J Med*. 2014;371(14):1316-1323.; McNicholas C, et al. *Clin Obstet Gynecol*. 2014;5(4):635-643.; Turok DK, et al. *Fertil and Steril*. 2016;106(6):1273-1281.

Studies: Same Day IUD/ Implant Placement and Infection Risk

- **Same day IUD/implant placement**
  - Increases uptake and decreases pregnancy rate
    - One study showed only 54% uptake for women requiring a second visit for IUD placement
    - Other studies show decreased short-term pregnancy rates with same-day insertion, including postpartum and post-abortion
- **Infection risk**
  - Infection rates considered low
    - Study at Kaiser Permanente Northern California – over 57,000 participants looked at safety of IUD placement with STI testing
      - Overall PID rates were 0.54%
      - No difference in infection rates between those in the same-day STI tested group, those screened 3 months later or those no screening
    - Other studies have confirmed low infection rates, similar findings PID rates ~0.5%, consistent even in women with high risks for STIs

Bingcsson NE., et al. *Journal of Women's Health*. 2015;24(5):354-359.; Turok DK, et al. *Am J Obstet Gynecol*. 2016; 215(5):599e1-599e6.; Sufrin CB, et al. *Obstet Gynecol*. 2012;120(6):1314-1321. Turok DK, et al. *Fertil and Steril*. 2016;106 (6):1273-1281.

Patient Case

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What are some contraceptive options for TL and some considerations regarding therapy choice for TL?

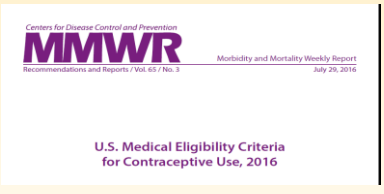
Pharmacist's Role in LARC Patient Care

- Determine type of LARC
- Determine if it is a levonorgestrel based
- Other things to consider/to counsel on
  - Very important when taking a medical history to also ask about LARC therapies to assess the following issues:
    - Drug-drug interactions
    - Adverse drug reactions
    - Prevention of STIs
    - Teratogenicity

Pharmacist's Role in LARC Patient Care

- Other things to consider/to counsel on
  - Open dialog is key. May phrase question as:
    - "Are you currently using any forms of birth control such as over-the-counter spermicides, condoms, oral tablets, patch, vaginal ring, intrauterine device or implant?"
    - Open-ended, "What forms of birth control are you using, if any, such as over-the-counter spermicides, condoms, oral tablets, patch, vaginal ring, intrauterine device or implant?"

CDC Medical Eligibility Criteria for Contraceptive Use (MEC)



CDC. http://www.cdc.gov/mmwr/volumes/65/rr/pdfs/rr6503.pdf. Accessed March 11, 2017.

Contraindications for LARC

Based on CDC Medical Eligibility Criteria 4 categories:

Category 1. A condition for which there is no restriction for the use of the contraceptive method.

Category 2. A condition where the advantages of using the method generally outweigh the theoretical or proven risks.

Category 3. A condition where the theoretical or proven risks usually outweigh the advantages of using the method.

Category 4. A condition that represents an unacceptable health risk if the contraceptive method is used.

CDC. *MMWR Recomm Rep.* 2016;65(RR-3):1–103.

CDC Medical Eligibility Criteria (MEC) I vs C

Initiation "I"
- Condition present when initiating the contraceptive agent

Continuation "C"
- Condition presents while woman is using the contraceptive agent

CDC MEC for LARC

Condition	LNG IUD	Implant	CU IUD
Obesity	1	1	1
Hypertension (controlled)	1	1	1
Hypertension (uncontrolled)	2	2	1
Diabetes	2	2	1
Multiple cardiovascular risk factors	2	2	1
History of DVT/PE/Thrombogenic mutations (Lower/higher risks for recurrent DVT/PE)	2	2	1
Acute DVT or DVT/PE on anticoagulant therapy (Lower and higher risk for recurrent DVT/PE)	2	2	2
Stroke	2	2 I 3 C	1
Migraines with aura	1	1	1
HIV infection (well receiving ARV)	1	2	1
HIV (not clinically well or not on ARV therapy)	2 I 1 C	2	2 I 1 C

CDC. *MMWR Recomm Rep.* 2016;65(RR-3):1–103.; CDC. https://www.cdc.gov/reproductivehealth/contraception/pdf/summary-chart-us-medical-eligibility-criteria_508tagged.pdf. Accessed January 12, 2017.

