Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Long Acting Reversible Contraception***
-April 2021-

Background:
The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a drug class review of Long Acting Reversible Contraception (LARC) including the levonorgestrel intrauterine devices (IUD), copper IUD, and etonogestrel subcutaneous implant. There is a trend of increasing LARC use both within IHS and nation-wide. In the IHS, the number of LARC insertions has increased yearly, from approximately 4,300 in 2015 to over 6,600 in 2019. In the United States, it is estimated that 10% of women aged 15-49 years used a form of LARC in 2019[1].

The NPTC reviewed the topic of contraception in 2016, at which time all three options for LARC were added to the IHS National Core Formulary. Clinical trials[1-4], systematic reviews[5-9], and guidelines[1,10] from the most recent American College of Obstetrics and Gynecology (ACOG) practice bulletin and committee opinion were reviewed. Following this clinical review and analysis, the NPTC made **no changes to the National Core Formulary**.

Discussion:
LARCs provide the most effective form of contraception with a failure rate of less than 1 per 100 years of use, which is >20x more effective than hormonal pills, patches, or rings (HR 21.8, 95% CI: 13.7-34.9, p<0.001)[2]. Multiple studies also confirm that access to, and use of LARC results in reduced incidence of abortion (4.4 vs 17.0 per 1,000 p<0.001)[2,9].

LARCs are generally well tolerated, and are continued longer than other forms of contraception (67.2%, CI: 65.4-68.9 vs 31.0%, CI: 28.5-33.5 at 3 years, p<0.001)[2]. LARCs are also the most cost efficient form of contraception when used for at least 3 years[5]. When compared to the levonorgestrel IUD, the etonogestrel subcutaneous implant has a higher discontinuation rate, most commonly due to increased bleeding (ARR -7.2%, CI: -13.2 to -1.2, p=0.0092)[6]. The copper IUD is more effective than injectable progestogens for prevention of unintended pregnancy (RR 0.47, CI: 0.26-0.85, p=0.01)[6].

There are currently 4 options within the class of levonorgestrel IUDs with various sizes, daily doses, and durations of use. Although head to head study data is lacking, evidence suggests that efficacy is the same regardless of dosage over a three year period[7].

LARCs have defined duration of use, with levonorgestrel IUDs lasting for 3-6 years depending on the product, copper IUDs for 10 years, and etonogestrel subcutaneous implant for 3 years. However, extended use (beyond approved duration) is being studied for each type of LARC with promising data for use up to 7, 12, and 5 years respectively[2].

Women who receive IUD placement in the immediate postpartum period (within 10 minutes of placenta delivery) are more likely to have successful placement (OR 4.07, CI: 0.54-30.4, p=0.17), and more likely to have continued IUD use at 6 months (OR 2.04, CI: 1.01-4.09, p=0.05) compared to routine postpartum IUD placement. The immediate placement group was also more likely to experience IUD expulsion (OR 4.89, CI: 1.47-16.32, p=0.01)[8]. IUD placement immediately following aspiration abortion procedures reduced the likelihood of repeat abortion (HR 0.38, CI: 0.27-0.53; p<0.001)[9].

ACOG recommends that LARC be offered routinely as safe and effective contraception for most patients, including nulliparous patients and adolescents[1]. LARC should be offered in the immediate postpartum and immediate post-abortion settings[10].

Findings:
LARCs are safe, well tolerated, and provide the most effective, reliable, and cost efficient reversible contraception. IHS should prioritize provider training and barrier reduction to ensure every patient has access to all types of LARC. Clinicians should provide counseling and engage in shared decision making to select the most appropriate contraceptive option for each individual patient.