Category 4 Contraindications

Condition	LNG IUD	Implant	CU IUD
Post-puerperal sepsis or septic abortion	4	1	4
Current PID, purulent cervicitis, chlamydia, or gonorrhea	4 I 2 C	1	4 I 2 C
Breast cancer	4	4	1
Unexplained vaginal bleeding	4 I 2 C	3	4 I 2 C
Cervical/endometrial cancer	4 I 2 C	2/1	4 I 2 C
Distorted uterine cavity	4	1	4
Pelvic tuberculosis	4 I 3 C	1	4 I 3 C
Gestational trophoblastic disease with elevated B-hCG levels or malignant disease	4 I 2C	1	4 I 2 C

CDC. *MMWR Recomm Rep.* 2016;65(RR-3):1–103.; CDC. https://www.cdc.gov/reproductivehealth/contraception/pdf/summary-chart-us-medical-eligibility-criteria_508tagged.pdf. Accessed January 12, 2017.

Other Contraindications

Copper IUD

- Wilson's disease
- Systemic lupus erythematosus with severe thrombocytopenia

Progestin LARC

- Acute liver disease or liver tumor (benign or malignant)
- Ischemic heart disease
- Systemic lupus erythematosus with positive or unknown antiphospholipids
- Solid organ transplant (initiation)

Paragard T380A [package insert]. North Wales, PA: Teva Women's Health Inc.; Sept. 2014.; CDC. *MMWR Recomm Rep.* 2016;65(RR-3):1-103

DVT and Hormonal LARC

Risk of DVT

Method	Adjusted Relative Risk of DVT (95% CI)
Non-user	1.0 Reference
Transdermal patch	7.9 (3.54 to 17.65)
Vaginal ring	6.48 (4.69 to 8.94)
COC with norgestimate	3.57 (2.98 to 4.27)
COC with LNG and 30-40 mcg of estrogen	3.21 (2.71 to 3.81)
Implant	1.40 (0.58 to 3.38)
Levonorgestrel IUD	0.57 (0.41 to 0.81)

Adapted from Lidegaard O, et al. *BMJ.* 2012;344:e2990.

DVT and LARC

Condition	Sub-Condition	Cu-IUD		LNG-IUD		Implant		DMPA		POP		CHC	
		I	C	I	C	I	C	I	C	I	C	I	C
Deep venous thrombosis (DVT)/Pulmonary embolism (PE)	a) History of DVT/PE, not receiving anticoagulant therapy												
	i) Higher risk for recurrent DVT/PE	1		2		2		2		2		4	
	ii) Lower risk for recurrent DVT/PE	1		2		2		2		2		3	
	b) Acute DVT/PE	2		2		2		2		2		4	
	c) DVT/PE and established anticoagulant therapy for at least 3 months												
	i) Higher risk for recurrent DVT/PE	2		2		2		2		2		4*	
	ii) Lower risk for recurrent DVT/PE	2		2		2		2		2		3*	
	d) Family history (*first-degree relatives*)	1		1		1		1		1		2	
	e) Major surgery												
	i) With prolonged immobilization	1		2		2		2		2		4	
	ii) Without prolonged immobilization	1		1		1		1		1		2	
	f) Minor surgery without immobilization	1		1		1		1		1		1	

*Means "May review CDC Recommendations for complete guidance and clarification for this classification"

CDC. *MMWR Recomm Rep*. 2016;65(RR-3):1-103.; CDC. https://www.cdc.gov/reproductivehealth/contraception/pdf/summary-chart-us-medical-eligibility-criteria_508tagged.pdf. Accessed January 12, 2017.

PTCE DIRECTIONS IN Pharmacy

Postpartum and LARC Use CDC Medical Eligibility Criteria

Condition	Sub-Condition	Cu-IUD		LNG-IUD		Implant		DMPA		POP		CHC	
		I	C	I	C	I	C	I	C	I	C	I	C
Breastfeeding	a) <21 days postpartum					2*		2*		2*		4*	
	b) 21 to <30 days postpartum												
	ii) With other risk factors for VTE					2*		2*		2*		3*	
	iii) Without other risk factors for VTE					2*		2*		2*		3*	
	c) 30-42 days postpartum												
	i) With other risk factors for VTE					1*		1*		1*		3*	
	ii) Without other risk factors for VTE					1*		1*		1*		2*	
	d) >42 days postpartum					1*		1*		1*		2*	
Postpartum (*nonbreastfeeding women*)	a) <21 days					1		1		1		4	
	b) 21 days to 42 days												
	ii) With other risk factors for VTE					1		1		1		3*	
	iii) Without other risk factors for VTE					1		1		1		2	
	c) >42 days					1		1		1		1	
Postpartum (*in breastfeeding or non-breastfeeding women, including cesarean delivery*)	a) <10 minutes after delivery of the placenta												
	i) Breastfeeding	1*		2*									
	ii) Nonbreastfeeding	1*		1*									
	b) 10 minutes after delivery of the placenta to <4 weeks	2*		2*									
	c) ≥4 weeks	1*		1*									
	d) Postpartum sepsis	4		4									

*Means "May review CDC Recommendations for complete guidance and clarification for this classification"

CDC. *MMWR Recomm Rep*. 2016;65(RR-3):1-103.; CDC. https://www.cdc.gov/reproductivehealth/contraception/pdf/summary-chart-us-medical-eligibility-criteria_508tagged.pdf. Accessed January 12, 2017.

Postpartum and Breastfeeding

Postpartum Use of IUD/Implant

- IUD
  - Considered safe and effective
  - Overall higher chance of expulsion postplacental vs delayed insertion 4-8 weeks later, but higher continuation in postplacental
  - Immediately postpartum (within 10 minutes after delivery) associated with:
    - lower expulsion rates
    - less discomfort
  - 12 month expulsion rates for copper IUD similar between c-section (9 to14%) and vaginal births (13 to 19%)
- Implant
  - High continuation rates

Breastfeeding

- Copper IUD has no effect on breastfeeding
- Levonorgestrel IUD/Implant
  - Isolated reports of decreased breast milk production
  - No adverse effects have been associated with health, growth or development of infant
  - LNG may pass into breast milk and reach infant
  - Raises theoretical concern
  - May recommend to wait 6 weeks postpartum before use if breastfeeding

Mirena [package insert]. Wayne, NJ: Bayer Healthcare Pharmaceuticals; December 2016.; Skyla [package insert]. Wayne, NJ: Bayer Healthcare Pharmaceuticals; December 2016.; Liletta [package insert]. Parsippany, NJ: Actavis Pharma, Inc.; May 2016.; Paragard T380A [package insert]. North Wales, PA: Teva Women's Health Inc.; Sept. 2016; Sucak A, et al. *BMC Pregnancy Childbirth*. 2015;15:202.; ACOG. http://www.acog.org/-/media/Committee-Opinions/Committee-on-Gynecologic-Practice/co642.pdf?dmc=1. Accessed January 12, 2017.; Lopez LM, et al. *Cochrane Database Syst Rev*. 2015;(6):CD003036.; Wilson S, et al. *Contraception*. 2014;90(3): 259-64. Goldthwaite LM, et al. *Curr Opin Obstet Gynecol*. 2015;27(6):460-464.

Drug Interactions

Summary Chart for U.S. CDC Medical Eligibility Criteria for Contraceptive Use

Condition	Sub-Condition	Cu-IUD		LNG-IUD		Implant		DMPA		POP		CHC	
		I	C	I	C	I	C	I	C	I	C	I	C
Drug Interactions													
Antiretroviral therapy All other ARV's are 1 or 2 for all methods.	Fosamprenavir (FPV)	1/2*	1*	1/2*	1*	2*		2*		2*		3*	
Anticonvulsant therapy	a) Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine)	1		1		2*		1*		3*		3*	
	b) Lamotrigine	1		1		1		1		1		3*	
Antimicrobial therapy	a) Broad spectrum antibiotics	1		1		1		1		1		1	
	b) Antifungals	1		1		1		1		1		1	
	c) Antiparasitics	1		1		1		1		1		1	
	d) Rifampin or rifabutin therapy	1		1		2*		1*		3*		3*	
SSRIs		1		1		1		1		1		1	
St. John's wort		1		1		2		1		2		2	

CDC. *MMWR Recomm Rep*. 2016;65 (RR-3):1-103.; CDC. https://www.cdc.gov/reproductivehealth/unintendedpregnancy/pdf/legal_summary-chart_english_final_tag508.pdf. Accessed January 13, 2017.