****Resources for clinicians****

1. Use this CDC-sponsored phone application (app) for selecting safe contraception based on comorbid conditions
2. Use this interactive website for patients to compare all available contraceptive methods

Product	Components	FDA Approved Indications	Off-Label Use	Mechanism of Action	Approved Duration
TCu380A IUD (ParaGuard®)	T-shaped device of polyethylene wrapped with copper wire on stem and arms covering 380mm	Contraception in parous women (1988)	Contraception in nulliparous women Emergency Contraception	Inhibition of sperm migration and viability	10 years
LNG-IUD 52mg (Mirena®)	T-shaped device with polydimethylsiloxane sleeve that contains levonorgestrel 52mg total, 20ug/day	Contraception in parous women (2001) Treatment of heavy menstrual bleeding in women using IUD for contraception (2009)	Contraception in nulliparous women Abnormal uterine bleeding Endometriosis/ Endometrial atypia	Thickening of cervical mucus (stopping sperm passage)	5 years
LNG-IUD 52mg (Liletta®)	T-shaped device with polydimethylsiloxane sleeve that contains levonorgestrel 52mg total, 18.6ug/day	Contraception regardless of parity (2015)	Abnormal uterine bleeding	Thickening of cervical mucus (stopping sperm passage)	6 years
LNG-IUD 19.5mg (Kyleena®)	T-shaped device with polydimethylsiloxane sleeve that contains levonorgestrel 19.5mg total, 17.5uq/day	Contraception regardless of parity (2016)		Thickening of cervical mucus (stopping sperm passage)	5 years
LNG-IUD 13.5mg (Skyla®)	T-shaped device with polydimethylsiloxane sleeve that contains levonorgestrel 13.5mg total, 14ug/day	Contraception regardless of parity (2013)		Thickening of cervical mucus (stopping sperm passage)	3 years
ENG-SCI 68mg (Nexplanon®)	Ethyline vinyl acetate copolymer core that contains 68mg of etonogestrel surrounded by ethylene vinyl acetate copolymer skin	Contraception regardless of parity (2006)	Endometriosis Dysmenorrhea Adenomyosis	Suppression of ovulation Thickening of cervical mucus Alteration of endometrium	3 years

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the NPTC website.

References:

1. Winner B, Peipert JF, Zhao Q, et al. Effectiveness of long-acting reversible contraception. N Engl J Med. 2012 May 24;366(21):1998-2007.
2. Committee on Practice Bulletins-Gynecology, Long-Acting Reversible Contraception Work Group. Practice Bulletin No. 186: Long-Acting Reversible Contraception: Implants and Intrauterine Devices. Obstet Gynecol. 2017 Nov;130(5):e251-e269.
3. Apter D, Briggs P, Tuppurainen M, et al. A 12-month multicenter, randomized study comparing the levonorgestrel intrauterine system with the etonogestrel subdermal implant. Fertil Steril. 2016 Jul;106(1):151-157.e5.
4. Goodman S, Hendlish SK, Reeves MF, et al. Impact of immediate postabortal insertion of intrauterine contraception on repeat abortion. Contraception. 2008 Aug;78(2):143-8.
5. Trussell J, Hassan F, Lowin J, Law A, Filonenko A. Achieving cost-neutrality with long-acting reversible contraceptive methods. Contraception. 2015 Jan;91(1):49-56.
6. Hofmeyr GJ, Singata M, Lawrie TA. Copper containing intra-uterine devices versus depot progestogens for contraception. *Cochrane Database System Rev.* 2010, Issue 6. Art. No.: CD007043.
7. Krashin J, Tang JH, Mody S, et al. Hormonal and intrauterine methods for contraception for women aged 25 years and younger. *Cochrane Database System Rev* 2015, Issue 8. Art. No.: CD009805.
8. Lopez LM, Bernholc A, Hubacher D, et al. Immediate postpartum insertion of intrauterine device for contraception. *Cochrane Database System Rev.* 2015, Issue 6. Art. No.: CD003036.
9. Goodman S, Hendlish SK, Reeves MF, et al. Impact of immediate postabortal insertion of intrauterine contraception on repeat abortion. Contraception. 2008 Aug;78(2):143-8.
10. American College of Obstetricians and Gynecologists' Committee on Obstetric Practice. Committee Opinion No. 670: Immediate Postpartum Long-Acting Reversible Contraception. Obstet Gynecol. 2016 Aug;128(2):e32-7.
11. U.S. Centers for Disease Control and Prevention. Products - Data Briefs - Number 388- October 2020. *Centers for Disease Control and Prevention*, 20 Oct. 2020.