PTCE DIRECTIONS IN Pharmacy

Recommendations for Drug Interactions with LARC

- Copper IUD
  - No known drug interactions (CDC Category 1, CDC 1/2 for ARV*)
- Levonorgestrel IUDs
  - No known interactions with ARV therapy (Category 1/2*) or antiepileptic medication (CDC Category 1), but inducers or inhibitors of CYP3A4 are known to affect progestins.
- Progestin Implant
  - Concomitant use of drugs that decrease effectiveness progestin levels requires a back-up birth control method, such as condoms. (CDC Category 2)

*No known interaction exists between ARVs and IUD use. Insertion of IUD is category 2 if the woman is not clinically well or not receiving ARV therapy, otherwise it is category 1.

CDC. *MMWR Recomm Rep*. 2016;65 (RR-3):1–103.; Paragard T380A [package insert]. North Wales, PA: Teva Women's Health Inc.; Sept. 2014.

PTCE DIRECTIONS IN Pharmacy

Drug Interactions

CYP3A4 Inducers may decrease progestin effectiveness:

- Examples: Itraconazole, ketoconazole
- HIV protease inhibitors or non-nucleoside reverse transcriptase inhibitors may significantly increase or decrease LNG levels

CYP3A4 Inhibitors may increase progestin levels:

- Barbiturates
- Bosentan
- Carbamazepine, phenytoin, oxcarbazepine, topiramate, felbamate
- Efavirenz
- Griseofulvin
- Rifabutin, rifampin
- St. John's wort

Mirena [package insert]. Wayne, NJ: Bayer Healthcare Pharmaceuticals; October 2016.

PTCE DIRECTIONS IN Pharmacy

Return to Fertility

- Pilot data from Contraceptive CHOICE project
  - Return to fertility time with IUDs is similar to shorter-acting contraceptive methods
  - Looked at 69 IUD users (19 copper and 50 LNG IUDs) vs 42 non-users
  - Found pregnancy rates similar at 12 months, 81% of users vs 70% of non-users
- Copper IUD – ovulation is not suppressed
- LARC methods do not cause infertility

Paragard T380A [package insert]. North Wales, PA: Teva Women's Health Inc.; Sept. 2014.; Stoddard AM, et al. *Eur J Contracept Reprod Health Care*. 2015; 20(3):223-30.; Zieman M, et al. *Managing Contraception*. 2016. Tiger, Georgia: Bridging the Gap Foundation, 2016.; ACOG. http://www.acog.org/~/media/Committee%20Opinions/Committee%20on%20Adolescent%20Health%20Care/co539.pdf. Accessed January 12, 2017.

Adolescents and LARC: ACOG Recommendations

- LARC methods should be considered for all adolescents, and accessibility to these methods should be assured
- Counseling about LARC methods should be provided to sexually active adolescents at every health care provider visit.
  - Low failure rates, easy adherence
  - High satisfaction and continuation
  - Also discuss importance of condom use for STI prevention
  - Complications are low, expulsion may be higher in adolescents

ACOG. http://www.acog.org/~/media/Committee%20Opinions/Committee%20on%20Adolescent%20Health%20Care/co539.pdf. Accessed January 12, 2017.

Conclusion

- Pharmacists play an important role with LARC in:
  - Providing information
  - Identifying and referring appropriate patients
  - Taking comprehensive medication histories
  - Managing drug-drug interactions
  - Recommending additional contraception for STI protection
  - Manage and assess side effects
  - Working with institutions to encourage provision
- LARC therapies are:
  - Very effective in preventing pregnancy
  - Quickly reversible
  - Have high continuation rates
  - Cost-effective

Additional Resources

- Centers for Disease Control and Prevention
  - U.S. Medical Eligibility Criteria for Contraceptive Use, 2016. Source: *MMWR*. 2016;65(RR03):1-103.
  - Selected Practice Recommendations for Contraceptive Use, 2016: MMWR. 2016;62(RR05):1-46.
- Hatcher RA, et al. *Contraceptive Technology*, 20th ed. New York: Ardent Media, 2011.
- ACOG LARC Clinical Education and Training
  - http://www.acog.org/About-ACOG/ACOG-Departments/Long-Acting-Reversible-Contraception/LARC-Clinician-Education-and-Training
- American Reproductive Health Professionals
  - www.arhp.org
- Bedsider
  - www.bedsider.org
- Guttmacher Institute
  - www.guttmacher.org
- The Choice Project
  - www.choiceproject.wustl.edu
- LARC First
  - www.larcfirst.com